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DEVELOPMENT AND VALIDATION OF AMANTADINE HYDROCHLORIDE IN NEW ANALYTICAL BY USING UV-SPECTROPHOTOMETRIC METHOD

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ABSTRACT

A novel and simple Zero order derivative spectroscopic method was developed and validated for the estimation of Amantadine hydrochloride in bulk and Pharmaceutical dosage forms and has an absorption maximum at 260 nm using distilled water. The Linearitywas found to be in the concentration range of 2-10µg/ml and the correlation coefficient was found to be 0.9991 and it has showed good linearity, reproducibility, precision in this concentration range. The regression equation was found to be Y = 0.0656X -0.0173. The % recovery values were found to be within 100.27-101.25 % showed that the method was accurate. The LOD and LOQ were found to be 0.02002 and 0.06006µg/ml respectively. The % RSD values were less than 2. The developed method was validated according to ICH guidelines for linearity, accuracy, precision, and ruggedness. Limit ofdetection and limit of quantitation. The developed method was successfully applied for the quantitative estimation of Amantadine hydrochloride.

KEYWORDS: Amantadine hydrochloride Zero order derivative spectroscopy, water linearity, precision, reproducibility and accuracy.

INTRODUCTION

Amantadine hydrochloride

Amantadine is used to treat Parkinson's disease-related dyskinesia and drug-induced parkinsonism syndromes. Amantadine may be used alone or in combination with another

anti-Parkinson or anticholinergic drug. The specific symptoms targeted by Amantadine therapy are dyskinesia and rigidity.[1][2]

Amantadine sold under the brand name Gocovri among others, is a medication used to treat dyskinesia associated with parkinsonism and influenza caused by type A influenzavirus, though its use for the latter is no longer recommended due to widespread drug resistance.[3][4] It acts as a nicotinic antagonist, dopamine agonist, and noncompetitive NMDA antagonist.[5][6] The antiviral mechanism of action is antagonism of the influenzavirus A M2 proton channel, which prevents endosomal escape (i.e. the release of viral genetic material into the host cytoplasm).[7][8]

Amantadine was first used for the treatment of influenza A. After antiviral properties were initially reported in 1963, Amantadine received approval for prophylaxis against the influenza virus A in 1976.[9] However, Amantadine-resistant influenza viruses were first reported during the 1980 influenza A epidemic and resistance frequency continued to rise into the early 2000s. Currently, Amantadine is no longer recommended for the treatment of influenza A due to a high level of Amantadine resistance among circulating influenza A viruses.[10] In 1973, the FDA approved Amantadine for use in the treatment of Parkinson's disease. In 2017, the extended release formulation was approved for use in the treatment of levodopa-induced dyskinesia. Off-label uses include improvement of fatigue in multiple sclerosis and accelerating the rate of functional recovery and arousal following a brain injury.

Amantadine has a mild side effect profile. Common neurological side effects include drowsiness, light headedness, dizziness, and confusion.[11] Due to its effects on the central nervous system, it should not be combined with additional CNS stimulants or anticholinergic drugs. Amantadine is contraindicated in persons with end stage kidney disease, given that the drug is cleared by the kidneys.[12] It should also be taken with caution in those with enlarged prostates or glaucoma, due to its anticholinergic effects.[13] Live attenuated vaccines are contraindicated while taking Amantadine, as it may limit the efficacy of the administered vaccine.

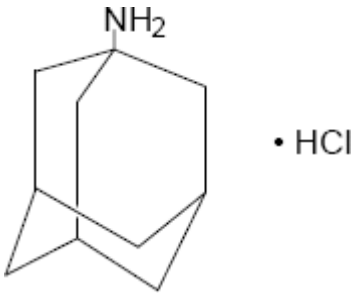

Fig. 1: Chemical structure of Amantadine hydrochloride.

MATERIAL AND METHOD

Instrument

UV-visible double beam spectrophotometer, SHIMADZU (model UV-1800) with UV probe software. All weights were taken on analytical balance.

Chemicals

Amantadine hydrochloride drug was obtained as a gift sample from INM research private limited.

Solvent

Water.

Selection of analytical wavelength

Appropriate dilutions were prepared for drug from the standard stock solution and the solution was scanned in the wavelength range of 200-400 nm. The absorption spectra thus obtained were derivatized from zero order method. It shows maximum absorbance at 260 nm was shown in fig.2

Preparation of standard stock solution

Accurately weigh 100mg of Amantadine hydrochloride was transferred into 100 ml volumetric flask and diluted with purified water up to the mark (stoke solution 1) From this pipette out 10ml in to 100ml volumetric flask and diluted with water up to mark(stoke solution 2), from this solution pipette out 2, 4, 6, 8, And 10.ml into 10ml individual volumetric flask and add water up to the mark, this gives2, 4, 6, 8, and 10.µg/ml concentrations.

Method validation

The method is validated according to the ICH guidelines.

RESULT AND DISCUSSION

Method: zero order derivatives spectroscopy

1. **Linearity:** The linearity of analytical method is its ability to elicit test results that are directly proportional to the concentration of analyte in sample within a given range, the linearity of the method was demonstrated over the concentration range of 2- 10µg/ml of the target concentration. Aliquots of 2,4,6,8, and 10µg/ml are prepared from Stock solution-II; calibration curve was plotted and presented.
2. **Range:** The range of analytical method is the interval between the upper and lower levels of analyte that have been demonstrated to be determined within a suitable level of precision, accuracy and linearity.
3. **Sensitivity:** The sensitivity of the proposed method for the measurement of Amantadine hydrochloride was estimated in terms of Limit of Detection (LOD) and Limit of Quantification (LOQ). The LOD and LOQ were calculated by using the average of the slope and SD of the intercept. The mean slope value and SD of the intercept wereobtained after plotting six calibration curves. The LOD and LOQ obtained are reported.
4. **Precision:** The precision of an analytical method is the degree of agreement among individual test results when the method is applied repeatedly to multiple samplings of homogenous samples. It provides an indication of random error results and was expressed as coefficient of variation (CV).
5. **Accuracy:** Accuracy is the closeness of the test results obtained by the method to thetrue value. To study the accuracy, Recovery studies were carried out at three different levels i.e. 50%, 100% and 150% by adding standard drug solution to the sample solution. The % recovery was calculated and reported.
6. **Ruggedness:** The solutions were prepared and analyzed with change in the analytical conditions like different laboratory conditions and different analyst and are presentedin.

Table 5.1: Results of calibration curve at 260nm for Amantadine hydrochlorideby zero order spectroscopy.

SL NO	Concentration inµg/ml	Absorbance ± Standard Deviation*
1	0	0
2	2	0.227±0.000816
3	4	0.421±0.000894
4	6	0.611±0.000753
5	8	0.803±0.001049
6	10	0.994±0.001414

* Average of six determinations.

Table 5.2: Optimum condition, optical characteristics and statistical data of the regression equation in UV method.

Optimized conditions	Amantadine hydrochloride
Range(µg/ml)	2-10
λmax(nm)	260
Regression Equation	Y= 0.0984x-0.0173
Slope(b)	0.0984
Intercept (a)	0.0173
Correlation Coefficient (r2)	0.9991
Sandell's equation	0.0147
Limit of detection (µg/ml)	0.0200
Limit of quantification (µg/ml)	0.0600

** Average of six determinations.

Table 5.3: Determination of precision results for Amantadine hydrochloride at 260 nm by zero order derivative spectroscopy.

Concentration (µg/ml)	Intra-day Absorbance ±SD**	%RSD	Inter-day Absorbance ±SD**	%RSD
2	0.227±0.000577	0.25	0.227±0.001	0.44
4	0.421±0.001	0.23	0.421±0.001	0.23
6	0.611±0.001	0.26	0.611±0.000577	0.09
8	0.803±0.001155	0.14	0.803±0.001155	0.14
10	0.993±0.001528	0.15	0.994±0.001528	0.15

** Average of six determinations.

Table 5.4: Determination of LOD and LOQ results for Amantadine hydrochloride by Zero order derivative spectroscopy.

Sl. No	Parameters	Values
1	SD of Intercepts*	0.00039
2	Average of Slopes*	0.0656
3	LOD(3.3×SD of Intercepts/average of slopes)	0.02002
4	LOQ(10×SD of Intercepts/ average of slopes)	0.06006

*Mean value obtained from 6 calibration curves.

Table 5.5: Determination of accuracy results for Amantadine hydrochloride by Zero order derivative spectroscopy.

Drug	Spiked levels %	Amountof sample (µg/ml)	Amount of standard (µg/ml)	Amount recovered	% Recovery ±SD**	%RSD
Amantadine hydrochloride	50	4	2	6.84	100.48±0.595	0.592
	100	4	4	8.03	100.27±0.361	0.360
	150	4	6	10.22	101.25±1.123	1.109

**Average of six determination.

Table 5.6: Ruggedness results for Amantadine hydrochloride at 260 nm by zero order derivative spectroscopy.

Analysts	Analyst-1	Analyst-2
Mean absorbance	0.611	0.6113
Standard deviation	0.001	0.00057
%RSD	0.163	0.0943

**Average of six determinations.

Figures

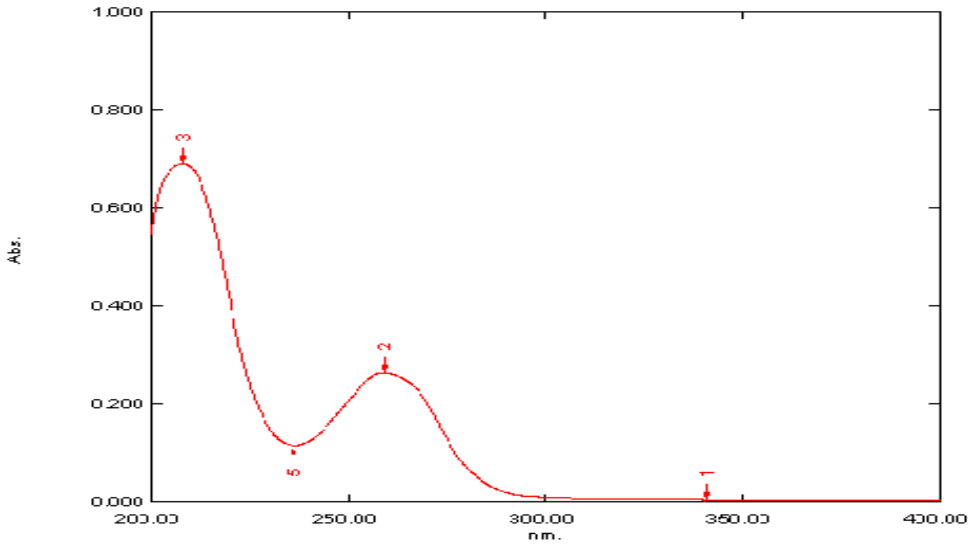

Fig.2: Zero order spectrum of Amantadine hydrochloride at 260nm.

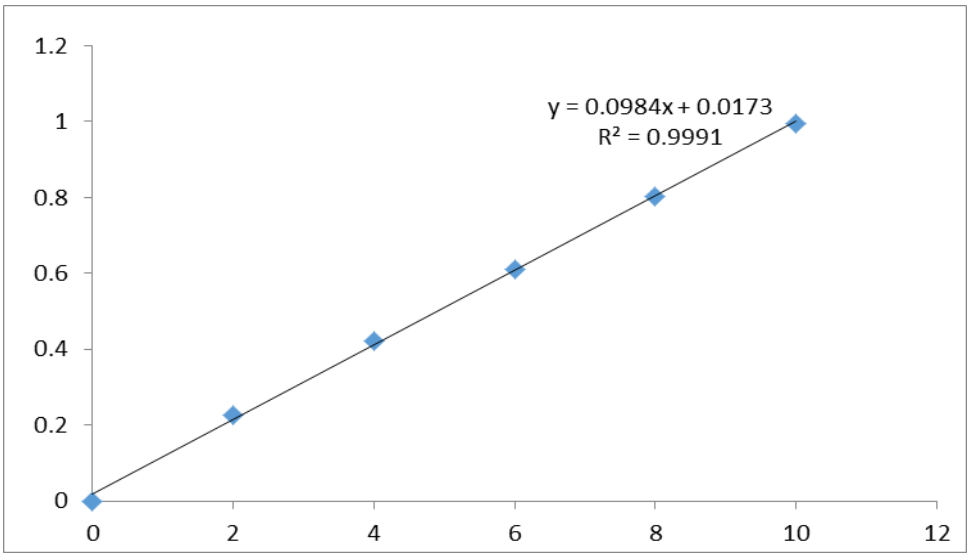

Fig.3: Calibration curve of Amantadine hydrochloride.

CONCLUSION

From the above it can be concluded that all validation parameters (precision, accuracy, linearity, LOQ, LOD, Ruggedness) met the predetermined acceptance criteria as mentioned in ICH guidelines. The developed spectrophotometric method is simple, rapid, accurate, and precise of Amantadine hydrochloride.

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