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UV-spectrophotometric method development and validation for estimation of Galantamine Hydrobromide in tablet dosage form

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Abstract

Two innovative, new, simple and low cost UV-spectrophotometric and first order derivative methods were developed and validated for estimation of Galantamine Hydrobromide in bulk drug and tablet dosage form. Galantamine Hydrobromide was estimated at 289 nm in Distilled Water. In first order derivative, it showed amplitude at 284.8 nm and λ_{minima} = 290.4 nm with 286.4 nm as zero crossing point (ZCP). In both the methods linearity was found to be in the range of 20-100 µg/ml; for UV spectrophotometric method (y = 0.007x - 0.002, r^2 = 0.999) and for first order derivative spectrophotometric method (Y=0.0012 x+0.00045; r2=0.999), respectively. These methods were analyzed and validated for various validation parameters according to USP guidelines. The quantitation limits were found to be 0.50 and 1.54 µg/ml, for UV-Spectrophotometric method and 3.3 and 10 µg/ml for the 1st order derivative method. The proposed methods were successfully applied for the determination of Galantamine Hydrobromide in tablet dosage forms. The results demonstrated that the procedure is simple, accurate, cost effective, precise and reproducible (relative standard deviation <2%), while being simple, cheap and less time consuming and can be suitably applied for the estimation Galantamine Hydrobromide in different dosage forms.

Keywords: Galantamine Hydrobromide, UV-Spectrophotometric method.

Introduction

Galantamine Hydrobromide is a reversible, competitive acetyl cholinesterase inhibitor. It is known chemically as (4*aS, 6R, 8aS*)-4a, 5, 9, 10, 11, 12-hexahydro-3-methoxy-11-methyl-6H-benzofuro [3a, 3, 2-*ef*] [2] benzazepin-6-ol Hydrobromide. The structural formula for Galantamine Hydrobromide is as described in figure 1. Galantamine Hydrobromide is available in opaque hard gelatin extended release capsules of 8 mg (white), 16 mg (pink), and 24 mg

(caramel). Galantamine Hydrobromide is indicated for the treatment of mild to moderate dementia of the Alzheimer's type. Treating mild to moderate impairment of memory, judgment, and abstract thinking as well as changes in personality caused by Alzheimer disease.

Literature survey revealed, few analytical methods which include liquid chromatography with tandem mass spectrometry, simultaneous quantification of Galantamine Hydrobromide in human plasma using high- performance liquid chromatography after solid phase extraction. Sensitive determination of Galantamine Hydrobromide in human plasma samples using reversed-phase liquid chromatography. Galantamine Hydrobromide is not official in IP, BP and USP. The present work deals with estimation of Galantamine Hydrobromide in tablets by UV-spectrophotometry and first order derivative spectrophotometry

Material and methods

Instruments and Apparatus:

- UV-visible spectrophotometer, Double beam, Model 1700(shimadzu)
- Balance, Model ALC 210.4 (Acculab)
- Ultra Sonicator (Fast Clean Ultrasonic Cleaner)
- Volumetric flasks – 10ml, 100ml
- Pipettes – 1ml, 5ml, 10ml, beakers, measuring cylinders etc.

Reagents:

- Galantamine Hydrobromide
- Distilled water is used throughout the study

Preparation of standard stock solution

Standard stock solution containing 100 µg/ml of Galantamine Hydrobromide was prepared in Distilled water. From the stock, different aliquots were taken and diluted to 10 ml mark with same solvent to obtain series of concentrations. The solutions were scanned on spectrophotometer in the UV range 200-400 nm. Galantamine Hydrobromide showed absorbance maxima at 289 nm (fig. 1). The same solutions were subjected to first order derivative, using UV probe software of instrument, where $\Delta\lambda = 2$ (fig. 2). The absorbance was measured at λ_{maxima} = 284.8 nm and λ_{minima} = 290.4 nm with 286.4 nm as zero crossing point (ZCP) and amplitude difference was measured for the respective concentration of standard and was plotted against concentration and regression equation was calculated. In both the methods, drug follows linearity in the concentration range of 5-40 µg/ml ($y = 0.007x - 0.002$, $r^2 = 0.999$and $y = 0.0012x - 0.0004$, $r^2 = 0.999$), respectively.

Preparation of sample solution

For analysis of commercial formulation; twenty tablets were weighed, average weight determined and crushed into fine powder. An accurately weighed quantity of powder equivalent weight of Galantamine Hydrobromide was transferred into 100 ml volumetric flask containing 30 ml, Distilled water, shaken manually for 10 min., volume was made up to mark with same solvent and filtered through Whatmann filter paper. 3 ml of this solution was transferred to 10 ml volumetric flask and diluted upto 10 ml with distilled water to get 30 µg/ml concentrations, volume was adjusted to the mark and absorbance was recorded at 289 nm. The same solution was subjected for first order derivative using UV probe software and amplitude of the trough was recorded at 284.8 and 290.4 nm. The concentration of the drug was calculated from linear regression equation; results are shown in table 2.

Result and Discussion

The zero order UV spectrum of Galantamine Hydrobromide in Distilled water has showed maximum absorbance at 289 nm. The First derivative spectrum of Galantamine Hydrobromide has sharper and well- defined peak. The structural features are sharpened to give improved resolution of overlapping peaks. In first order derivative spectrum, the amplitude of the trough was recorded at 284.8 and 290.4 nm. The amount of drug determined was in the good agreement with the label claim as shown in table 1. The methods were validated for accuracy, precision, ruggedness and robustness. The accuracy of the methods was assessed by recovery studies by Standard addition method. The precision of the methods were studied as intra-day, interday and repeatability. The % RSD values less than 2 indicate the methods are accurate and precise.

Ruggedness of the proposed methods was studied with the help of two analysts. Robustness of the methods was studied in two different laboratories using UV-visible spectrophotometer. The results did not show any statistical difference between operators and environmental conditions, suggesting that methods developed were rugged and robust. The results from validation studies are shown in table 2.

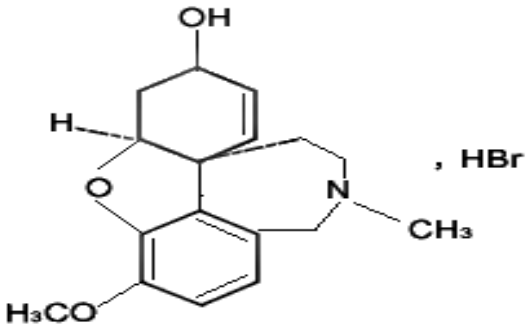

Figure 1. Galantamine Hydrobromide

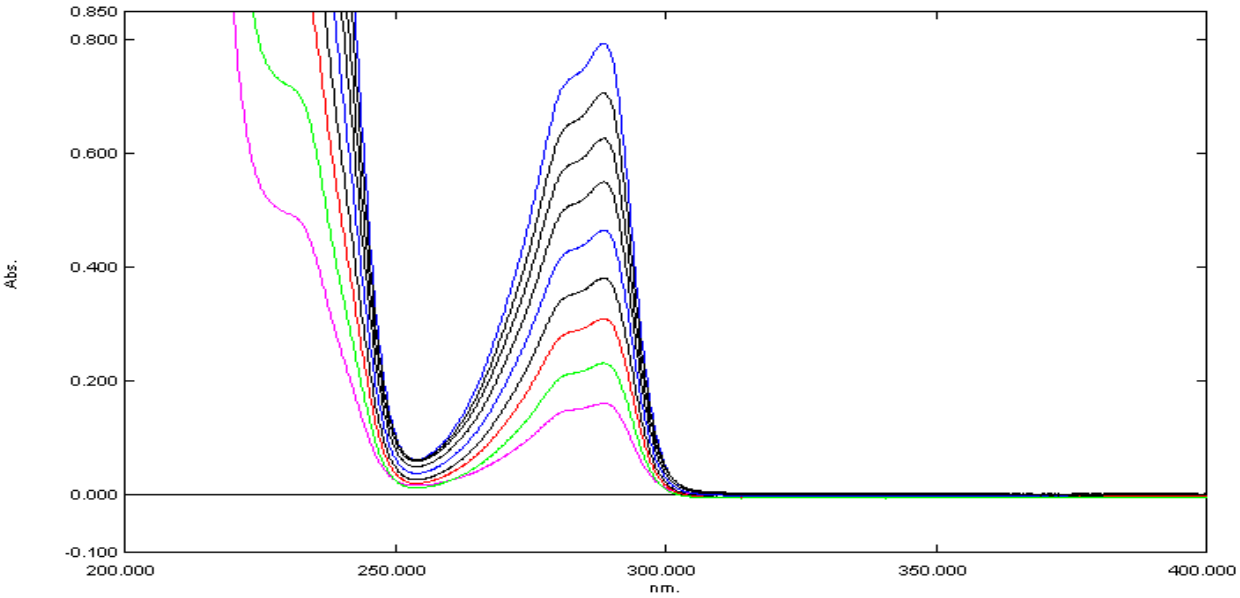

Figure 2. An overlain UV Spectra of Galantamine Hydrobroie

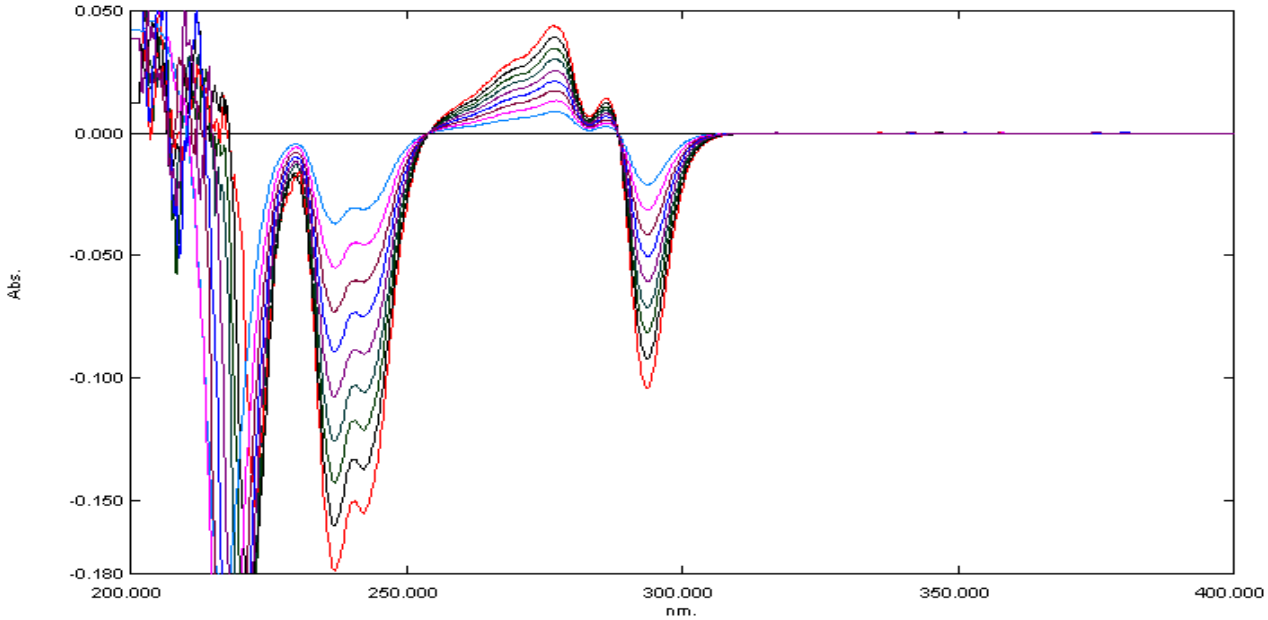

Figure 3. An overlain First Derivative Spectra Of Galantamine Hydrobromide

Table1. Characteristics of the UV method derived from the standard calibration curve

Method	LOD	LOQ	Linearity Range µg/mL	Linearity Equation	Correlation Coefficient	Slope of curve
Simple UV	0.50	1.54	20-100	y = 0.007x - 0.002	0.999	0.007
1st Derivative	3.3	10.0	20-100	y=0.0012x + 0.0004	0.999	0.0012

Table2. Precision

Method	Precision	% Assay mean ± SEM	% RSD
Simple UV	Repeatability	98.4±0.356	0.97
	Intra-day	99.1±0.125	0.94
	inter-day	99.5±0.541	0.74
1st Derivative	Repeatability	98.4±0.356	0.61
	Intra-day	99.1±0.125	0.84
	inter-day	99.5±0.541	0.86

Table3. Accuracy by Simple UV Method

Initial conc. (µg/ml) (A)	Quantity of std. Added (µg/ml) (B)	Total Amount (A + B)	Total quantity Found Mean ± S.D.	% Recovery± S.D
30	10	40	39.87 ± 0.29	99.67 ± 1.22
30	20	50	50.23 ± 0.67	100.6 ± 1.95
30	30	60	60.12 ± 0.032	100.2 ± 0.99
30	40	70	69.68 ± 0.12	99.54 ± 1.89

Table4. Accuracy by 1st Derivative Method

Initial conc. (µg/ml) (A)	Quantity of std. Added (µg/ml) (B)	Total Amount (A + B)	Total quantity Found Mean ± S.D.	% Recovery± S.D
30	10	40	39.80 ± 0.018	99.5 ± 1.39
30	20	50	50.19 ± 0.061	100.38 ± 1.96
30	30	60	60.26 ± 0.11	100.43 ± 1.94
30	40	70	69.43 ± 0.092	99.18 ± 0.64

Table5. Method robustness (% RSD) in Normal and Changed condition (n=5)

Method	Robustness(% RSD) (n = 3)	
	Laboratory-I	Laboratory-II
Simple UV	0.47	0.59
1st Derivative	0.67	0.38

Table6. Result of Assay

Label Claim	Amount found (mg/tablet)	Amount found (%) (n=5) (Mean± SEM)	
		UV-Spectro-photometric	First order derivative spectrophotometry
Galantamine Hydrobromide (4 mg/tablet)	3.98	99.75 ± 1.32	99.5 ± 0.91

Conclusion

This developed method is reliable, simple, rapid, low cost and accurate and precise and can be used for routine analysis of Galantamine Hydrobromide from tablet formulations.

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