Estimation of the galanthamine using derivative spectrophotometry in bulk drug and formulation

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ABSTRACT

Two simple, rapid, accurate, precise, reliable and economical spectrophotometric methods have been proposed for the determination of galanthamine hydrobromide (GH) in bulk and pharmaceutical formulation. First method is zero order UV spectrophotometry and second is 1st derivative zero crossing spectrophotometry. The developed methods have shown best results in terms of linearity, accuracy, precision, LOD and LOQ for bulk drugs and marketed formulations. Absorbance was measured at 287 nm for zero order and 277.4 nm for first derivative. It obeyed Lambert-Beer's law in the range of 30-80 μg mL-1. Both methods have good linearity (r2 = 0.9997) and accuracy found to be 100.5% and 101.2% for both methods respectively.

Keywords: Galanthamine Hydrobromide (GH); Zero Order UV-Spectrophotometry; First Derivative Zero Crossing Spectrophotometry

1. INTRODUCTION

Figure 1 is the structure of galanthamine hydrobromide (GH), which is (4a*S*,6*R*,8a*S*)-5, 6, 9, 10, 11, 12-hexahydro-3-methoxy-11-methyl-4a*H*-[1] benzofuro [3a,3,2-*ef*] [2] benzazepin-6-ol [1,2]. It is used for the treatment of mild to moderate Alzheimer's disease and various memory impairments [3,4]. The molecular weight of GH is 368.27 and melting point is 258-264°C. GH is very soluble in water [5].
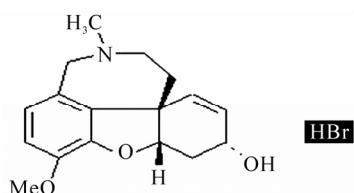

Figure 1. Structure of GH.

The official monograph of USP [6] describes assay method for GH using HPLC but compare to that spectrophotometric methods are more economic and simple. Under computer-controlled instrumentation, derivative spectrophotometry is playing a very important role in the analysis of drugs by giving more resolved spectra than the zero order spectra [7,8].

The aim of the present work is to investigate utility of derivative spectrophotometry and to develop reliable spectrophotometric procedure for determination of GH either in bulk and marketed formulation.

2. MATERIALS AND METHODS

2.1. Instruments and Reagents

Spectrophotometric measurements were made on a Shimadzu 1700 double beam UV-VIS spectrophotometer with a fix slit width of 1 nm coupled with computer loaded with Shimadzu UV PC software (UV probe) version 2.31. Double distilled water was used and pure GH was obtained from Alembic Pharmaceuticals Ltd. Vadodara, India. The marketed formulation of GH was obtained commercially from Sun Pharmaceuticals Ltd (Galmer-40 tablets labeled 4 mg of pure drug, Batch Number-GK 90964).

2.2. Standard and Test Solutions

Stock solution of 1 mg mL-1 of pure GH and its formulation was freshly prepared in double distilled water. Test solution of GH was tested for stability in solution during the actual analysis. The behaviour of GH was found to be stable over the period of 24 hr from their preparation at room temperature.

2.2.1. Zero Order UV-Spectrophotometry (Method 1)
The working solutions were prepared by accurately diluting aliquots of the standard solution with water to obtain the concentration in range of 30-80 μg mL-1. The absorption spectra of the samples were recorded between 200-400 nm against double distilled water using a 1.0 cm

quartz cell. Zero order spectra of pure drug GH were stored individually within mentioned concentration ranges and absorbance was measured at 280 nm.

### 2.2.2. First Derivative Zero Crossing Spectrophotometry (Method 2)

The zero order absorption spectra of GH were derivatized in first order using delta lambda 4 and scaling factor 10. The first derivative amplitudes were recorded at 277.4 nm.

3. RESULTS AND DISCUSSION

The absorption spectra of the GH were recorded at wavelength 287 nm for zero order UV-spectrophotometry and 1st derivative was measured at 277.4 nm. It is observed from the spectra that GH shows a good linearity in the range of 30-80 μg mL-1. **Figure 2** explains the zero order spectra of GH. While, **Figure 3** describes first derivative spectra of GH which showed more resolution than zero order spectra. Both methods were validated, all the validation parameters were in limit as per the ICH guidelines [9]. **Table 1** exhibits the detailed validation parameters for both the methods. **Table 2** represents results of recovery studies of both methods and **Table 3**
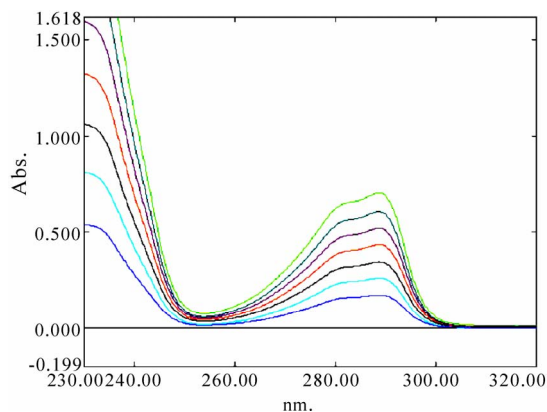
Figure 2. The zero order spectra of GH of 30-80 μg mL^{-1}.
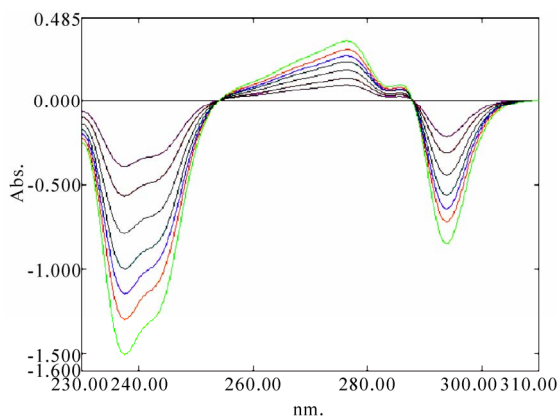
Figure 3. The first derivative spectra of GH of 30-80 μg mL^{-1}.

Table 1. Validation parameters obtained by method 1 and method 2.

Parameters	Method-1	Method-2
Linearity	0.9996	0.9997
Range (μg mL^{-1})	30-80	30-80
Accuracy	100.5 ± 2.39	101.2 ± 1.63
Precision	% R.S.D-0.8315	% R.S.D-1.7052
LOD (μg mL^{-1})	1.46	0.72
LOQ (μg mL^{-1})	4.45	2.19
Assay (%Purity)	98.02	99.94

Table 2. The results of recovery studies of the method 1 and method 2.

Amt added (μg mL^{-1})	% Recovery Method 1	% Recovery Method 2
16	99.25	101.6
20	99.05	99.4
24	103.3	102.6
Mean recovery	100.5	101.2
SD	2.39	1.63

Table 3. The statistical comparison of the results of validated methods.

t-Test	F-Test
$t_{calculated} = 0.419$	$F_{calculated} = 2.14$
$t_{theoretical} = 3.52$	$F_{theoretical} = 19.0$

explains the statistical comparison of results of both the validated methods.

The results obtained were compared statistically by Student *t*-test and by the variance ratio *F*-test with those obtained by each method. The calculated values of the Student *t*-values at 95% confidence level and the variance ratio *F*-values did not exceed the theoretical values indicating that there were no significant differences among the results of the developed two methods.

4. CONCLUSIONS

The developed spectrophotometric methods for determination of GH are simple, specific, accurate, precise, rapid and economical which indicates its adequacy for routine pharmaceutical analysis. It is concluded that derivative spectrophotometry is successfully utilized for the estimation of GH.

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