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Spectrophotometric Estimation of Donepezil Hydrochloride in Bulk and Tablet Formulation

[1]J.N. Sangshetti, [2]P.R. Mahaparale, [2]S. Paramane and [1]D.B. Shinde
[1]Department of Chemical Technology,
Dr. Babasaheb Ambedkar Marathwada University,
Aurangabad (Maharashtra), India
[2]Dr. D.Y. Patil College of Pharmacy, Pimpri,
Pune-411018, Maharashtra, India

Abstract: Two simple, accurate, rapid and sensitive methods were developed for the estimation of Donepezil Hydrochloride (DH) in bulk and tablet formulation. Method A and B describes simple UV spectrophotometric and colorimetric method in methanol, respectively. For method A and method B λ max was found to be at 231 and 454 nm, respectively. In method B orange coloured complex was observed due to reaction of keto group of donepezil with 2, 4-dinitrophenyl hydrazine in dilute sulphuric acid. Molar absorptivity of the drug was found to be at 1.38×10^5 and 3.077×10^4 for method A and B, respectively. The Beer Lambert's law was obeyed in the concentration range of 5-40 and 10-60 μg mL^{-1} for method A and B, respectively.

Key words: Donepezil hydrochloride, 2, 4, dinitrophenyl hydrazine, spectrophotometry

INTRODUCTION

Donepezil Hydrochloride (DH) is a new antialzeimer drug. It is the potent acetylcholine esterase inhibitor (Barner and Grey, 1998; Martindale, 2002). Chemically it is 2,3-Dihydro-5, 6-dimethoxy- 2-{{1- (phenylmethyl)- 4 piperidinyl} methyl} -2, 3, dihydro- 1 H-indene- 1-one (Fig. 1). This drug is not official in any Pharmacopoeia. So far only HPLC methods have been reported for its estimation from plasma (Yasui-Furukori *et al*., 2002; Nakashima *et al*., 2006; Wada *et al*., 2007). No spectrophotometric method has been reported for the estimation of DH in bulk and its formulation. In the present paper, we are reporting two simple spectrophotometric methods that can be used for routine analysis of DH in bulk and tablet formulation.

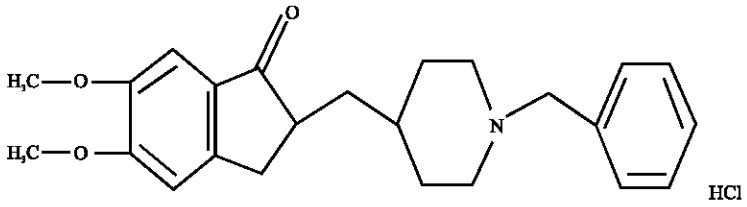

Fig. 1: Chemical structure of donepezil hydrochloride

Corresponding Author: D.B. Shinde, Department of Chemical Technology,
Dr. Babasaheb Ambedkar Marathwada University,
Aurangabad (Maharashtra), India

MATERIALS AND METHODS

Apparatus

A Shimadzu model 1601 double beam UV-visible spectrophotometer with a pair of 10 mm matched quartz cells was used to measure absorbance of the resulting solutions. Shimadzu electronic one pan balance, ultrasonicator were also used in the study. Drug was supplied by Wockhardt Research Centre, Aurangabad. DH tablets were purchased from a local market. All analytical grade reagents were used. Double distilled water was used throughout the study.

Solutions

Donepezil hydrochloride standard stock solution was prepared by dissolving 10 mg of drug in 100 mL methanol (100 μg mL^{-1}). Solution of 2, 4-dinitrophenyl hydrazine (2% w/v) was prepared in 0.1 N sulphuric acid.

Construction of Calibration Curve

For method A, aliquots of the working standard solution of DH (0.5-4 mL) were transferred in a series of 10 mL volumetric flask and suitably diluted with methanol to get concentration of 5, 10, 15 upto 40 μg mL^{-1}. These solutions were scanned in spectrum mode between 400 to 200 nm to determine λ max. The λ max of DH was found to be 231 nm. The absorbances of resulting solutions were measured at 231 nm and calibration curve was plotted.

For method B, aliquots of the working standard solution of DH (1-6 mL) were transferred in a series of 10 mL volumetric flask so as to get concentration of 10, 20, 30 to 60 μg mL^{-1}. Then 2 mL of 2, 4-dinitrophenyl hydrazine in 0.1 N sulphuric acid was added in each flask. The volume was adjusted with methanol. The flasks were kept aside for 30 minutes for development of colour. The keto group of DH was reacted with 2, 4-dinitrophenyl hydrazine to form orange coloured complex. The solution of 40 μg mL^{-1} was scanned between 800 to 400 nm to determine λ max. The λ max of DH was found to be 454 nm. The absorbance of resulting solutions was measured at 454 nm and the calibration curve was plotted.

Procedure for Assay of Donepezil Hydrochloride in Tablet Formulations

For analysis of drug in tablet dosage form, twenty tablets were weighed accurately and triturated in the mortar to get fine powder. The amount of tablet powder equivalent to 10 mg of DH was weighed and transferred to 100 mL volumetric flask and dissolved in methanol for method A and B. The solution was kept in ultrasonicator for 10 min and filtered through Whatman's filter paper No. 41. The tablet solution was further diluted to get final concentration of 10, 15, 20, 25, 30, 35 and 40 μg mL^{-1} for method A and B. Appropriate aliquots of drug solution were taken and the individual assay procedure was followed for the estimation of drug content in tablets. The concentration of drug present in tablets was calculated using calibration curve.

RESULTS AND DISCUSSION

Determination of λ Max

Donepezil hydrochloride when treated with 2,4, dinitrophenylhydrazine orange color is formed. To determine λ max a solution of 40 μg mL^{-1} was scanned between 800 to 400 nm. The λ max of DH was found to be 454 nm. The effect of time on maximum absorbance was tested by measuring absorbance of solution at regular interval and it was found that solution showed maximum absorbance after 30 min and was stable for 2 h.

Table 1: Optical characteristics of the proposed methods

Parameters	Method A	Method B
λ max (nm)	231	454
Beer's law limit (μg mL^{-1})	5- 40	10- 60
Molar absorptivity (mol^{-1} cm^{-1})	1.38×10^{5}	3.077×10^{4}
Sandell's sensitivity (μg cm^{-2}/ 0.001 A)	3.81×10^{-2}	1.12×10^{-2}
Correlation coefficient (r)	0.9983	0.9961
Regression equation		
Slope	0.0558	0.0115
Intercept	0.012	0.0146

Where, A is simple UV spectrophotometric method and B is colorimetric method

Table 2: Analysis of donepezil hydrochloride in tablet formulations

Formulation	Method	Label claim (mg)	(%) of label claim* ±SD	Amount added in mg	(%) recovery* ±SD
D_1	A	10	99.73±0.083	10	99.40±0.020
	B	10	99.53±0.153	10	98.70±0.040
D_2	A	10	99.82±0.136	10	98.90±0.134
	B	10	99.73±0.320	10	99.35±0.146

Where, A is simple UV spectrophotometric method and B is colorimetric method; D_1 and D_2 are two different brands of tablet formulations; *: n = 6, average of six readings

Optical Characteristics and Validation of Method

Optical characteristics for DH such as Beer's law limit, molar absorptivity, Sandell's sensitivity are shown in Table 1. The recovery was carried out by standard addition method (Table 2).The percent recovery obtained indicates noninterference of drug with common excipients used in formulations. The reproducibility, repeatability and accuracy of two methods were found to be good, which is evidenced by low standard deviation.

Interference Studies

To study interference of commonly used excipients on absorbance a recovery study was done. Under the experimental condition employed to a known amount of drug different excipients were added. The excipients up to concentration of 40 mg mL^{-1} do not interfere in studies. Recovery for all excipients was close to 100%. The precision of method was confirmed by their low RSD.

CONCLUSION

All proposed spectrophotometric methods for determination of DH are simple, sensitive, accurate, precise and reproducible. In method B, colour reaction neither requires any stringent condition nor any specific reagent or buffers. These methods can be successfully applied for routine estimation of DH in bulk and pharmaceutical dosage forms.

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