International Journal for Pharmaceutical Research Scholars (IJPRS)

V-6, I-4, 2017 ISSN: 2277 - 7873

RESEARCH ARTICLE

Development of UV Spectrophotometric Method for Estimation of Rivastigmine in Pharmaceutical Dosage Form

Amar Shripati Kulkarni*[1], Chandrashekhar Vishnu Babar[2], Amol Nivas Jadhav[3]

[1]*Anandi Pharmacy College Kalambe Tarf Kale, Kolhapur,* [2]*Eklavya College of Pharmacy, Tasgaon*

[3]*KLES's College of Pharmacy, Nipani.*

Manuscript No: IJPRS/V6/I4/00079, Received On: 23/11/2017, Accepted On: 28/02/2018

ABSTRACT

In this present research work we have developed a validated UV spectrometric method for estimation of Rivastigmine in pure and pharmaceutical dosage form. The developed method is accurate, cost effective for the estimation of Rivastigmine in pure and pharmaceutical dosage form. Based on measurement of absorption of UV light, the spectra of Rivastigmine in water + methanol (9:1) as a solvent show maximum absorption wavelength (λmax) at 221nm. The calibration curve was plotted over the concentration range from 10 - 90 µg/ml of Rivastigmine with correlation coefficient 0.999. Validation was performed as per ICH Q2 guidelines for linearity, precision and recovery. This method has good reproducibility with % RSD less than one. The limit of detection (LOD) & limit of quantification (LOQ) were found to be 0.501 & 1.52 respectively by simple UV spectroscopy. Thus, this proposed validated method can successfully apply for estimation of Rivastigmine in quality control, routine analytical work in pharmaceutical dosage forms.

KEYWORDS

Rivastigmine, Spectroscopic method, ICH Q2 guidelines

INTRODUCTION

Chemically Rivastigmine tartrate is N-Ethyl-N-methylcarbamic acid 3-[(1S)-1-(dimethylamino) ethyl] phenyl ester (2R,3R)-2,3-dihydroxybutanedioate.[1]

Rivastigmine tartrate is a white to off-white powder.[2] It is very soluble in water, soluble in ethanol and acetonitrile, slightly soluble in n-octanol and very slightly soluble in ethyl acetate. It has a molecular formula $C_{14}H_{22}N_2O_{22}.C_4H_6O_6$ having molecular weight 400.43 g/mol.[3] Rivastigmine tartrate is a reversible (or pseudoirreversible because it separates too slowly from AChE) nonselective cholinesterase inhibitor, which inhibits both AChE and BuChE in the central nervous system (CNS). It binds both esteratic and ionic sites of AChE just like a natural substrate, and it inhibits the metabolism of Ach. It is 4-6 times more effective on the G1 (monomeric) form of the enzyme, which is present at higher concentrations in the brain of AD patients. There is no affinity of rivastigmine tartrate for muscarinic, alpha- or beta-adrenergic, or dopamine receptors or opoid binding sites.[4]

*Address for Correspondence:
Mr. Amar Shripati Kulkarni,
Lecturer, Department of Pharmaceutics
Anandi Pharmacy College Kalambe Tarf Kale, Kolhapur, India.
E mail ID: amarkulkarni123@gmail.com

Objective of Present Research Work

1. Till the present day there is no valid UV spectrophotometric method available for estimation of Rivastigmine tartrate using a mixture of water + methanol (9:1) ratio.

2. The goal of our present research work was to develop a validated UV spectrometric method for estimation of Rivastigmine tartrate in pure and pharmaceutical dosage form.
3. Use this method for quality control and analysis of drugs in pharmaceuticals containing Rivastigmine tartrate.
4. To develop rapid, economical, and reproducible UV spectroscopic method for quality control of pharmaceutical formulations containing Rivastigmine tartrate.

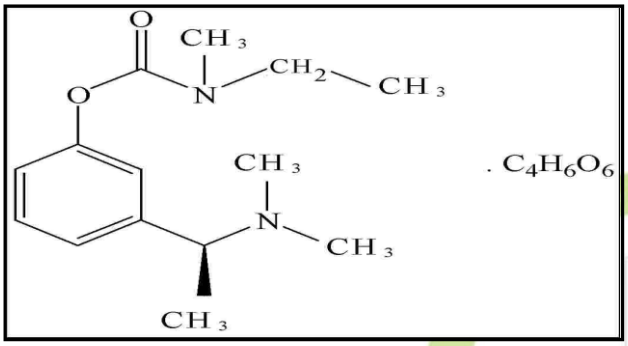

Figure 1: Structure of Rivastigmine tartrate

MATERIALS AND METHODS

Instrumentation, Reagents and Chemicals

Instrument

UV-Visible double beam spectrophotometer Shimadzu UV1800 with 1cm matched quartz cells. Electronic Balance. The absorption spectra of reference and test solution were carried out in a one cm quartz cell over the range of 200-400nm.

Materials

Pure Sample

Rivastigmine tartrate was purchased from Swapnroop Drugs & Pharmaceuticals, Aurangabad, Maharashtra, India.

Reagents and Chemicals

Methanol was obtained from Loba Chemie Pvt. Ltd, Mumbai, Maharshtra, India. Other chemicals & reagents used were of analytical grade.

Preparation of Standard Stock Solutions

Stock Solution-I

Standard drug solution of Rivastigmine tartrate was prepared by dissolving 100mg of pure Rivastigmine tartrate in small amount of water + methanol (9:1) in 100ml volumetric flask and the volume was adjusted with water + methanol (9:1) as a solvent the resultant solution gives the concentration of 1mg/ml i.e.1000µg/ml.

Stock Solution-II

From stock solution-I, 10ml solution was taken and then diluted up to 100ml with the same solvent in a volumetric flask and the concentration of this stock solution was 100µg/ml.

Determination of lambda max (λmax)

10µg/ml solution was prepared by withdrawing 10ml of solution from stock solution-II and further diluted with water + methanol (9:1) to get concentration solution. This solution was then scanned at a wavelength of 200 to 400 nm against the blank. The λmax was found to be at 221nm wavelengths where absorbance was maximum at this wavelength. Hence this is considered as absorption maxima which are used for preparation of the calibration curve (Figure 2).

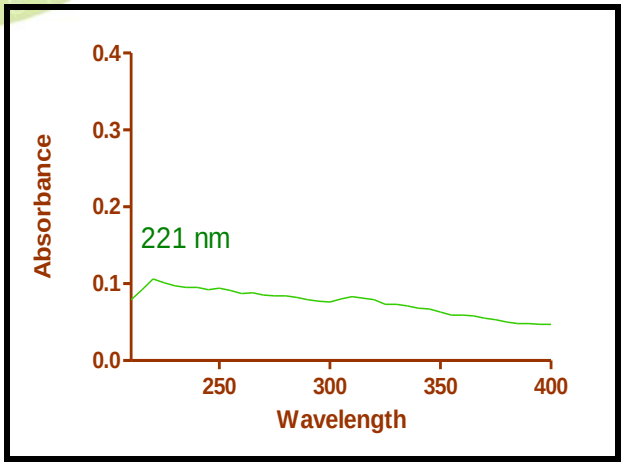

Figure 2: Determination λmax of Rivastigmine tartrate

Preparation of Calibration Curve

I-Stock solution

Standard drug solution of Rivastigmine tartrate was prepared by dissolving 100 mg of pure Rivastigmine tartrate in small amount of mixture of water + methanol (9:1) in 100ml volumetric flask and then the volume was adjusted with the same solvent. The resultant solution gives the concentration of 1mg/ml, i.e. 1000µg/ml.

II-Stock Solution

From I-stock solution 10ml solution was taken and then diluted up to 100ml with same solvent in a volumetric flask and then the concentration of this stock was 100µg/ml. From this II-stock solution 10, 20, 30, 40, 50, 60, 70, 80 and 90ml solutions were pipetted and volume was made to 100ml using a mixture of water + methanol (9:1) as a solvent to get concentrations of 10, 20, 30, 40, 50, 60, 70, 80 and 90µg/ml respectively. The absorbance of these solutions was measured at 221nm (λmax of Rivastigmine tartrate). The standard calibration curve was obtained from data of concentration v/s absorbance; standard calibration curve data reported in Table 1, Figure 3.

Table 1: Calibration data for the method development for Rivastigmine tartrate

Sr. No.	Concentration(µg/ml)	Absorbance at 221nm ± SD
1	10	0.102±0.00152
2	20	0.214±0.00200
3	30	0.303±0.00200
4	40	0.415±0.00321
5	50	0.512±0.00251
6	60	0.601±0.00200
7	70	0.727±0.00378
8	80	0.819±0.00208
9	90	0.909±0.00305

SD- Standard Deviation

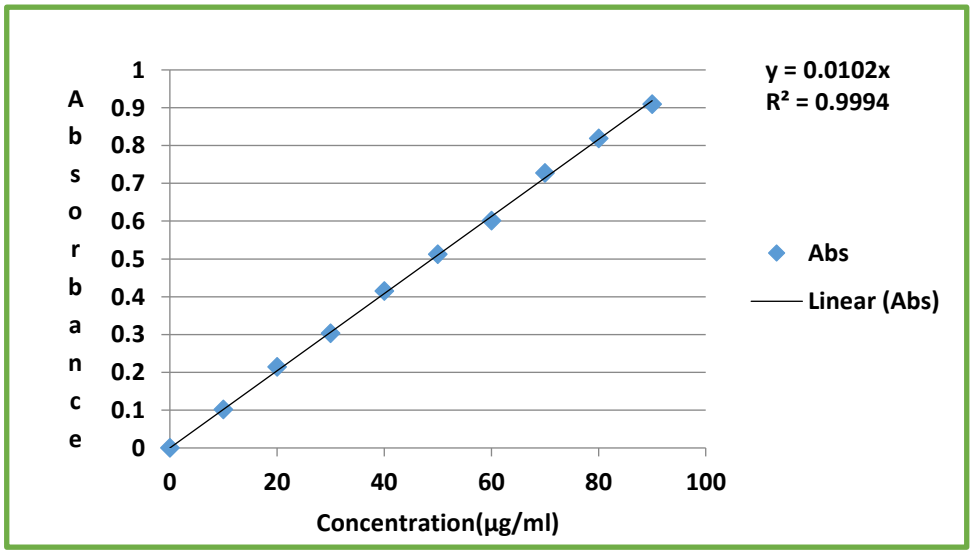

Figure 3: Calibration curve of Rivastigmine tartrate

Validation Method

Linearity and Range

The linearity of response obtained between 10 to 90 µg/ml concentrations. The calibration curve was obtained by plotting the absorbance versus concentration data and treated by linear regression analysis (Table 1).

Precision

Precision of the method was analyzed to repeatability and determined by analyzing µg/ml of Rivastigmine for six times the results are reported in (Table 2).

Precision

Precision of the method was studied as intra-day & inter-day variations. Intra-day and precision was determined by analyzing 20, 40 and 60 (µg/ml) of Rivastigmine for three times within the day; the results are reported in (Table 3).

Recovery Study

To analyze the accuracy of developed method, it was applied to analyze commercially available Rivastigmine capsules (Rivamer 3mg-Sun Pharma). Ten capsules accurately weighted and powder removed. The amount of the powder equivalent to 30mg of Rivastigmine accurately weighted and transferred to the 100ml volumetric flask. The drug content of preparation was calculated using the standard calibration curve and amount of drug estimated by this method is given in (Table 5).

Table 2: Data showing Repeatability of Absorbance's

Sr. No	Conc (µg/ml)	Wavelength (nm)	Absorbance	Mean SD	% RSD
1		221	0.514		
2		221	0.513		
3	50 µg/ml	221	0.517	0.516 ± 0.00282	0.546
4		221	0.521		
5		221	0.515		
6		221	0.516		

Table 3: Results for Intra-day & Inter-day Precision of Rivastigmine

Drug	Conc. (µg/ml)	Intra-day Mean Abs	Absorbance ± SD	%RSD	Inter-day Mean Abs	Absorbance ± SD	%RSD
	20	0.213	0.00208	**0.976**	0.207	0.001	**0.497**
Rivastigmine	40	0.419	0.00351	**0.837**	0.425	0.00404	**0.950**
	60	0.605	0.004	**0.661**	0.610.	0.00416	**0.681**
Mean %RSD				**0.824**			**0.709**

SD-Standard Deviation, RSD- Relative Standard Deviation

Table 4: Validation parameters for Rivastigmine tartrate

Sr. No.	Parameters	Results
1	Absorption maxima (nm)	221nm
2	Linearity range (µg/ml)	10-90(µg/ml)
3	Standard Regression Equation	y=0.010x
4	Correlation coefficient (R^2)	0.999
5	Specificity	A 40 µg /ml solution of Rivastigmine tartrate in mixture of water and methanol (9:1) at UV detection of 221 nm will show an absorbance value of 0.423±0.00147
6	Accuracy (%Recovery)	98.35%
7	Precision %RSD Repeatability (n=6)	0.546
	Inrta-day(n=3)	0.824
	Inter-day(n=3)	0.709
8	Molar absorptivity	$0.3683*10^4$L/mol.cm
9	LOD	0.501(µg/ml)
10	LOQ	1.52(µg/ml)

Table 5: Determination of Accuracy by Percentage Recovery Method

Drug	Tablet amount (µg/ml)	Level of addition (%)	Amount added (µg/ml)	Amount recovered (µg/ml)	% Recovery	Average % Recovery
Rivastigmine	10	80	6	7.6	98.67	
	10	100	8	6.1	98.36	98.35
	10	120	10	5.1	98.03	

RESULTS & DISCUSSION

This method has been made to develop rapid, precise & accurate analytical method. The proposed method based on UV spectroscopic absorption in UV region using water + methanol (9:1) as a solvent, maximum absorbance was found to be 221nm LOD & LOQ were found to be 0.501 & 1.52 respectively. The calibration curve of Rivastigmine plotted at 221nm (Figure 3) and linear relationship was obtained between 10 – 90 µg/ml. The accuracy of the method was determined by calculating mean percentage recovery it was found to be 98.35% (Table). Further precision was calculated as respectively, inter and intraday variations and % RSD was less than one given in (Table 3).

CONCLUSION

A UV spectrophotometric method for Rivastigmine in pure and pharmaceutical dosage form has been developed and validated in water + methanol (9:1) solvent.

REFERENCES

1. https://www.tocris.com/products/rivastigmine-tartrate_4440#.U-m2ZvQW1SQ
2. http://www.mhra.gov.uk/home/groups/par/documents/websiteresources/con226931.pdf
3. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=0e20124c-725a-0145-996c-2ff908703162
4. Mutlu, N. B., & Degim, Z. (2005). Bioavailability file: rivastigmine tartrate. Journal of Pharmaceutical Sciences, 30, 150-157.