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Full Length Original Research Paper

Development and Validation of a Spectrophotometric method for estimation of Rasagiline Mesylate in bulk and tablet dosage Form

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Abstract: Rasagiline mesylate is a new molecule which acts as irreversible monoamine oxidase inhibitor used for the treatment of idiopathic parkinson's disease. The aim of present work was to develop a simple, accurate, reproducible and cost effective spectrophotomeric method for determination of Rasagiline mesylate in a pharmaceutical dosage form using phosphate buffer pH 6.8 as a solvent. The drug in solution form showed absorption maxima at 265 nm and obeys Beer's Lambert's law in concentration range 100-300 µg/ml. The regression equation was y = 0.003x + 0.0056 and correlation coefficient of (R^2) 0.9995. The limit of detection and limit of quantification was found to be 2.915 µg/ml and 8.833 µg/ml. Percent relative standard deviation values for the intra-day and inter-day precision were found to be 0.4308 and 0.6160 respectively. Mean % recovery was 100.45%. The proposed method was successfully applied for determination of Rasagiline mesylate in a tablet dosage form without any interference from common excipients.

Keywords: Rasagiline Mesylate, Validation, UV Spectrophotometric.

Introduction:

Parkinson's disease is degenerative disorder of the central nervous system. It results from the death of dopamine-generating cells in the substantia nigra which is a region of the midbrain. The cause of cell-death is unknown[1]. Rasagiline mesylate (Figure 1) is a new molecule which acts as irreversible monoamine oxidase inhibitor used for the treatment of idiopathic parkinson's disease. Chemical name for Rasagiline mesylate is (R)-2, 3-dihydro-N-2-propynyl-1H-inden-1-amine methanesulfonate, Molecular Formula is $C_{13}H_{17}NO_3S$ and Molecular Weight is 267.34 g/mol[2,3].

Rasagiline Mesylate is not official in any Pharmacopoeia. Literature survey reveals that U.V Spetrophotometric method for the determination of Rasagiline Mesylate in bulk and pharmaceutical formulations employed distilled water as solvent. The drug in aqueous solution showed absorption maxima at 271.6 nm[4]. A rapid and sensitive liquid chromatography-tandem mass spectrometry is also developed and validated for assay and has been applied to human pharmacokinetic studies[5]. Literature search also showed a RP-HPLC method for estimation of Rasagiline Mesylate in bulk and tablet dosage form[6] and a stability indicating HPTLC method for its analysis in tablet dosage form[7]. Already published UV spectrophotometric method employs water as a solvent for the assay of Rasagiline Mesylate. Since Rasagiline mesylate is absorbed from the upper portion of small intenstine, henceforth Phosphate buffer pH 6.8 was used in the study. The present paper describes the development and validation of UV spectrophotometric method for assay of rasagiline mesylate in tablet dosage form.

Materials and Methods:

Instrument and Materials: Only AR grade chemicals and solvents were used for analysis of Rasagiline mesylate. The reference standard Rasagiline Mesylate (99.50 % w/w) was obtained from Lupin Pharmaceuticals Limited, Pune (Maharashtra, India). The commercial formulation Rasalect 0.5 mg (Sun pharmaceutical Limited, India, Label claim- Rasagiline Mesylate-0.5 mg), was purchased from local market.

The spectrometer used was Shimadzu UV (1800 model, Japan) with 1 cm matched quartz cells, spectral bandwidth of 3 nm and wavelength accuracy of 0.5 nm connected to computer loaded with UV Prob Software. Digital balance of Shimadzu (AX200, Japan) and Sonicator of Spectrolab ultrasonicator (UCB 40, Germany) were used. All the instruments and apparatus were calibrated and validated as per calibration and validation protocol.

Experimental Methods:

Preparation of standard solution:

Stock standard solution was prepared by dissolving 100 mg of Rasagiline Mesylate in 100 ml Phosphate Buffer pH 6.8 (1000 µg/ml). The working standard solution of 100µg/ml was prepared and scanned in the range of 400-200 nm against solvent Phosphate Buffer pH 6.8 as blank. The standard solutions were prepared by dilution of the stock solution with Phosphate Buffer pH 6.8 to reach a concentration range of 100 µg/ml -300 µg/ml of Rasagiline Mesylate.

Preparation of sample solution for assay:

For the present work Rasalect tablet (Sun pharmaceutical Limited, India, label claim: 0.5 mg of Rasagiline Mesylate per tablet) was selected. To determine the content of Rasagiline Mesylate in Rasalect, twenty tablets were weighed and powdered. Average weight of powder equivalent to 10 mg of Rasagiline Mesylate was transferred to 50 ml volumetric flask and dissolved in about 30 ml of Phosphate Buffer pH 6.8 (200µg/ml). This was sonicated for 10 minutes. Finally, the volume was made up to the mark using same solvent. The solution was then filtered through syring filter (PVDF, 0.45µm) and this solution was analyzed at 265 nm (Table 1).

Validation of the developed method:

The developed method was validated as per ICH guidelines[8] for the following parameters.

Linearity and range:

The standard solutions were prepared by dilution of the stock solution with Phosphate Buffer pH 6.8 in the range of 100-300 µg/ml. The spectrums of these solutions were recorded and overlay spectra was taken (Figure 2). The Absorbances were measured at 265 nm and plotted against the corresponding concentrations to obtain the calibration graph (Figure 3).

Precision:

Intra and inter-day precision studies were performed by measuring the absorbance of standard solution of 200µg/ml at 6 independent series in the same day and three subsequent days within a week respectively. The percentage relative standard deviation (%RSD) was calculated (Table 2).

Limit of Detection (LOD) and Limit of Quantitation (LOQ):

LOD and LOQ were calculated using the formulae as LOD = 3.3 (SD)/S and LOQ = 10 (SD)/S, where S is average value of slopes of calibration plots and

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SD is calculated using values of y intercepts of regression equations.

Accuracy:

Recovery studies were carried out by applying the method to drug sample at which Rasagiline Mesylate corresponding to 50, 100, 150% of label claim was present. Total three determinations at each level were performed and the results were expressed as % RSD (Table 3).

Result and Discussions:

The standard solution of Rasagiline Mesylate, when scanned in UV range, showed the λmax at 265 nm. Linear relationships between drug concentrations were obtained over the range of 100-300µg/ml. Assay of Rasagiline Mesylate tablet formulation was successfully performed and the percentage purity of tablet was found to be 100.46%. Percent relative standard deviation values for the intra-day and inter-day precision were found to be satisfactory. The limit of detection and limit of quantitation values were found to be 2.915µg/ml and 8.833µg/ml respectively. Results of the accuracy studies indicated good recovery of the drug. No interference from the excipients of tablet formulation was found. The summary of validation parameters is shown in (Table 4).

Conclusion:

A simple, accurate and precise UV Spectrophotometric method for estimation of Rasagiline Mesylate was developed. The method is suitable for routine estimation of Rasagiline Mesylate in pharmaceutical tablet dosage form as it is an immediate release formulation.

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Figure 1: The structure of Rasagiline Mesylate

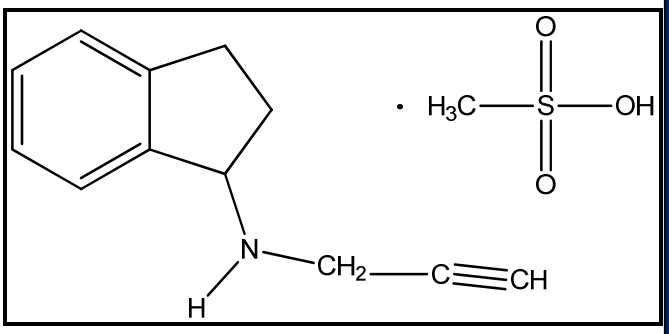

Figure 2: UV spectrum of Rasagiline Mesylate (100-300 µg/ml)

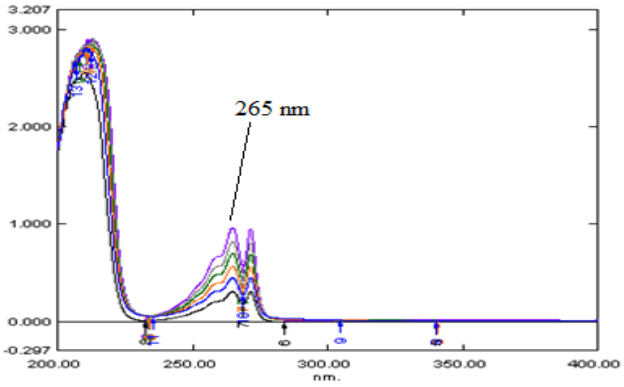

Figure 3: Calibration curve of Rasagiline Mesylate(100-300 µg/ml)

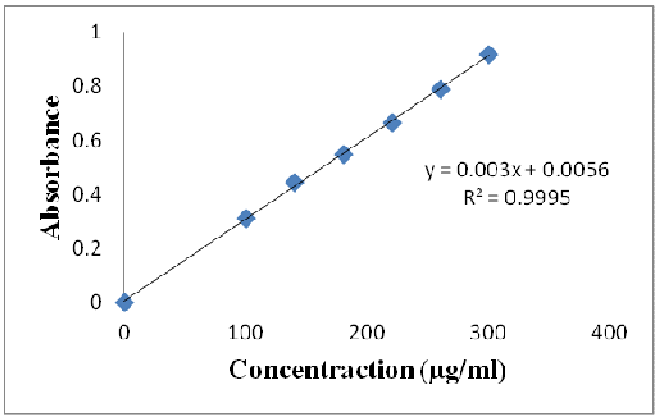

Table 1: Assay of Tablet dosage form

Tablet solution containing (µg/ml)	% Found	Mean % Found*	% RSD*
200	100.65	100.46	0.168
200	100.48		
200	100.32		

*n=3

Table 2: Precision data of Rasagiline mesylate

Parameters	Intra-day precision	Inter-day precision
Sample solution concentration (µg/ml)	200	200
% Assay*	100.45%±0.45	100.54%±0.61
%RSD	0.451	0.616

*n=6

Table 3: Accuracy data of Rasagiline mesylate

Accuracy Level	Amount addad (µg/ml)	%Recovery*	Mean % Recovery*	% RSD*
I (50%)	100	101.06±0.66	100.45%	0.523
II (100%)	200	100.10±0.56		
III (150%)	300	100.21±0.64		

*n=3

Table 4: Summary of Validation Parameters

Parameters	Rasagiline Mesylate
λmax (nm)	265
Linearity range (µg/ml)	100-300
Correlation coefficient (r^2)	0.9995
Slope (m) ± SD*	0.003
Intercept (c) ± SD*	0.0056
Regression equation (y=mx+c)	y=0.003x+0.0056
LOD (µg/ml)	2.915
LOQ (µg/ml)	8.833
Precision % RSD*	
Intraday	0.451
Interday	0.616
Accuracy (Mean % Recovery)	100.45%

*n=6

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Article History:----------

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