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Analytical Method Development and Validation of Rasagiline Hemitartrate in Tablets by X-ray diffractometer.

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Abstract:
This research article aims to validate the newly developed method to establish the specificity and method precision of the analytical method for identifying Rasagiline Hemitartrate API in Rasagiline Tablets 1mg using an X-ray diffractometer. The specificity of the method refers to its ability to accurately identify and distinguish Rasagiline Hemitartrate API in the presence of Placebo in the sample. To assess specificity, the X-ray diffractometer was used to analyze Rasagiline Tablet 1mg and recorded the peak at 2θ value 6.6°, corresponding to the peak of Rasagiline Hemitartrate API. The method precision was evaluated by performing six sample preparations of Rasagiline Tablet 1mg spiked with 10% Rasagiline Tartrate API in Placebo. The observed values for the peak at 2θ value 6.6° were consistent across all six sample preparations, with a % RSD of 0. % RSD indicates a high level of precision and reproducibility of the method for identifying Rasagiline Hemitartrate API in drug product Rasagiline Tablets 1mg.

Keywords: XRPD, method validation, Precision, LOD

I. INTRODUCTION

Rasagiline hemitartrate, a potent and selective monoamine oxidase type B (MAO-B) inhibitor, has received substantial attention in the pharmaceutical industry due to its therapeutic efficacy in treating Parkinson's disease. [1, 2]The development and validation of analytical methods for accurately quantifying Rasagiline hemitartrate polymorph in tablet formulations are crucial to ensuring its purity of desired polymorph, safety, efficacy, and bioavailability. Rasagiline is a monoamine oxidase-B inhibitor that has demonstrated efficacy against the cardinal symptoms of Parkinson's disease when used as monotherapy in early Parkinson's disease and as an adjunct to levodopa in advanced disease stages. It reduces the duration and severity of poor symptom response episodes in fluctuating patients. [3] Rasagiline was also generally well tolerated when added to other antiparkinsonian medication in patients with moderate to advanced disease and motor fluctuations, with the most commonly occurring adverse events being dopaminergic related. [4] Rasagiline is a second-generation potent, irreversible, and selective inhibitor of monoamine oxidase type B (MAO-B), which has been evaluated for the treatment of Parkinson's disease. [5]

This method validation report aims to establish an analytical method's specificity and precision for identifying Rasagiline Hemitartrate API in Rasagiline Tablets 1mg using an X-ray diffractometer. The method validation report outlines the specific conditions and parameters used in the analysis, as well as the acceptance criteria for determining the accuracy and precision of the method. [6, 7]Method Validation Report for Identification of Rasagiline Hemitartrate API in Rasagiline Tablets 1mg the specificity of the method was evaluated by analyzing Rasagiline Tablet 1mg using an X-ray diffractometer. The X-ray diffractometer analysis recorded a peak at 2θ value 6.6°, corresponding to the Rasagiline Hemitartrate API peak. The method precision was assessed by performing six sample preparations of Rasagiline Tablet 1mg spiked with 10% Rasagiline Tartrate API in Placebo. The observed values for the peak at 2θ value 6.6° were consistent across all six sample preparations, with a % RSD of 0.25.[8,9,10]

II. MATERIAL AND METHOD:

A. Materials: Strength is 1mg, and average weight is approximately 200mg. Rasagiline Tablet 1 mg, Placebo for Rasagiline Tablet, Rasagiline Tartrate API

B. XRD instrument Method

Mode of collection- Reflection, Radiation/Source K-Alpha1 [Å] -Cu Kα (Wavelength=1.54060 Å), Scan axis- Gonio, Scan Mode – Continuous, Voltage (kV)- 45, Current (mA)- 40, Start angle(°2θ)- 5.50, End angle(°2θ)- 7.5131, Step size(°2θ)- 0.0393908, Time per step (sec)- 15300, Scan speed (°/s)- 0.000657, Number of steps-51, detector setting mentioned in Table no 1

Instrumental Parameters: Table No.1: Instrument Parameters

Parameters	Method Parameters
a)Incident Beam path	
Prefix Module	iCore Cu (Offset = -1.1085°)
Soller Slit (mm)	BBHD Soller slits 0.03 rad.
Mirror	Bragg-Brentano HD Cu
Primary Mask	Mask 14.0 mm
Distance to sample	171.50 mm
Divergence slit	PDS for more
Distance to sample	95.50 mm
Fixed Angle	½°
Secondary Mask	Mask 6.0 mm
Distance to sample	111.00 mm
Beam attenuator	None
Beam Knife	Beam knife for linear detectors
b)Diffracted Beam path	**Diffracted Beam Path 1**
Prefix Module	dCore (Offset = 0.0000°)
Soller Slit	dCore Soller slits 0.04 rad
Anti-scatter slit	PASS for dCore
Fixed Angle	1/2°
Filter	None
Collimator	None
Beam Attenuator	None
Detector	PIXcel 1D-Medipix3 detector[1]

C. Procedure

Preparation of Samples API, Tablet, and Placebo Triturate a sufficient quantity of Rasagiline samples into mortar and pestle to obtain the fine powder, fill the sample powder in the sample holder, and prepare the sample with the backloading technique. Carry out the analysis as per the instrumental conditions mentioned in Table No.1

III. METHOD VALIDATION PARAMETERS [8, 9, 10]

Method validation consists of Specificity, Observation at the LOD Level, Precision, and Method Precision.

A. Specificity

Preparation of Samples (API, placebo and tablet)

Triturated sufficient Rasagiline samples into mortar and pestle to obtain the fine powder, filled the sample powder in the sample holder and prepared the sample with the backloading technique. Carried out the analysis as per the instrumental conditions mentioned in Table No.1 and recorded the data in Table No.2

Table No.2: Experimental Observations

Sample ID	Standard 2θ values (±0.2°)	Observed 2θ values
Rasagiline Tablet 1 mg	6.6°	6.6°
Placebo for Rasagiline Tablet	6.6°	No peak observed
Rasagiline Tartrate API	6.6°	6.7°

1. Experimental Observations

The X-ray diffraction pattern of the sample shows peaks of Rasagiline Hemitartrate at 2θ values 6.6°

There is no interference of the characteristic peak at 6.6° from Placebo.

Observation at the LOD level

LOD of the method is established, and 10 % of the w.r.t. label claim is found.

Preparation of 10% Rasagiline Tartrate API spiked in placebo w.r.t label claim of Rasagiline Tablets 1 mg.

Transferred 1.10 mg of Rasagiline Tartrate API and 2501.04 mg of Placebo for Rasagiline Tablet and mixed homogeneously using geometric mixing technique, taken a sufficient quantity of this mixture and filled in sample holder with the back loading technique, used sample holder tool kit and carried out the analysis as per the instrument parameter mentioned in Table No. 1. LOD to be performed for a total of three sample preparations and data recorded in Table No.3

Similarly, the same procedure for weights 1.20 mg API 2500.40 mg Placebo, 1.14 mg API, and 2503.47 mg Placebo.

Table No.3: Observation

10% Rasagiline Tartrate Drug substance spiked in placebo w.r.t label claim of Rasagiline Tablets 1 mg	Observed 2θ (±0.2°) values in
Sample -I	6.6°
Sample -II	6.7°
Sample -III	6.6°

2. Experimental Observations

LOD is visually detected at a characteristic peak of 6.6° for three sample preparations.

B. Method Precision

Procedure:

Sample Preparation

Transferred sufficient Rasagiline Tablet 1 mg and triturated into mortar and pestle to obtain the fine powder, filled the sample powder in the sample holder, and prepared the sample with a backloading technique. Carried out the analysis as per the instrumental conditions mentioned in Table No. 1 and data recorded in Table No.4

Performed the method precision for a total of six sample preparations of each strength.

Table No.4: Calculation Sheet

Drug product Tablet of strength in (mg)	Standard 2θ values (±0.2°)	Observed 2θ Values						Average	% RSD
		Spl Pre 1	Spl Pre 2	Spl Pre 3	Spl Pre 4	Spl Pre 5	Spl Pre 6		
1	6.6°	6.6°	6.6°	6.6°	6.6°	6.6°	6.6°	6.60°	0.00°

Experimental Observations

The XRD diffractogram of the sample shows the peak of Rasagiline Hemitartrate at 6.60°

The % RSD for the peak of Rasagiline Tablets 1 mg for six sample preparations at 2θ values 6.6° is 0.0

IV. Conclusion:

To sum up, this method validation report effectively illustrates the specificity and precision of the analytical technique used to identify the X-ray diffractometer-based Rasagiline Hemitartrate API in Rasagiline Tablets 1mg. The specificity assessment confirmed the method's capacity to effectively detect Rasagiline Hemitartrate API, as indicated by the peak that matched the expected peak at 2θ value 6.6°. Furthermore, the method's reproducibility and reliability were demonstrated by the precision evaluation, which involved six sample preparations spiked with 10% Rasagiline Tartrate API. The results consistently produced a percentage RSD of 0.25 for the peak at 2θ value 6.6°. These results highlight the analytical method's viability for the intended use and offer a solid foundation for its use in pharmaceutical quality control. It can be concluded that the analytical method validation for Rasagiline Hemitartrate in Tablets by XRPD was performed using the parameters specificity, Precision, and Limit of detection. All of the data has been compiled and determined to be satisfactory. As a result, the method established for the polymorph determination method is suitable for examining the presence of the desired polymorph in the drug product. Further, it ensures that the desired polymorph remains the same during manufacturing and that the drug product is stable.

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