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Method development and validation for determination of methane sulphonic acid in Rasagiline Mesylate drug substance by ion chromatography with suppressed conductivity detector

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ABSTRACT

A simple method for the detection of Methanesulphonic acid content in Rasagiline Mesylate drug substance using ion chromatography with suppressed conductivity detection is presented. A mixture of 1.3mM Sodium carbonate and 2.0mM Sodium bicarbonate was used as an eluant. The method showed linear responses over the sample target concentration ranges7-13µg/ml. The correlation coefficient was found to be 0.9993. The accuracy of the method was determined by preparing the sample concentration in the ranges 50%, 100% and 120% in triplicate and the % recovery was found to be within 98.0 to 102.0. The Method precision and the intermediate precision were demonstrated by the relative standard deviations (%RSD) of <2% for both the analyst. The Ruggedness was determined by changing the variables such as instrument and different analyst on different days. The method was fully validated for the determination of Methanesulphonic acid content in Rasagiline Mesylate drug substance. And the developed method was validated. The validated method is accurate, reproducibility, repeatability, linear, sensitive, convenience, ease of automation and the cost of analysis.

Keywords: Methanesulphonic acid, Rasagiline Mesylate, Conductivity detector, Ion chromatography.

INTRODUCTION

Ion chromatography is a process that allows the separation of ions and polar molecules based on their charge [1]. A column packed with solid ion exchange materials is used to perform the separation. Complex mixtures of anions or cations can usually be separated and quantitative amount of individual ions measured in the relatively short time. Ion chromatography [6] permits the determination of both inorganic and organic ionic species, often in concentration of 50µg/l

(ppb) and less. It has found increasingly application in a number of areas of chemical analysis [3] and particularly for the quantitative determination of anions [2].

Rasagiline Mesylate is the Methanesulphonic acid salt of rasagiline, inhibits MAO type B and Anti-parkinsonian drug. It is chemically described as 1H-Inden-1-amine, 2, 3-dihydro-N-2-propyny (1R)-, methanesulfonate. Its empirical formula is $C_{12}H_{13}N{\cdot}CH_4O_3S$.

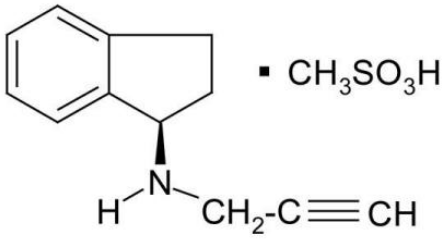

Fig:1 Structure of Rasagiline Mesylate

A reverse phase liquid chromatography method and LC–MS/MS method for quantitative determination of rasagiline [7]. The work describes the validation of an ion chromatographic method for the determination of Methanesulphonic acid in Rasagiline Mesylate drug substance using the parameters linearity, specificity, precision, ruggedness, accuracy and robustness.

MATERIALS AND METHODS

Rasagiline Mesylate was obtained from Orchid Chemicals and Pharmaceuticals Ltd., R&D Centre, Sholinganallur, Chennai, Sodium carbonate AR Grade (Aldrich), Sodium bicarbonate AR Grade (Riedel-de Haen®), Sulphuric acid AR Grade (Rankem), Methanesulphonic acid LR grade, Milli Q water was used in mobile phase, suppressor solution, standard and sample solutions preparation.

Ion Chromatographic Conditions:

The content of mobile phase was a mixture of 1.3sodium carbonate and 2.0 mM Sodium bicarbonate. Suppressor solutions were Milli Q water and 20mM sulphuric acid. They were filtered before use through a 0.2µm membrane filter and pumped to the column packed with Polymethacrylate functionalized with quaternary ammonium groups at a flow rate of 0.7mL/min which yielded a column backpressure of about 4.5MPa. The run time was set at 30min and an ambient column temperature was maintained. The volume of the injection loop was 10µL. Prior to injection of the drug solution the column was equilibrated with mobile phase for at least 45 min.

Standard Preparation:

Accurately weigh and transfer about 100mg of Methanesulphonic acid into a 100mL volumetric flask. Dissolve and dilute to volume with water. Dilute 10mL of this solution to 100mL with water. From the above dilution 4mL of solution make up to 100mL in volumetric flask with water. Filter this solution through a 0.2µm membrane filter.

Sample Preparation:
Accurately weigh and transfer about 100mg of sample to 100ml volumetric flask and dissolve the sample. 10ml of the above solution is dissolved with water and make up to 100mL in volumetric flask. From the above dilution 10mL of solution make up to 100mL in volumetric flask with water. Filter this solution through a 0.2µm membrane filter.

Methodology:
10µl of the sample solution was injected in to ion chromatography, using the given chromatographic condition. The retention time of Methanesulphonic acid was found to be 5.3 min. the content of Methanesulphonic acid was calculated by comparing the peak areas of the sample with that of the standard.

RESULTS AND DISCUSSION

Full method validation of the procedure was performed as per ICH guidelines which include precision, linearity, specificity, ruggedness, accuracy and robustness.

Precision:
The system precision of the procedure was determined by performing six replicate injections of standard Methanesulphonic acid with 4ppm of concentration and then determining the relative standard deviation (R.S.D) of the areas of Methanesulphonic acid peaks. The Method precision was determined by injecting six independent preparations of sample (Analyst 1). The precision of the replicate injections of the samples was <2% and the content of Methanesulphonic acid in Rasagiline Mesylate drug substance was calculated and found to be within the limit between 34.2% to 37.8%. The results are shown in Table 1.

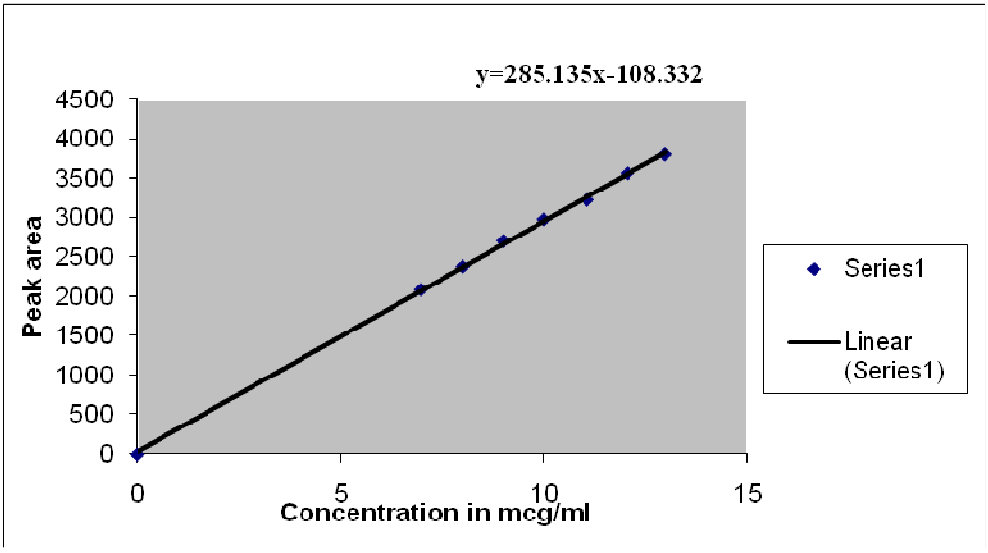

Figure 1: Linearity Curve of Methyl sulphonic acid in Rasagiline Mesylate

Linearity:
Linearity of the method was assessed by performing single measurement at several analyte concentrations. From the sample stock solution, a volume of about 70, 80, 90,100,110,120 and

130mg of sample Rasagiline mesylate was weighed and make up to the concentration around 7,8,9,10,11,12,13µg/ml. 10µl of above solutions was injected and the chromatogram was recorded. A calibration curve was determined by plotting a graph with the peak area against the concentration, which is shown in figure 1 and the linearity data's are given in Table 1. A correlation coefficient of 0.9993 was obtained.

Specificity:

The specificity of the method was evaluated by injecting the blank and check for interference, if any, at the retention time of Methanesulphonic acid. And individual injections of 10µl of standards bromide, chloride, Methanesulphonic acid and sample Rasagiline Mesylate were done. Further, the specificity was evaluated by spiking of bromide, chloride, Methanesulphonic acid with Rasagiline Mesylate sample solution. It was observed that there was no interference at the retention time of Methanesulphonic acid. As the obtained peaks are with the area 1110.199 for standard Bromide ion in 1000ppm, 2519.966 for standard Chloride ion in 1000ppm and the same area obtained while done in spiking of these with MSA and Sample. The chromatogram was shown in figure 2.

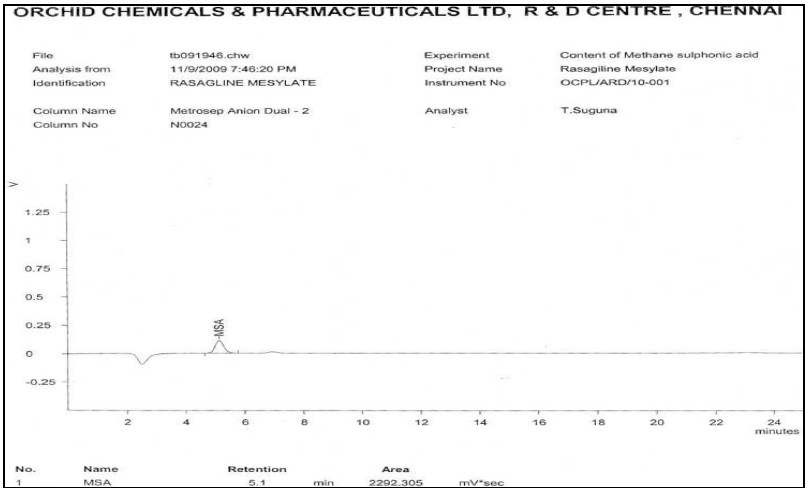

Figure 2: Chromatogram of Methyl Sulphonic acid in Rasagiline Mesylate

Ruggedness:

The ruggedness of the method for validation was studied by using different analyst (Analyst-2) on different day (Day-2). The content of Methanesulphonic acid was determined by the same condition. Table -13 shows the calculated values for the content of Methanesulphonic acid and overall %RSD for the two analysts was found to be <1%. This indicates the ruggedness of the method.

Accuracy:

The accuracy of the method was determined by preparing the sample in the ranges 50%, 100% and 120% of sample concentration in triplicate and analyzed as per the procedure. The % recovery was calculated by comparing the values of Methanesulphonic acid with the mean of precision value and the % recovery was found to be within 98-102%. The results are shown in Table -8.

The recovery was calculated by using the formula

$$\% \text{ Recovery} = \frac{\text{True value obtained x100}}{\text{Mean of Precision}}$$

50% recovery level of sample was prepared by adding 2mL of standard stock solution (Solution-1) in 10ppm of sample solution. Similarly 100% and 120% recovery level was prepared by adding 4mL and 4.8mL of standard stock solution (Solution-1) in 10ppm of sample solution.

Solution stability:

It is critical procedure to demonstrate the analyte are stable over the time required for analysis. In particular the stability of the analyte was of interest in this study because the sample is slightly soluble in water. Here a single stock solution was prepared and prepare a diluted sample concentration as per the procedure. This solution was injected initial and for every one hour by storing at room temperature for six hours. The cumulative %RSD was calculated from the peak areas of Methanesulphonic acid and it is not more than 5.0%. The results are summarized in Table 1.

Table 1: Validation Summary

Validation parameters (Units)	Results
Precision (%RSD)	
System Precision	*1.72*
Method Precision	*1.14*
Intermediate Precision	*0.85*
ACCURACY:	*%Recovery*
50%	*98.473*
100%	*99.772*
120%	*101.387*
Linearity	
Linearity Range	*7-13µg/ml*
Correlation Coefficient	*0.9993*
Specificity	
Spiking with bromide, chloride, MSA in to sample	*no interference*
Robustness	
Control	*1.05% RSD*
-10% flow	*1.80% RSD*
+10% flow	*1.90% RSD*
Solution Stability	
Stable till 360 minute	*% RSD is NMT 5%*
Ruggedness	
Over all % RSD	*NMT 2%*
System suitability	
Theoretical plates (N)	*2055*
% RSD	*1.72*

Robustness:
The robustness of the method was determined by carrying out the content of Methanesulphonic acid during which the flow rate was altered by ±10%. The %RSD was found to be 1.80 at -10% and 1.90 at +10% changes in flow rate. The Table 1 shows the value of robustness flow with ±10%.

CONCLUSION

The results of the validation study demonstrated that the analytical method for estimation of Methanesulphonic acid in Rasagiline Mesylate drug substance is reliable and reproducible. The results met all the acceptance criteria of ICH method validation guidelines. This method is found to be capable of determining the concentration of Methanesulphonic acid in Rasagiline Mesylate drug substance.

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