



## The Hydrogen bond in Rasagiline Mesylate drug substance interaction with moisture studies by FTIR, XRD, and TGA

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### Abstract:

This article mainly reports the Inductive effect on Rasagiline Mesylate drug substance by FTIR Spectroscopy. The Inductive effect is a temporary effect that produced a partial shifting of  $\sigma$  electrons towards a more electronegative atom of  $\sigma$  bond. This means  $\sigma$  (or single-bond electrons) shifts towards a more electronegative atom. Because of this, partial charges develop, the OH group from the water molecule attacking to the carbon carbon triple bond to form carbon double bond and the molecule gets Partial charge developed and it is a temporary effect, so once the water is removed, the partial charge removed and molecule goes back to its original state. Due to this, here there is no shifting of the Carbon carbon triple bond to the carbon carbon double bond take place and resulting in The IR spectra showing two vibration frequencies in the region of 3219.20  $\text{cm}^{-1}$  and 3278.99  $\text{cm}^{-1}$  Sample treated with a mixture of Ethyl acetate and Isopropyl alcohol, followed by drying at 105°C does not involve in the Inductive effect. And IR spectra show one vibration frequency at 3278.99 $\text{cm}^{-1}$  and there is no shifting of carbon carbon triple bond to carbon carbon double bond take place and does not involve the Inductive effect.

*Index Terms* - Inductive Effect, Hygroscopic, FTIR spectroscopy, Rasagiline Mesylate.

### I. INTRODUCTION

### INTRODUCTION

Rasagiline is an irreversible inhibitor of monoamine oxidase-B used as a monotherapy to treat symptoms in early Parkinson's disease or as an adjunct therapy in more advanced cases.[1,2] Rasagiline is a potent, selective, irreversible Monoamine Oxidase-B (MAO-B) inhibitor, developed to prolong the action of dopamine in the brain. It has been demonstrated that Rasagiline can improve motor and some non-motor symptoms (NMS) in both early and advanced Parkinson's disease (PD) patients. [3] It has shown efficacy in both early and advanced Parkinson's and appears to be especially useful in dealing with non-motor symptoms like fatigue. Parkinson's disease (PD) is a progressive neurodegenerative disease characterised by reduced dopamine levels in the substantial nigra. This may lead to typical motor features such as bradykinesia, resting tremors and rigid muscles, as well as non-motor symptoms such as neuropsychiatric symptoms, sleep disorders, autonomic dysfunction, and sensory disturbances. [4] There is a risk of psychosis or bizarre behaviour if rasagiline is used with dextromethorphan and there is a risk of non-selective MAO inhibition and hypertensive crisis if rasagiline is used with other MAO inhibitors. [5, 6, 7].Rasagiline mesylate is known to be a moderately hygroscopic material [8, 9].

Rasagiline Mesylate IR spectra differ and found that was not concordant with that of moisture absorbed sample. After an extensive literature search found that there is not enough work and scientific explanation available regarding any polymorphic change or moisture impact on Rasagiline molecule. This research article is basically dealing with the impact of moisture on rasagiline mesylate molecule which by using different analytical tools like XRD TGA, IR. Phenomenon Leads to shows different spectra in IR spectroscopy analysis. FTIR Spectroscopy is an important analytical technique that detects various characteristic functional groups in molecules of organic molecule [10]. On the interaction of infrared light with matter, chemical bonds would stretch, contract, and bend, and as a result, each chemical functional group tends to absorb infrared radiation in a specific wavelength with

respect to the structure of the rest of the molecule. Based on the principle, functional groups present in composite materials are identified.

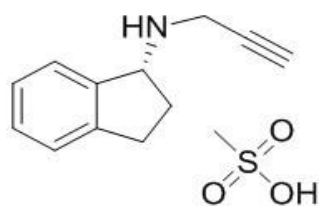


Figure 1: Structure of Rasagiline Mesylate

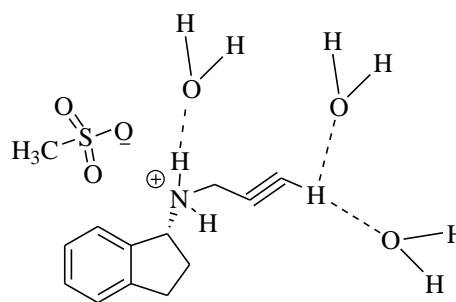


Fig. 2 Hydrogen bonding interaction with Rasagilin

## MATERIALS AND METHODS

### Materials

Rasagiline Mesylate uses in-house, Isopropyl alcohol, Ethyl acetate.

Instrumentation: FTIR Spectroscopy -Shimadzu, Model – IR Affinity 1S. Hydraulic Press, Vacuum Oven, Mortar and Pestle. XRD-PANalytical, TGA-TA (Waters)

### Method

#### General Procedure for TGA

Thermogravimetric Analysis were performed on a TA, Model-Q500, instrument conditions like Equilibrate 30°C, Ramp rate 10°C/min up to 300°C, isothermal for 5 min.

#### General Procedure for XRD

Powder XRD was carried out with a Cu-Ka radiation source PANalytical Corporation, Eindhoven, and the Netherlands). Data were collected at a step size of 0.0131303 and time per step 49.725 over a range of (2 $\theta$ ) 2 to 40. The generator settings were 45kV and 40 mA.

#### General Procedure for IR

Fourier transform infrared (FTIR) spectroscopic measurements were performed on a Shimadzu, model IR Affinity 1-S, The scanning range was from 4000 to 400 cm<sup>-1</sup>

## RESULTS AND DISCUSSION

### 1. TGA Analysis

Thermo gravimetric analysis was used to study the relative Rasagiline Mesylate sample moisture absorbed and treated sample, when equilibrate at 30°C, ramp rate 10°C/Min up to 300°C, Isothermal for 5 min, then from the data it was observed that, loss at 105°C is 0.07% in treated sample and sample moisture absorbed, it was observed that loss at 105°C is 3.161%

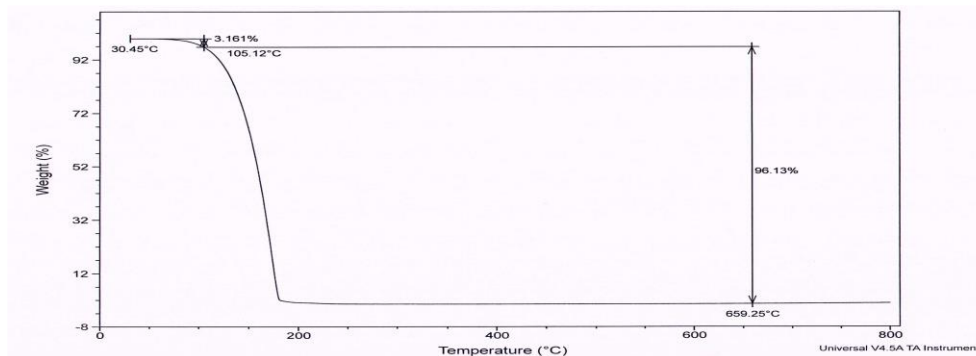


Figure 3: TGA Thermo gram with moisture

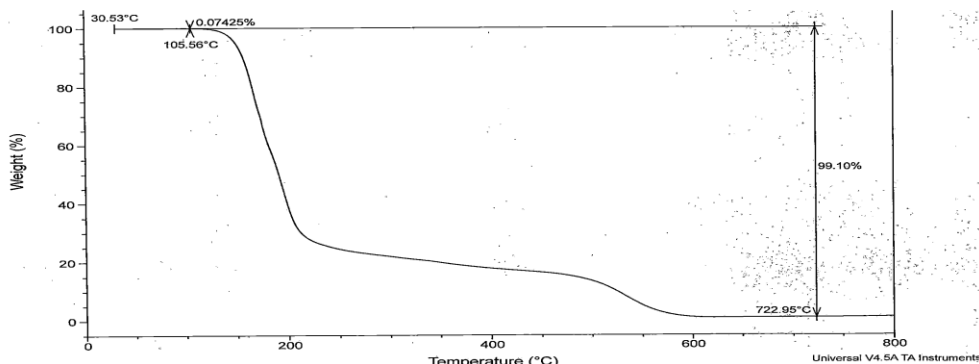


Figure 4: TGA Thermo gram without moisture

## 2. XRD Analysis

The PXRD patterns obtained experimentally Rasagiline Mesylate sample moisture absorbed and treated sample showed excellent agreement (Fig.2), demonstrating that there was no change in polymorphic form along with there is no any differences in peak relative intensities

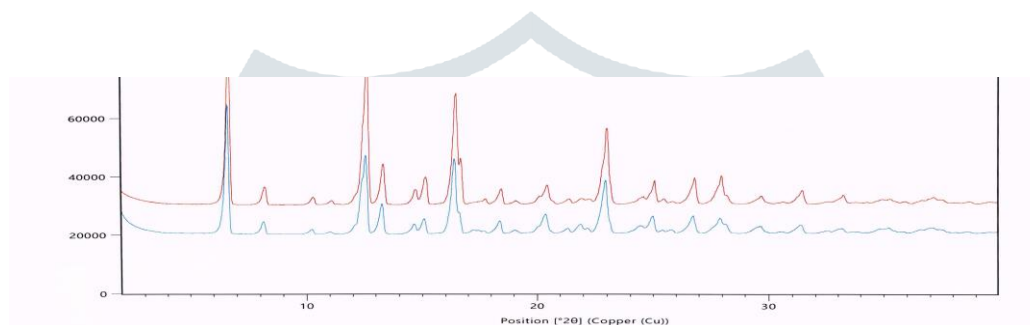


Figure 5: The XRD Diffractogram overlay of Rasagiline Mesylate sample moisture absorbed and treated sample

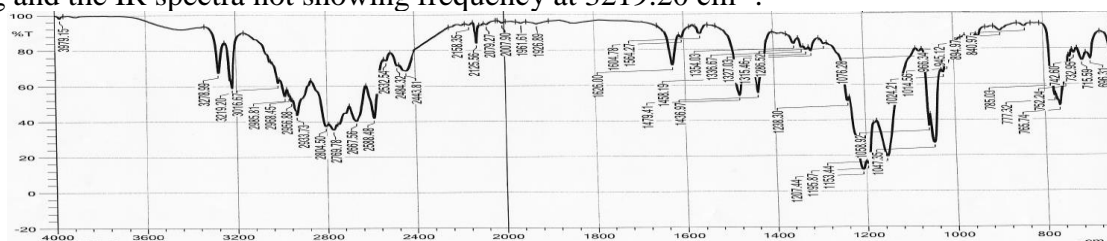
## FT-IR Analysis

Rasagiline Mesylate sample with 3.161% moisture triturate 2 mg with 300 mg of finely powdered and dried potassium bromide and grind the mixture. Prepare the pellet and record IR absorption spectrum in the range of 4000  $\text{cm}^{-1}$  to 650  $\text{cm}^{-1}$ .

Rasagiline mesylate is hygroscopic in nature so it absorbs water molecule from the environment, OH group from water molecule negatively charged reagent attacks such a molecule, it causes a complete transfer of sigma bond from the carbon atom, movement of electrons from one atom to another atom takes place and partial charged develop in molecule. It is a temporary effect, so once the reagent is removed, the partial charge molecule goes back to its (original state). Due to this, here shifting of the triple bonded carbon-Hydrogen stretch take place and resulting and IR spectra showing two vibration frequencies in the region of 3219.20 & 3278.99  $\text{cm}^{-1}$ .

Rasagiline Mesylate sample treated with Ethyl acetate and IPA. Keep this petri dish in a vacuum oven at 105°C for about 1 hour triturate about 2-4 mg of the above sample with about 200-400 mg of finely powdered and dried potassium bromide and grind the mixture. Prepare the pellet and record the IR absorption spectrum in the range of 4000  $\text{cm}^{-1}$  to 650  $\text{cm}^{-1}$ .

There is no transfer of the sigma bond from the carbon atom, movement of electrons from one atom to another atom does not take place, and. it is a temporary effect, Rasagiline molecule partial uncharged state (original state). Due to this, here shifting of the carbon-carbon triple bond to the carbon-carbon double bond doesn't take place and resulting and the IR spectra not showing frequency at 3219.20  $\text{cm}^{-1}$ .

Figure 6: The IR spectra showing vibration frequency occurred in the region of 3219.20  $\text{cm}^{-1}$ . Showing Temporary Inductive effect

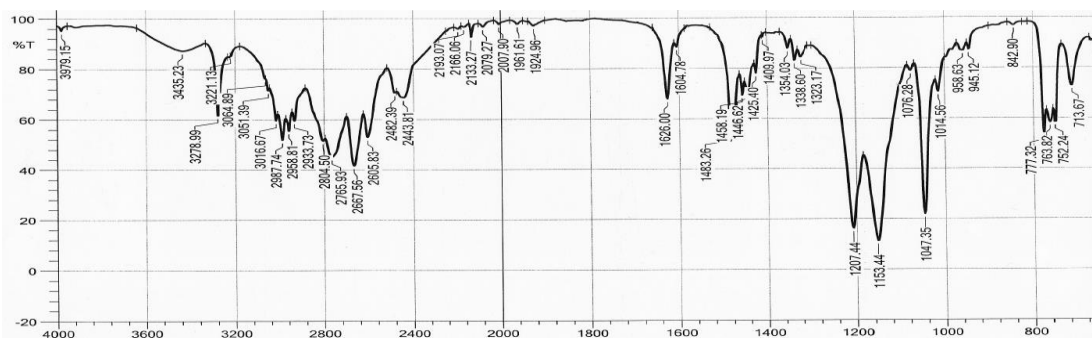


Figure 7: Sample IR spectra doesn't showing frequency at 3219.20 cm<sup>-1</sup> does not showing Inductive Effect.

## CONCLUSION

The study of potential polymorphism Changes in the development of new Active pharmaceutical Ingredient is of paramount importance for the pharmaceutical world, The API of reference in this study, Rasagiline Mesylate, 3.161% moisture-containing sample and dried sample differ in the FT-IR spectral study.

The Inductive effect on Rasagiline Mesylate were investigated using FTIR method, showing Inductive effect on Rasagiline mesylate of complete shift of sigma bond to either of the two atoms. OH group from water molecule, Movement of electrons from one atom to another atom take place and molecule gets the partial charged develop. it is a temporary effect, its occur in multiple bonds in presence of sigma bond and attacking agents, so once the reagent is removed, the partial charged develop molecule goes back to its partial uncharged state (original state). Due to this, here IR spectra show vibration frequency in the region of 3219.20 cm<sup>-1</sup>. XRD data shows that there is no change in the polymorph of Rasagiline mesylate and theta values matches with each other.

Overall, the present study demonstrated that impact of moisture on rasagiline mesylate studied by TGA found that sample absorb 3% moisture and further Inductive effect evaluated by using IR. Whereas the XRD Diffractogram shows no change in the Diffractogram of moisture absorbed and dried sample proves that there is no change in the polymorphic nature of the compound.

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