Evaluation of Some Anti-Parkinson's Disease Drug by Differential Scanning Colorimetry Method Using Salt

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Abstract: - Safinamide (SAF) is an anti-Parkinson's disease (PD) drug that has selective monoamine oxidase type-B (MAO-B) inhibition activity. In 2017, SAF was approved by the U.S. Food and Drug Administration (FDA) as safinamide mesylate (SAF-MS, marketed as Xadago). In this study, salts of safinamide with hydrochloric acid (HCl), hydrobromic acid (HBr), and maleicacid (MA) were obtained and characterized using differential scanning calorimetry (DSC). Differential scanning calorimetry methods are usually employed to assess the thermodynamic stability of solid forms the proposed method provides accurate and precise quality control tool for routine analysis of Safinamide mesylate in bulk and in tablet dosage form 2013 Trade Science Inc. – INDIA.

Key Words: —*Parkinson's disease (PD), Safinamide (SAF), Differential scanning calorimetry (DSC), Hydrochloric acid (HCl), acid (HBr), and Maleicacid (MA).*

I. INTRODUCTION

Safinamidemesylate (SAF) is an orally available derivative from chemical class of a amino amides, with multiple mechanisms of action involving inhibition of MAO-B and Dopamine reuptake used in the treatment of epilepsy and Parkinson.s disease. Chemically, Safinamidemesylate is, (S)-(+)-2-[4-(3-fluorobenzyloxybenzylamino) propanamide] methanesulfonate(1:1 salt).The chemical structure is shown in Figure 1.[1, 2].

Previous studies on the solubility of SAF and related salts have been conducted using the excessive powder dissolution method.

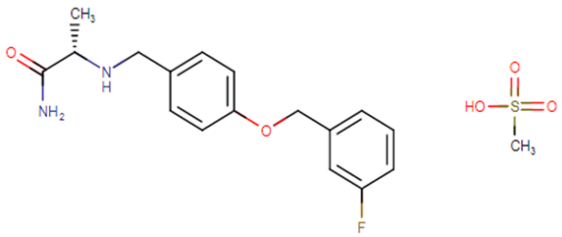

Fig.1. Chemical structure of Safinamide Mesylate.

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Literature survey reveals a validated chiral liquid chromatographic method for the enantiomeric separation of safinamidemesylate[3] and bioassay of safinamide in biological fluids of humans and various animal species [4].

Except this, so far no analytical method was available forestimation of SAF as indicated by detail literature survey. The therapeutic effectiveness and less methods available for its estimation encourage us to undertake this work, so that quantitative estimation of SAF can be done and hence can be used for routine analysis of bulk and formulation as well.

The antiparkinson mechanism of safinamide is through reversible inhibition of selective MAO-B, as a mesylate salt, thus reducing the degradation of dopamine.

It inhibits glutamate release and dopamine reuptake in the brain. Safinamide also blocks sodium and calcium channels, although the clinical significance of this to PD is unknown.

II. EXPERIMENTAL AND STABILITY STUDIES

Safinamide (SAF) was gifted from Alembic Pharma, Munbai. (M S). Differential scanning calorimetry(DSC) was performed on a Mettler-Toledo machine at a rate of heating of 10 0C/min within the range of 25–250oC under nitrogen flow at a rate of 20 mL/min.

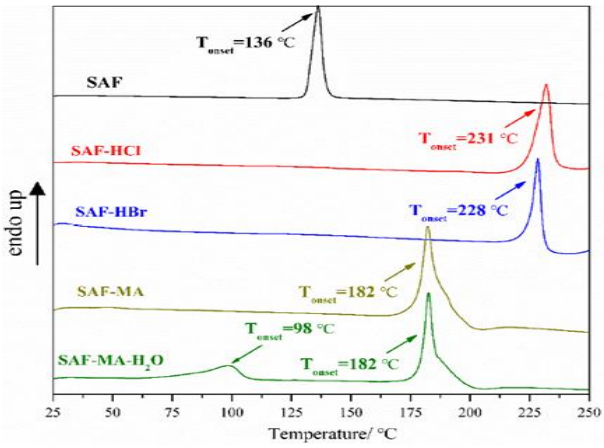
The stability studies of SAF and its salts was performed under different humidity environments at 25oC. The different relative

humidity treatments were 75% (sodium chloride in saturated state), 85% (potassium chloride in saturated state), and 97% (potassium sulfate in saturated state). The samples were placed in an incubator after 14 days and assessed using PXRD data.

III. Results And Discussion

A. *Thermal Analysis:*

Differential scanning method is usually employed to assess the thermodynamic stability of solid forms. Herein, the DSC and TG curves of SAF and all salts are shown in Figure 7 and Figure S1. The DSC curves of SAF, SAF-HCl, SAF-HBr, and SAF-MA showed an end of thermic peak at 1360C, 2310C, 2280C, and 1820C, respectively, with the temperature attributed to Crystals 2020, 10, 989 7 of 11the melting point of the solid forms. The DSC curve of SAF-MA-H2Oexhibited abroad peak in the range of 50–1100C, which may be attributed to the release of water in the crystal cell. Another end of thermic peak at 182 0C was observed, which was assigned to the melting point of SAF-MA-H2O. The TGcurves of SAF, SAF-HCl, SAF-HBr, and SAF-MA began to decompose with the formation of volatile compound(s) at 200 0C, 224 0C, 2220C, and 177 0C, respectively. The TG curves of SAF-MA-H2Oshowed a weight loss of 4.38% at the range of 50–110 0C, which was attributed to water loss (calculated4.13%). SAF-MA-H2O began to decompose at 177 0C, which meant that the melting observed was a melting/degradation due to the fact that the baseline was not reached after the phase transition, experiments that confirmed the decomposition phenomenon.



IV. Conclusion

The formulations of safinamide were subjected to accelerated stability studies after filling into hard gelatin capsules shells. The evaluated method is very simple. Therefore, the DSC method was proved to be suitable for the safinamide determination in tablets.

V. Acknowledgement

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