

Thermal-Dependent Dehydration of NSB L-Tartrate Monohydrate: Solid-state characterisation of Anhydrous Form II and Form III

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NSB is a novel mixed monoamine re-uptake inhibitor and a possible development candidate for treatment of diseases in the CNS area. Various salts have been crystallised and the L-Tartrate Monohydrate (Form I) was chosen as the preferred salt form for further development. Early development DSC traces showed that the Monohydrate after dehydration probably could exist either as the dehydrated hydrate or in one or two distinct anhydrous polymorphic forms. The present study was initiated in order to identify the nature of the thermal events encountered.

Two anhydrous forms (Form II & Form III) were identified and characterised. Form II was prepared by thermal dehydration of the Monohydrate and subsequent re-crystallisation at 125 °C. Form II was prepared by thermal dehydration and re-crystallisation at 160 °C. Form I and Form II showed different powder x-ray diffraction patterns, FT-IR spectra, water vapour sorption profiles and crystal morphology. The anhydrous forms were irreversibly re-hydrated to the monohydrate Form I above the critical re-hydration humidity, which was determined to approx. 30 % RH for Form II and approx 40% RH for Form III. It was concluded that the anhydrous Form II and Form III are true polymorphic forms and that Form II probably is metastable compared to Form III.