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THERMAL STUDIES ON MEBENDAZOLE

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Although mebendazole (I) is a widely used broad-spectrum antihelminthic, less than 0.2% of an oral dosage is absorbed due to the low solubility and slow dissolution. The existence of three polymorphic forms of mebendazole identified as A, B, and C, exhibiting significant therapeutic differences supports the fact that the solubility and rate of dissolution of the drug are important factors to be considered.

This paper presents the results of a study of the thermal degradation of mebendazole in order to provide insight into the existence of the various polymorphic forms in suspension and the solid-state and the resulting effect not only on the physical properties, but also on the efficacy of the dosage form. Polymorph C, which is pharmaceutically favoured, was used in this study and the identity confirmed using infrared (IR) spectra, X-ray powder diffractograms (XRD) and differential scanning calorimetry (DSC). The DSC curves showed the melting endotherm at 320°C, preceded by transition endotherms at 170 and 235°C. An LC-MS method was developed to confirm the solid-state degradation of mebendazole and together with TG-FTIR, was used to identify the degradants (II) and (III) shown in Figure 1.

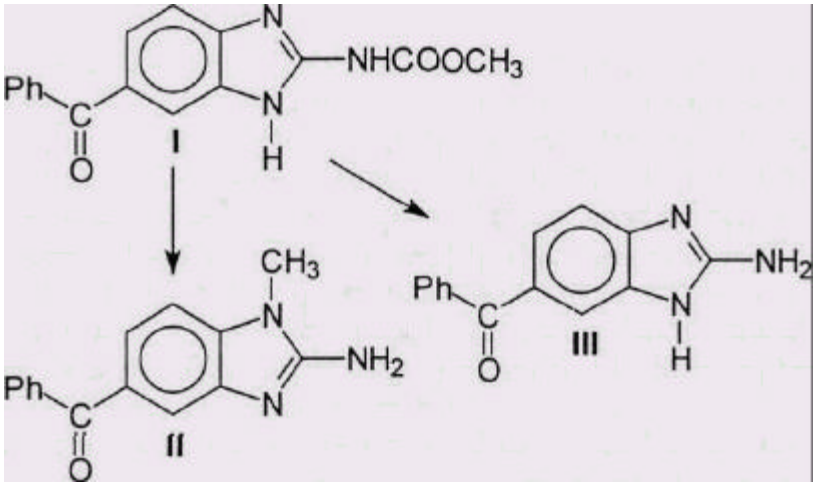

Figure 1: Thermal Degradation of Mebendazole

These results will be of use in the further understanding of the three polymorphic forms of mebendazole in selected dosage forms.

References:

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2. M. Himmelreich, B.J. Rawson and T.R. Watson, Australian Journal of Pharmaceutical Sciences, 6(4) 123-125 1977