INCOMPATIBILITY BETWEEN ISONIAZID AND LACTOSE IN A PAEDIATRIC MIXTURE CONFIRMED BY DIFFERENTIAL SCANNING CALORIMETRY

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Purpose. Differential scanning calorimetry (DSC), shown to be a powerful tool in preformulation studies, has been used to evaluate the compatibility of drug substances and excipients. Due to the unavailability of commercial isoniazid (INH) liquid dosage formulations, a paediatric INH mixture is commonly prepared in pharmacy practice from readily accessible INH tablets. The original British Pharmaceutical Codex (BPC) INH mixture is intended for formulation utilizing INH powder and not tablets. Although the incompatibility of INH and lactose is well documented in the BPC, the compounded INH mixture (formulated with tablets) was prepared without considering the potential for lactose to be present as an excipient in the tablet.

Methods. The stability of INH in this mixture was assessed by high performance liquid chromatography (HPLC). DSC methods were used to determine the compatibility of INH with lactose.

Results. The INH mixture was shown to exhibit significant degradation (> 10% after 3 days of storage at 4 and 25°C). The BPC mixture claims a 30-day expiry, which was demonstrated in a mixture compounded with INH powder (> 90% remaining at 30 days). This formulation, then spiked with lactose, was shown to produce a statistically similar degradation profile to that of the formulation made from INH tablets (p>0.05). These results indicate that the tablet excipient, lactose, is responsible for the observed degradation of INH. The thermoanalytical studies confirmed the above results with the DSC curve of INH/lactose broadening and shifting the $T_{\text{onset}}$ from 171°C for pure INH to 166°C, confirming the presence of an impurity.

Conclusions. The DSC results, confirming the incompatibility between INH and lactose, demonstrate its value as a rapid technique to identify potential incompatibilities between drug substances and excipients. This study also highlights the importance for stability data on all extemporaneously compounded preparations.