**CAPTISOL® IMPROVES THE SOLUBILITY OF ANTI-TUBERCULAR DRUGS**

**A Haywood**, **GD Grant**, **BD Glass**

1School of Health Science, Gold Coast Campus, Griffith University, QLD; 2Discipline of Pharmacy, School of Pharmacy and Molecular Sciences, James Cook University, Townsville, QLD

**Purpose.** There are global concerns on the quality of anti-tuberculosis (TB) fixed dose combination (FDC) products, a matter receiving attention from the World Health Organisation (WHO). The bioavailability of rifampicin (RIF) has been found to reduce when in combination with other anti-tubercular agents due to the formation of insoluble complexes. The availability of a combination liquid dosage form for the treatment of TB in children is limited by both solubility and stability issues. This study was undertaken to investigate the effect of selected cyclodextrins (CDs) such as Captisol® (a sulfobutylether-β-CD) and 2-hydroxypropyl-β-CD (HPB) on the solubility of RIF alone and in combination with the other anti-tuberculosis agents, namely; isoniazid (INH) and pyrazinamide (PZA). **Methods.** A stability-indicating HPLC method was developed and validated for the quantitation of these three drugs in combination. Sample preparation involved the addition of excess drug candidate, alone and in combination, to aqueous cyclodextrin solutions of varying concentrations. The resulting suspensions were agitated at room temperature (25 ± 0.5°C) for 12 hours and the supernatant analysed for the drug candidate. **Results.** The solubility of RIF and PZA was enhanced in the presence of Captisol® (0.092 M) from 1.236 to 7.700 mg/ml and 20.331 to 23.460 mg/ml respectively while for HPB (0.141 M) increases in solubility of RIF and PZA from 1.611 to 4.757 mg/ml and 18.116 to 23.959 mg/ml were achieved. These results demonstrate the superior solubilising ability of Captisol® over that of HPB especially for RIF whose inclusion in liquid dosage forms in adequate concentrations has proved to be problematic. **Conclusions.** Captisol® has enhanced the solubility of RIF and PZA, providing new formulation opportunities for FDC products for the treatment of TB in the paediatric population.