

## DEVELOPMENT OF CONTROLLED RELEASE TABLET FORMULATIONS USING HYDROPHILIC POLYMER MATRIX SYSTEMS

C. Ramani<sup>1</sup>, J. Wang<sup>2</sup>, A. Kane<sup>1</sup>, K. Chow<sup>1</sup>, J. Lambing<sup>2</sup>

<sup>1</sup>Patheon Inc., <sup>2</sup>Portola Pharmaceuticals

**Purpose:** To Develop Large Diameter, Non-Disintegrating Controlled Release Tablet Formulations Using Hydrophilic Polymer Matrix Systems for pH-sensitive low solubility drugs.

**Methods:** Formulations containing a pH-solubility sensitive drug and a combination of hydrophilic polymers (HPMC and Polyox) and alkalizers (such as Calcium Carbonate, Magnesium Oxide and Sodium Bicarbonate) were designed and manufactured using direct compression or roller compaction followed by compression using rotary tablet press. The investigation was aimed to provide an alkaline micro-environment to a chemical entity which has very poor solubility up to pH of 6.8. The tablets were subjected to prolonged exposure to various pH environments (pH Range 1.0 to 7.4) and studied for effect of various pHs on the *in-vitro* release profile using USP Dissolution Apparatus III method. Selected formulations were tested for physical appearance, dissolution, content and impurities after storage at 25°C/60% RH and 40°C/75%RH for up to 6 months.

**Results:** Large, non-disintegrating controlled release tablet formulations using hydrophilic polymer matrix systems were designed and developed to release the drug for 7-9 hours and 10-12 hours respectively with zero to pseudo zero order release profiles. No significant changes in physical appearance, stability and dissolution were observed from the stability samples. The data showed significant influence of the alkalizers on the dissolution profile of the tablets. The molecular weights and type of hydrophilic polymers also influence the tablet strength and drug release mechanisms (i.e., erosion or diffusion) from the matrix tablets during *in-vitro* dissolution. With suitable combination of excipients, floating tablets in dissolution fluids were produced.

**Conclusion:** The results indicated that interactions of drug, excipients and polymers play an important role in modulating the physical properties and dissolution profiles of controlled released tablets. This approach may be useful for improving the bioavailability of pH-solubility sensitive drugs.