DEVELOPMENT OF ORALLY DISINTEGRTING TABLETS COMPRISING CONTROLLED-RELEASE MULTIPARTICULATE BEADS

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Abstract

Purpose: To characterize and deliver a once daily controlled release orally disintegrating tablet (ODT) formulation comprising Diffucaps® sustained-release (SR) melperone beads.

Methods: Target dissolution profiles were derived from pharmacokinetic modeling using maximum drug concentration (Cmax), time to Cmax (tmax), area under the curve (AUC), and the drug concentration (C) versus time (t) for a 50-mg SR beaded formulation. Drug release in vitro was performed with a USP apparatus II (200 rpm) against water (pH 5.6) at 37°C. Two ODTs were manufactured: one containing low-dose pellets (50 mg SR); and the other containing medium-dose pellets (50 mg SR). In vitro and in vivo bioequivalence was determined using a randomized crossover study with 16 normal volunteers receiving, under fasting conditions, four treatments: 25-mg syrup formulation A (50% of CR capsules) and 25-mg ODT-CR (50% of CR capsules). Two ODTs with release profiles similar to those shown in Figure 1 were prepared for bioequivalence studies.

Results: SR beads exhibited a mean particle size of <150 μm, while the melperone content was 20% (SR-1) and 25% (SR-2) by weight. Bead porosity was determined by the density of consolidated pellets. The SR-1 and SR-2 bead formulations were blended with AdvaTab® rapidly dispersing microgranules, and subsequently compressed into tablets. Composite tablet samples were collected and tested for potential for fracture during compression. SR capsules containing SR beads were blended with AdvaTab® rapidly dispersing microgranules, and subsequently compressed into tablets. Composite tablet samples were collected and tested for potential for fracture during compression. Two ODTs with release profiles similar to those shown in Figure 1 were prepared for bioequivalence studies.

Conclusions: Two ODTs, containing equivalent concentrations of melperone and excipients, were successfully developed using a novel technology that allows delivery of extended-release melperone from orally disintegrating tablets. The release profiles of the SR beads and the corresponding ODT-CR tablet batches (data not shown), indicate that the ODT-CR formulations were bioequivalent to the 50-mg SR capsule formulation. The oral bioavailability of tablet formulations was similar to that of the syrup formulation, indicating that the tablet formulations effectively and consistently deliver the drug to the small intestine. The oral bioavailability of tablet formulations was similar to that of the syrup formulation, indicating that the tablet formulations effectively and consistently deliver the drug to the small intestine.