Dissolution of Piroxicam in Capsule Formulations studied with USP and Real-Time UV Imaging Methods

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Introduction

Poor aqueous solubility of an active pharmaceutical ingredient (API) is one of the most pressing problems in formulation development, with as many as 90% of new API candidates in this category besides approximately 40% of the drugs on the market. Low solubility and dissolution rate often lead to poor bioavailability and efficacy problems, regardless of the administration route (Duret *et al*., 2012). Among several approaches have been adopted for improving the drug dissolution and/or solubility, the usage of multifunctional excipients confers many advantages, as manufacturing efficiency and reduced production costs (Builders *et al*., 2010). LoxOral™ (PCCA), is a innovative excipient that has been used in capsule formulations, where it displays an improved dissolution of all types of APIs, excellent flowability, and reduced static state.

The present study was designed to evaluate the *in vitro* potential of LoxOxal to enhance the dissolution properties of piroxicam, as well as its utility in comparison to microcrystalline cellulose (MCC) delivery systems. In addition to the conventional USP dissolution method, an approach based on UV imaging was utilized as a non-intrusive technique for investigating both the real-time, spatially and temporally resolved (projected 2D) at a selected wavelength, drug dissolution phenomena (Ye *et al*., 2012). Piroxicam (class II drug) was selected as a model of a low solubility–high permeability API.

Methods

Dissolution studies of piroxicam (3.5 mg) in gelatin capsules containing LoxOral and MCC formulations were conducted using USP Apparatus 1 (basket method) (Distek Symphony 7100, North Brunswick, NJ) with 6 replicates/formulation, according to the USP monograph of the drug (US Pharmacopeia, 2000). The dissolution medium was 900 mL of USP simulated gastric fluid (SGF) without pepsin (pH 1.2), maintained at 37^0C. The basket rotation speed was kept at 50 rpm. In all experiments, samples (5ml) were withdrawn at 15, 30, and 45 minutes and replaced by 5 ml of fresh pre-warmed SGF. Samples were then filtered with an Acrodisc® syringe - 0.45 µm HT Tuffryn membrane and analyzed using UV-vis spectrophotometry (IMPLEN NanoPhotometer 300) at 333 nm. The cumulative percentage of the API released from the preparations was calculated using calibration equations.

A Sirius SDI UV imaging system (Sirius Analytical, East Sussex, UK) was used to study real-time dissolution behavior of piroxicam from the LoxOral formulation. The measurements were performed at ambient temperature in a quartz flow cell, designed to provide laminar flow across the surface of a compacted API powder. A pulsed xenon lamp was used as a light source and employing a 254 nm detection wavelength. The total area available for imaging was 9 mm × 7 mm (1280 × 1024 pixels; 7 x 7 µm2). A syringe pump was used for infusion of 0.1 N HCl as dissolution medium at the following programmed flow: 0.2 mL/min for 10 min (fasted flow); 0.8 mL/min for 10 min (fed flow); 2 mL/min for 0.5 min (quick flush); 0 mL/min for 5 min (static flow); 2 mL/min for 0.5 min. Images were recorded at a rate of 59 frames/s and analyzed by ActiPix D100 (v.1.4).

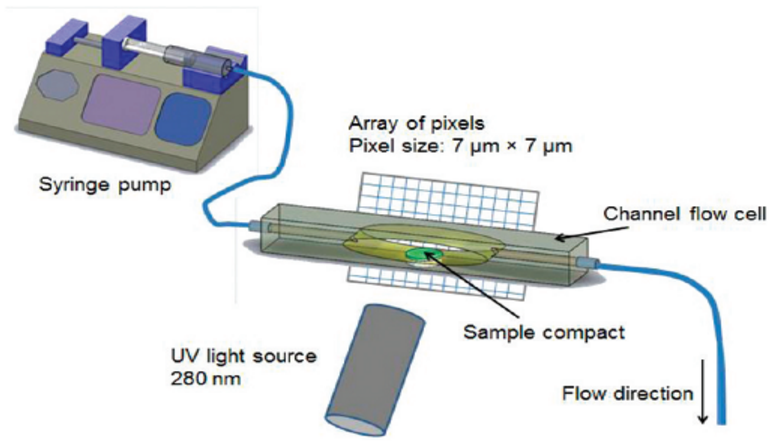

Figure 1: Schematic representation of the UV imaging setup.

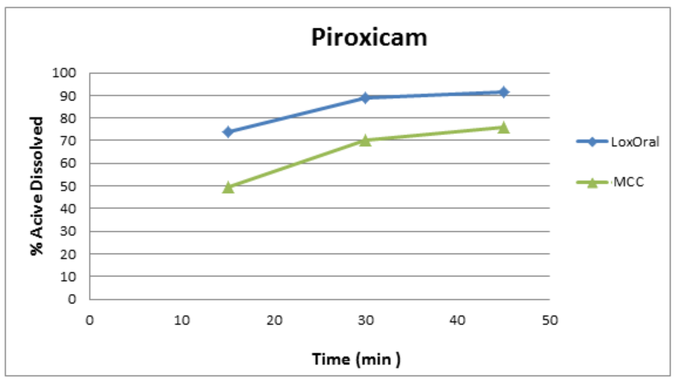

Figure 2: Dissolution profiles of piroxicam from capsules containing different excipients, LoxOral and microcrystalline cellulose (MCC).

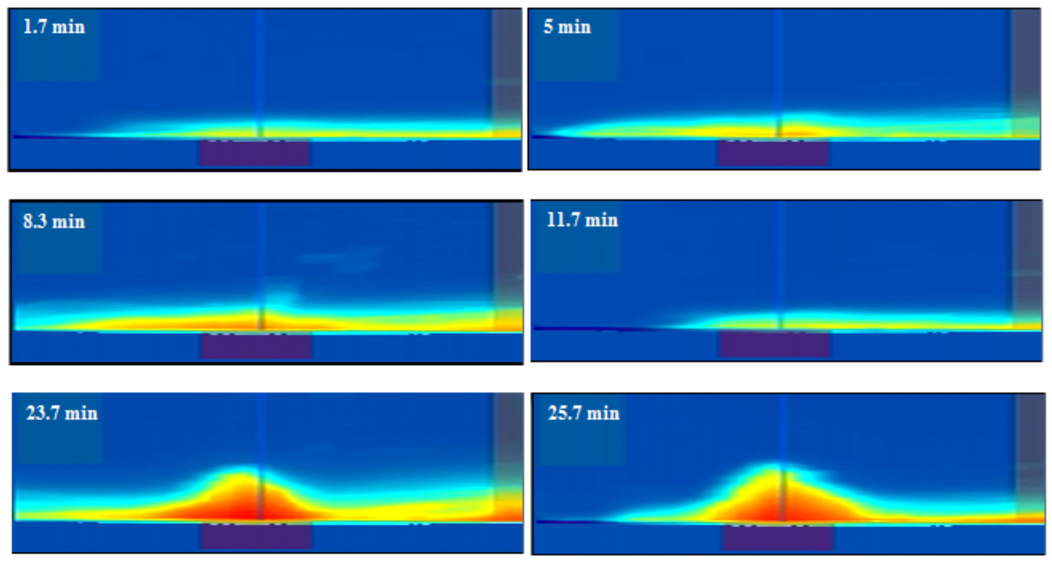

Figure 3: UV-surface dissolution imaging of the *in vitro* piroxicam release from LoxOral formulation in 0.1 N HCl at defined time points: 1.7 min, 5 min and 8.3 min (fasted flow); 11.7 min (fed flow); 23.7 min (static flow); 25.7 min (quick flow).

Results and Discussion

The data presented in Figure 2 clearly show the dissolution rate of the drug from LoxOral was significantly higher when compared to that of MCC. Although both formulations complied with the USP dissolution specification (not less than 75% of the labeled amount of the drug within 45 min in SGF without pepsin), the dissolved amount of piroxicam at 45 min was 91.5% in the LoxOral formulation. The increased drug release from the LoxOral formulation possibly resulted from a partial dissolution of the drug in the excipient, solubilization effects of LoxOral, and improved wettability in dissolution media because of the excipient`s amphiphilic character.

The UV image absorbance maps of released piroxicam at a series of selected time points (Figure 3), showed the dissolution of piroxicam from LoxOral formulation promotes a rapid formation of a thin layer at the surface which then steadily dissolved downstream with the flow over time. However, the sample showed some breaking down behavior from the static flow period, with a swollen appearance. Almost the whole sample dissolved at the end of the run.

Conclusion

LoxOral was shown to be a successful excipient to improve the dissolution rate of piroxicam. The increase in the rate would potentially provide the rapid bioavailability and onset of action after the drug is taken orally. The information from in situ experiments on UV imaging could reinforce the understanding during dissolution event, indicating an uniform and smooth release of piroxicam from LoxOral formulation, while in the presence of flow. LoxOral-based formulation has proven to be a most promising delivery system for oral bioavailability enhancement of BCS Class II drugs such as piroxicam.

Builders, P.F.; Bonaventure, A.M.; Tiwalade, A.; Okpako, L.C. and Attama, A.A. Novel multifunctional pharmaceutical excipients derived from microcrystalline cellulose–starch microparticulate composites prepared by compatibilized reactive polymer blending, Int. J. Pharm. 388, 159-167 (2010).

Duret, C.; Wauthoz, N.; Sebti, T.; Vanderbist, F. and Amighi, K. Solid dispersions of itraconazole for inhalation with enhanced dissolution, solubility and dispersion properties, Int. J. Pharm. 428, 103-113 (2012).

Ye, F.; Larsen, S.W.; Yaghmur, A.; Jensen, H.; Larsen C.; Østergaard, J. Real-time UV imaging of piroxicam diffusion and distribution from oil solutions into gels mimicking the subcutaneous matrix, Eur. J. Pharm. Sci. 46, 72-78 (2012).

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