# Technical Report:

## Comparison of Dissolution Properties of Piroxicam Using Microcrystalline Cellulose and a New Excipient (LoxOral®)

**Abstract:** Piroxicam is a nonsteroidal anti-inflammatory drug that is characterized by low solubility-high permeability (class II by BCS). The capability of a new excipient, LoxOral, manufactured by PCCA, to enhance the dissolution of poorly water-soluble drugs was investigated by USP dissolution testing and compared to microcrystalline cellulose (MCC). The capsules containing piroxicam in LoxOxal produced faster *in vitro* dissolution than the corresponding simple mixture using MCC and met USP dissolution standards for the drug (91.5% at 45 min). The results suggest that LoxOral, as an excipient, is a powerful tool to accelerate dissolution and potentially improve the oral bioavailability of poorly water-soluble drugs, having a good potential for use as a pharmaceutical excipient.

### Purpose:

The purpose of this study was to evaluate the potential of LoxOral to enhance the dissolution properties of piroxicam and to evaluate its utility in comparison to MCC delivery systems.

### Introduction:

During the last decade, the trend in drug discovery has increased the number of active pharmaceutical ingredients (APIs) that exhibit high lipophilicity and poor water solubility, also associated with poor dissolution characteristics (Vogt *et al*., 2008). Dissolution rate in the gastrointestinal tract is the rate limiting factor for the absorption of many of these drugs, which therefore suffer from poor oral bioavailability (Zimmermann *et al*., 2009).

In order to enhance the dissolution of poorly water-soluble drugs, an increasing number of pharmaceutical formulation technologies are being developed to address this challenge of drug product development (Uchiyama *et al*., 2010). Many pharmaceutical studies have focused their attention on the production of multifunctional excipients, once the choice of excipients becomes critical in terms of delivery system functionality and quality. Excipients with multiple functional properties confer many advantages such as manufacturing efficiency and reduced production costs (Builders *et al*., 2010).

Microcrystalline cellulose (MCC) is a purified, partially depolymerized cellulose prepared by treating alpha cellulose, obtained as a pulp from fibrous plant material with mineral acids (Gohel *et al*., 2007). It is widely used as filler, disintegrant and binder of oral tablets, pellets and capsules (Nikolakakis *et al*., 2006). MCC is considered one of the most useful fillers due to its excellent compatibility at low pressures, high dilution potential, chemical inertness and compatibility with most drugs (Kalita *et al*., 2013). However, according to Chamsai & Sriamornsak (2013), most drugs prepared with MCC show a tendency toward prolonged release due to a lack of disintegration.

LoxOral, manufactured by PCCA, is an innovative excipient for use in capsule formulations. It improves dissolution of all types of APIs, including drugs with poor water solubility. It is gluten- and casein-free, Sodium Lauryl Sulfate (SLS)-free, lactose-free, soy-free, dye-free and magnesium stearate-free. It also contains an ingredient (isomalt) which has shown potential prebiotic effects (Gibson *et al*., 2010). LoxOral is an all-in-one base with improved dissolution, excellent flowability and reduced static. It is minimally hygroscopic, resisting moisture absorption and providing optimal stability.

Piroxicam is a member of the oxicam group of nonsteroidal anti-inflammatory drugs (NSAIDs), and is indicated for treatment of acute or chronic signs and symptoms of osteoarthritis and rheumatoid arthritis (Karatas *et al*., 2005). According to the Biopharmaceutic Drug Classification System (BCS) proposed by Amidon *et al.* (1995), piroxicam is a class II drug, characterized by low solubility–high permeability. Over the years, several techniques have been used to improve the oral bioavailability of piroxicam by accelerating its dissolution rate in biological fluids at physiological pH (Yuksel *et al*., 2003).

### Methodology:

**Materials:** Piroxicam (lot number C153613) was obtained from PCCA (Houston, TX, USA). PCCA Formula #10825 (piroxicam + LoxOral) and PCCA Formula #6984 (piroxicam + MCC) were also supplied by the same company.

**Methods:** Dissolution studies of the capsule dosage form containing piroxicam were performed using a USP Apparatus 1 (rotating basket method) (Distek Symphony 7100, North Brunswick, NJ), according to the USP monograph of the drug (US Pharmacopeia, 2000). The test was conducted on 12 capsules (6 capsules of LoxOral and 6 capsules of MCC). An accurately weighed amount of piroxicam (3.5 mg) plus LoxOral or MCC excipients were placed in gelatin capsules. Each capsule was then placed in a dissolution media containing 900 mL of USP simulated gastric fluid (SGF) without pepsin (pH 1.2). The basket rotation speed was kept at 50 rpm and the dissolution medium maintained at 37°C. In all experiments, samples (5 mL) 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.

### Results and Discussion:

The data presented in Figure 1 clearly show the dissolution rate of the drug from LoxOral was significantly higher when compared to that of MCC. The *in vitro* dissolution studies showed that the dispersion systems containing piroxicam and LoxOral gave faster dissolution than the corresponding simple mixture using MCC. The USP specification for piroxicam dissolution has been stated as not less than 75% of the

labeled amount of the drug within 45 min in SGF without pepsin. Although both formulations complied with the USP dissolution specification, 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.

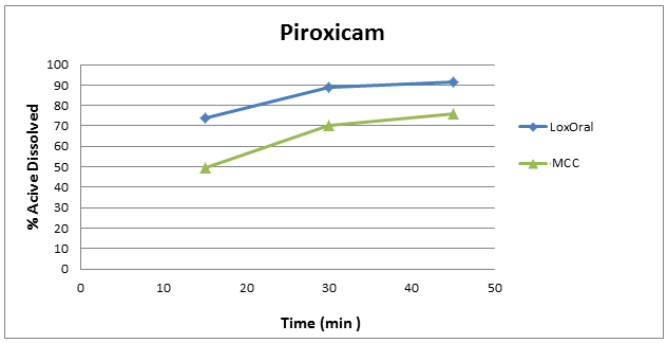


**Figure 1.** *Dissolution profiles of piroxicam from capsules containing different excipients, LoxOral and microcrystalline cellulose (MCC).*

## Conclusions:

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. LoxOral-based formulations have proven to be a most promising delivery system for oral bioavailability enhancement of BCS Class II drugs such as piroxicam.

## Financial Disclosure:


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