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Mechanical Influences During Dissolution Testing in a Novel Peristaltic Movement Simulating Stirring Device

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Mechanical stress caused by gastrointestinal motility might have a great impact on drug release from oral dosage forms. In our experiments different mechanical influences on the tablet during dissolution experiments were tested using extended release tablets containing diclofenac. Dissolution experiments were performed on the flow-through apparatus, developed on Faculty of Pharmacy, University of Ljubljana [1]. The novel peristaltic movement simulating stirring device contains a working vessel with a certain amount of small glass beads that are stirred by a magnetic stirrer. Tablets were kept in simulated gastric fluid (pH 1.2) for 2 hours and in simulated intestinal fluid (pH 6.8) afterwards. The intensity of mechanical stress on the tablet was modified by varying the amount of glass beads, stirring speed, and by using different barriers in the working beaker in a different position for 5 or 20 minutes.

Our experiments showed that mechanical stress induced by increasing stirring rate or decreasing the amount of glass beads resulted in increased diclofenac release. The insertion of different types of barriers into the working vessel increased the release rate, however, some crushing of tablets appeared. Thus, no subsequent decrease of release was observed when the barrier was removed. Namely, such dissolution kinetics was desired as we wanted to develop a dissolution test to predict double peaks in plasma profiles after oral administration of diclofenac extended release tablets. It seems that only squeezing the tablet and not other types of mechanical influences, simulates well *in vivo* situation [2]. Additionally, tablets were more sensitive to mechanical stress in intestinal than in gastric medium which is a consequence of different diclofenac solubility in both media. Thus, greater mechanical sensitivity of the tablet might also be expected *in vivo* when passing ileo-cecal sphincter than in pylorus. However, it is questionable if this influence could be observed *in vivo* as a large amount of drug has already been released when tablet reaches the end of ileum.

[1] Bogataj M, Cof G, Mrhar A. Peristaltic movement simulating stirring device for dissolution testing. PCT, WO 2010/014046 A1 (2010).

[2] Garbacz G, Wedemeyer R, Nagel S, Giessmann T, Mönnikes H, Wilson CG, Siegmund W, Weitschies W. Irregular absorption profiles observed from diclofenac extended release tablets can be predicted using a dissolution test apparatus that mimics in vivo physical stresses. Eur J Pharm Biopharm. 2008; 70: 421–428. doi:10.1016/j.ejpb.2008.05.029