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Dissolution properties of controlled-release matrix tablets containing pelubiprofen

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Pelubiprofen (PLB) is a propionic acid derivative with analgesic and anti-inflammatory properties and is widely used in the treatment of inflammatory diseases [1]. Because of the short half-life of PLB and its active metabolite (trans-OH form), it needs to be taken three times a day. Therefore, a controlled release formulation would benefit patients by elongating the dosing interval. Controlled release delivery systems can be classified as three categories: matrix, reservoir and osmotic systems. Among these systems, the matrix system has many advantages such as effectiveness, wide range of drug loading and the utilization of conventional manufacturing equipment [2]. In this study we employed the matrix system as controlled-release system to develop PLB-controlled release matrix tablets (CRT) to improving patient adherence and efficacy.

CRT were prepared by wet granulation method. PLB, lactose monolydrate and HPC(hydroxypropyl cellulose) L was mixed and granulated through wet-granulation with a high speed mixer. The wet granules were dried at 55°C ± 5°C for 2 hours and the dried granules were blended with various controlled-release agents (i.e. hypromellose 60SH-4000, hypromellose 60SH-10000, HPC HXF, Eudragit® RS PO, Kollidon® SR). The mixtures was blended with magnesium stearate and compressed. The formulations C1-C5 were prepared by 15 w/w % of controlled-release agents and the formulations P1-P3 containing 15, 20 and 25 w/w % of Kollidon® SR were also prepared. All of these formulations included 45 mg of PLB. The *in-vitro* dissolution studies of C1-C5 were carried out in FaSSIF and FeSSIF medium and dissolution studies of P1-P3 were performed at pH 6.8 buffer solution.

As shown in Fig. 1a, HPMC 60SH-10000 exerted the highest drug retarding effects on PLB,

and followed by HPMC 60SH-4000, HPC, Eudragit® RS PO, Kollidon® SR during 2 hours in FaSSIF. On the other hand, formulation C1-C4 showed no retarding effects in FeSSIF with the exception of C5 (Fig. 1b). These results show that as a controlled-release agent, Kollidon® SR would be less affected by environmental conditions such as ion concentration. Whereas in pH 6.8 buffer solution, formulations containing 15, 20 % Kollidon® SR released more than 90 % of drug in 3 hours and 6 hours, respectively (Fig. 1c). 25 % Kollidon® SR CRT released about 80 % of drug in 6 hours. 15-25 % Kollidon® SR CRT showed no significant swelling and maintained geometric shape of tablets until the end of the dissolution test.

Kollidon® SR had been selected for PLB-CRT because it would be less affected by environmental conditions. 15 % to 25 % Kollidon® SR containing CRT form stable matrix during dissolution. In conclusion, PLB- Kollidon® SR containing CRT could be applicable for development of a b.i.d. formulation.

Keywords: Pelubiprofen; Controlled-release matrix tablets; Kollidon® SR; Dissolution

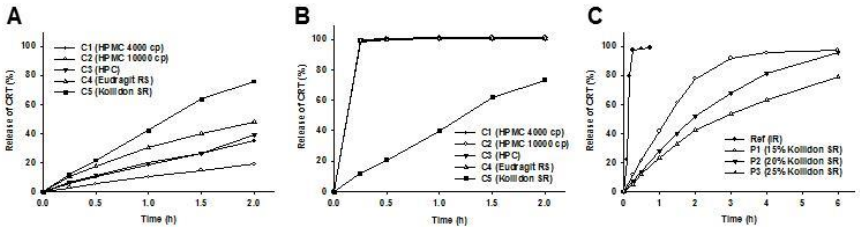

Fig. 1. Dissolution profiles of PLB in various CRTs at FaSSIF (A), FeSSIF (B) and pH 6.8 (C).

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