

as P-gp (Song *et al.* 2004). Nevertheless, drug delivery in this study is independent of gastric emptying because there is no significant difference in  $T_{max}$  between PRN alone and PRN with 200 mg/kg of GlcN was observed (Gainsborough *et al.* 1993; Shindo *et al.* 2008).  $pK_a$  and pH have a major effect on drug permeability and solubility as well as on the rate and extent of oral drug absorption (Palm *et al.* 1999; Ungell *et al.* 1998). GlcN is a basic cation with  $pK_a$  of 7.75 (Hofer and Kunemund 1985), and PRN is also a basic drug with  $pK_a$  of 9.4 (Salman *et al.* 2010). According to the pH partition theory, absorption of oral drugs takes place mainly by a passive diffusion of the un-ionized form of the drug molecule through the lipophilic intestinal membrane (Palm *et al.* 1999; Ungell *et al.* 1998). In an empty stomach, where the pH is low (pH 2-3), only a small fraction of the weak bases such as PRN or GlcN would be taken up, as the unionized fraction would be small. Therefore, PRN given on an empty stomach would be absorbed mainly after passage into the slightly alkaline duodenum where pH is more than 7 in the un-ionized form due to higher un-ionized fraction amount (Hurst *et al.* 2007; Liedholm and Melander 1990; Palm *et al.* 1999). Moreover, GlcN has been shown to be absorbed throughout the gut, where the highest absorption occurs in the small intestine, mainly the duodenum (Ibrahim *et al.* 2012). Although it seems that pH is an important factor for PRN BA. However, such factor was not studied in the current research (Amidon *et al.* 1995).

As for PRN site of absorption in the intestine, SPIP technique in rats has been used to study PRN permeability in the intestine. This model has been well elucidated for its correlation with human absorption. PRN absorption occurs along the whole