

## E-3

## Influence of Co-administered Antibiotics on Pharmacokinetic Fate of Paeoniflorin from Shaoyao-Gancao-tang

○Ju-Xiu He<sup>1)</sup>, Teruaki Akao<sup>2)</sup>, Tadato Tani<sup>1)</sup>

Institute of Natural Medicine, Toyama Medical and Pharmaceutical University<sup>1)</sup>,

Faculty of Pharmaceutical Sciences, Toyama Medical and Pharmaceutical University<sup>2)</sup>

**[Purpose]** Shaoyao-Gancao-tang (SGT, Shakuyaku-Kanzo-to in Japanese) composed of Paeoniae and Glycyrrhizae Radix may be used for ulcer together with some antibiotics, e.g. amoxicillin and metronidazole (AM). We have reported that AM significantly reduced the pharmacokinetic fate of glycyrrhizin from the co-administered SGT.<sup>1)</sup> The present study was designed to examine the influences of the antibiotics on the pharmacokinetic fates of paeoniflorin (PF) and paeonimetabolin I (PM-I), a metabolite derived from PF by intestinal bacteria in rats.

**[Method]** SGT was administered once together with AM or ofloxacin (OFLX) (*p.o.*, 10 times of human dose) to rats in single and multiple regimens (with three-day pre-administration of the antibiotics). Blood samples were collected at time intervals. Plasma PF and PM-I concentrations were determined by respective EIA methods. The variance of *AUC* were estimated by Bailer's method. PF-metabolizing activity of the intestinal bacteria in rat feces was determined by a newly developed HPLC method.

**[Results and Discussion]** 1. Both of AM and OFLX significantly reduced the *AUC* of PM-I, while significantly increased that of PF from the co-administered SGT in both single and multiple regimens. 2. The PF-metabolizing activity in rat feces was significantly decreased in the multiple regimens of both AM and OFLX. This evidence indicated that the reduction of *AUC* of PM-I in the co-administered groups was due to the effects of the co-administered antibiotics on the intestinal bacteria producing PF-metabolizing enzymes. The present study suggests that it is necessary to consider the influences of the antibiotics on SGT when they are to be used together.

1) He J-X., et al., *Biol. Pharm. Bull.*, **24**, 1395-1399, 2001.