PHARMACOKINETICS OF PAEONIFLORIN IS INFLUENCED BY CO-ADMINISTRATION OF SINOMENINE IN UNRESTRAINED CONSCIOUS RATS

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Paeoniflorin, a characteristic monoterpene glucoside present in the root of *Paeonia lactiflora* Pall., is an effective immunosuppressant in treating rheumatoid arthritis. However, the clinical use of paeoniflorin has been greatly impeded by its poor bioavailability owing to the bacterial transformation in gastrointestinal tract (Takeda *et al.*, 1997). Sinomenine, deriving from the stem of *Sinomenium acutum*, is another widely used antiarthritic agent (Liu *et al.*, 1996).

The aim of this study is to investigate the influences of co-administrated sinomenine hydrochloride on the pharmacokinetics of paeoniflorin in rats to identify the possible interactions between paeoniflorin and sinomenine.

A single dose of paeoniflorin (150mg/kg) alone or with sinomenine hydrochloride (90mg/kg) was administered by gastric gavage to unrestrained conscious male Sprague-Dawley rats (n=5, 250–300g). Blood samples (0.2ml/time point) were collected via a jugular vein catheter before dosing and from 10min to 12 hours post-dosing. A high-performance liquid-chromatographic assay calibrated with pentoxifylline as the internal standard was employed to determine the plasma concentrations of paeoniflorin. Non-compartmental pharmacokinetic parameters and profiles were derived and constructed by using the software *PK Solutions 2.0* (www.summitpk.com). The pharmacokinetic parameters were compared with unpaired Student *t*-test (P<0.05). All procedures involving animals and their care were approved by the Committee on the Use of Human & Animal Subjects in Teaching and Research of Hong Kong Baptist University.

In comparison with paeoniflorin given alone, the concomitant administration with sinomenine hydrochloride (90mg/kg) could elevate the plasma concentration, delay the peak time and consequently increase the bioavailability of paeoniflorin in rats. Mechanism of these changes is under investigation.