31C-03

Determination of Paeoniflorin and Paeonimetabolin I in Rat Plasma after Oral Administration of Toki-Shakuyaku-San (TS) and Shakuyaku-Kanzo-To (SK)

Research Institute for Wakan-Yaku, Toyama Medical and Pharmaceutical University, and Tsumura Central Research Laboratory, Tsumura & Co.*

○Meselhy R. Meselhy, Ola A. Heikal, Teruaki Akao, Masao Hattori, Hiromasa Ono*and Chiharu Sadakane*

【Purpose】 The present study was designed to investigate plasma concentrations of paeoniflorin (PF) and paeonimetabolin I (PM-I) after *p.o.* administration of two different Kampo prescriptions containing paeony roots, relative to that obtained after *p.o.* and/or *i.v.* administration of PF and/or PM-I, to emphasize the role of PM-I in the therapeutic effect of PF and Kampo prescriptions containing paeony roots.

【Method】 Doses of 100 and 500 mg/kg of the Kampo prescriptions TS and SK were orally administered to male Crj:CD (SD) rats. Similarly, PF (at doses of 0.5 and 5mg/kg) and PM-I (in equal molar doses) were administered. Blood samples were obtained at time intervals after administration. Concentrations of PF and PM-I in rat plasma were determined by the respective EIA methods.

【Results and Conclusion】 Following *p.o.* administration of PF, the maximal plasma concentrations (C_{max}) of PF were 9.9 and 20.3 (with *AUC* of 300 and 1174 ng•min/ml) and those of PM-I were 16.5 and 101.7 ng•min/ml at 0.5 and 5 mg/kg, respectively. The times to C_{max} (t_{max}) of PF were 11.6 and 13.3, and those of PM-I were 60 and 80 min, respectively. When PM-I was given orally at the same doses, C_{max} of 102.2 and 285 ng/ml were reached at t_{max} 6.2 and 7.5 min. The *AUC* values of PM-I after *p.o.* administration of PF (1873 and 12358 ng•min/ml) were comparable with those after *p.o.* and *i.v.* administration of PM-I (4145.6 and 14182.1, and 5614 and 13176 ng•min/ml, respectively) indicated that most of PF was transformed to PM-I by intestinal bacteria and PM-I was rapidly absorbed from the intestine. Following *p.o.* administration of TS, the C_{max} of PF (146.3 and 165.1 ng/ml) were reached at 60 and *ca.* 45 min (with *AUC* of 14305 and 19385 ng•min/ml), and those of PM-I were 184 and 400 ng/ml at 120 and 180 min (with *AUC* of 98497 and 182188 ng•min/ml) at 100 and 500 mg/kg, respectively. When SK was given orally, PF and PM-I were detected at considerable concentrations (C_{max} of 100.1 and 144 ng/ml, and 141.6 and 726.5 ng/ml, respectively. Relative to TS, the C_{max} of PF and PM-I were reached both at 5 min, and at 360 and 480 min, respectively, and retained in plasma for a longer period of time. From these observations, it seems likely that administration of TS or SK potentially affects absorption from GIT, plasma concentrations and elimination of both PF and PM-I.