

**Comparative pharmacokinetic study of three major bioactive components in normal and different course of liver-stagnation and spleen-deficiency syndrome depressive rats after intragastric administration of Zhi-Zi-Hou-Po decoction**

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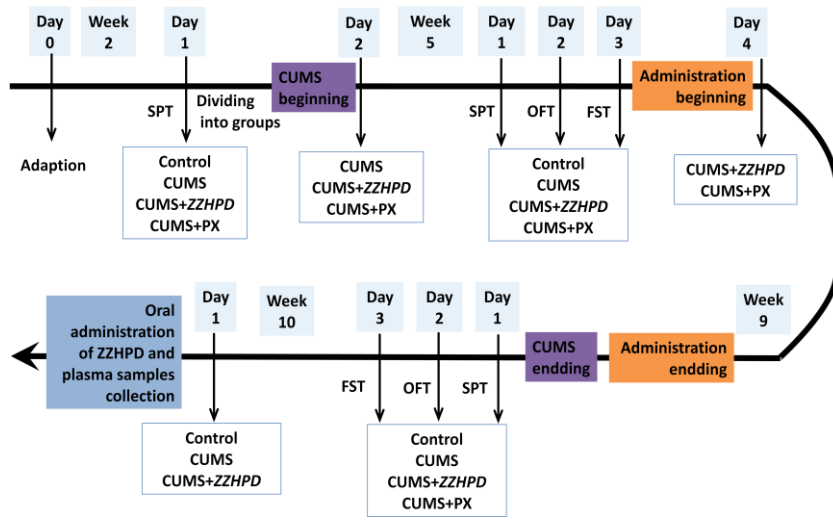
## Supplemental File

### Text S1: The conversion rule of oral dose of ZZHPD and PX.

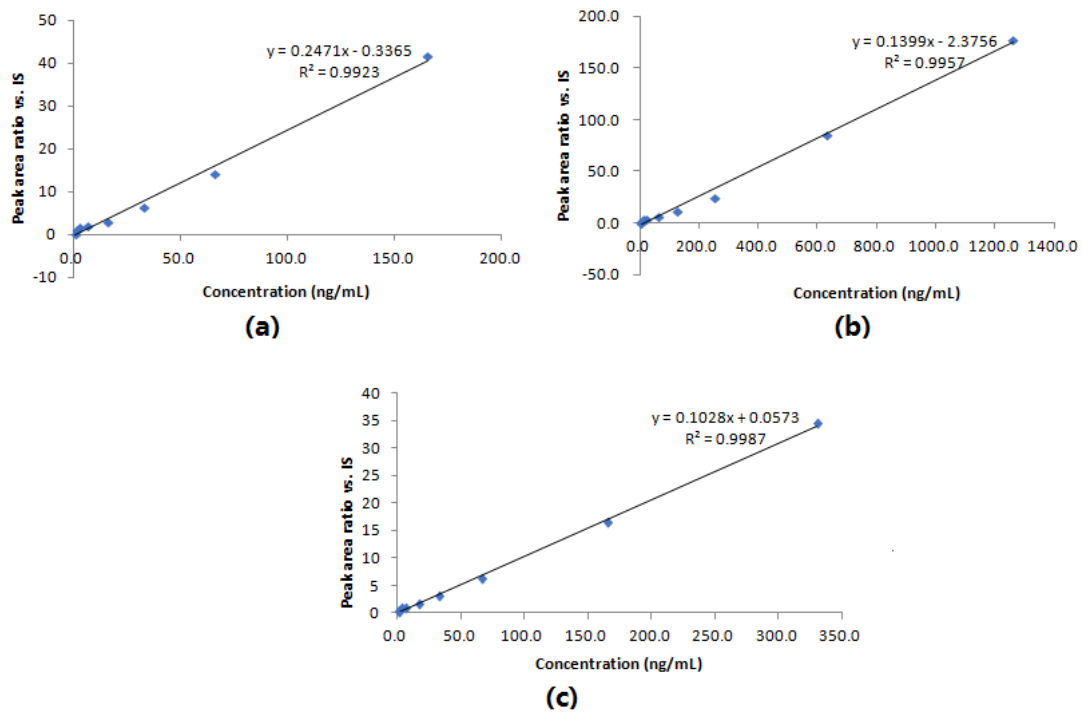
As recorded in *Shang-Han-Lun (Treatise on Febrile Caused by Cold)*, the oral dose of ZZHPD is 81.4 g/d (ZZ 9 g, HP 62.4 g and ZS 10 g) for a human being. In consideration of the average weight of human is 60 kg, the oral dose is 1.36 g/kg/d. After multiply by the reduction coefficient, which is 6.3, between human and rat, the oral dose for rat is 8.5 g/kg/d.

The recommended oral dose of paroxetine for human is 20 mg/d, then the oral dose for rat is 2.1 mg/kg/d according to the same conversion way.

### Animals experimental design



**FIGURE S1.** The animal experimental design of this study (10 weeks).



**FIGURE S2:** The standard curves of narirutin (a), naringin (b) and honokiol (c) ( $r > 0.99$ ).

**TABLE S1:** The intra-day and Inter-day precision, accuracy, extraction recovery and matrix effects of three analytes at low, middle and high concentration.

Analytes	Concentration (ng/mL)	Intra-day precision RSD (%)	Inter-day precision RSD (%)	Accuracy RE (%)	Extraction recovery (%, mean $\pm$ SD)	Matrix effects (%, mean $\pm$ SD)
Narirutin	2.5	0.45	1.31	3.45	92.25 $\pm$ 4.21	94.87 $\pm$ 2.17
	20.0	0.96	0.75	-4.16	93.56 $\pm$ 1.79	95.67 $\pm$ 3.01
	265.0	1.39	2.11	6.16	98.23 $\pm$ 5.36	95.06 $\pm$ 1.29
Naringin	9.5	0.59	0.73	7.35	89.62 $\pm$ 2.76	89.05 $\pm$ 2.85
	76.0	0.28	0.33	-5.21	90.72 $\pm$ 3.75	93.05 $\pm$ 0.87
	1011.2	1.57	2.01	7.91	99.69 $\pm$ 5.56	97.28 $\pm$ 0.96
Honokiol	2.5	2.39	2.14	4.83	91.92 $\pm$ 1.03	93.72 $\pm$ 0.56
	20.0	1.56	1.74	8.14	95.12 $\pm$ 2.06	93.52 $\pm$ 3.15
	264.0	2.17	1.78	-7.28	104.71 $\pm$ 3.43	89.51 $\pm$ 3.25

**TABLE S2:** The stability of three analytes at low, middle and high concentration.

Analytes	Concentration (ng/mL)	Stability at room temperature for 4 h		Stability in autosampler for 12 h		Stability of repeated freeze-thaw for three times		Stability at -20°C for 14 days	
		RE (%)	RSD (%)	RE (%)	RSD (%)	RE (%)	RSD (%)	RE (%)	RSD (%)
Narirutin	2.5	5.98	3.71	8.10	2.50	9.38	4.82	-6.11	5.92
	20.0	7.81	2.53	10.03	2.97	-8.32	3.72	9.32	6.21
	265.0	-5.32	2.11	-4.02	1.18	-3.21	1.07	1.05	4.02
Naringin	9.5	6.01	4.78	-5.22	1.57	8.93	4.19	5.32	7.29
	76.0	-4.01	1.76	5.91	3.50	4.73	2.89	-3.02	5.83
	1011.2	6.38	0.92	4.39	0.31	5.22	0.31	4.61	3.49
Honokiol	2.5	9.96	4.21	-3.29	0.90	3.02	3.78	7.65	8.46
	20.0	-7.53	2.41	4.41	0.04	5.92	2.15	-3.87	5.15
	264.0	3.29	1.55	-2.13	1.90	1.01	2.37	3.69	2.44