

Supplementary materials

Table S1. Summary of macroscopic findings of acute oral toxicity.

Dosage group (mg/kg)			0	500	1000	2000
Male	Abnormal lesions	Number examined	5	5	5	5
		Number unremarkable	5	5	5	5
	Abdominal cavity	Number examined	5	5	5	5
		Number unremarkable	5	5	5	5
	Thoracic cavity	Number examined	5	5	5	5
		Number unremarkable	5	5	5	5
Female	Abnormal lesions	Number examined	5	5	5	5
		Number unremarkable	5	5	5	5
	Abdominal cavity	Number examined	5	5	5	5
		Number unremarkable	5	5	5	5
	Thoracic cavity	Number examined	5	5	5	5
		Number unremarkable	5	5	5	5

Table S2. The numbers of mortality of acute oral toxicity.

Dosage group (mg/kg)		Treatment phase				Final Mortality *
		≤1 day	≤3 days	≤7 days	≤15 days	
Male	0	0	0	0	0	0/5
	500	0	0	0	0	0/5
	1000	0	0	0	0	0/5
	2000	0	0	0	0	0/5
Female	0	0	0	0	0	0/5
	500	0	0	0	0	0/5
	1000	0	0	0	0	0/5
	2000	0	0	0	0	0/5

* Number of animals with dead animals / Total animal number

Table S3. The numbers of mortality of chronic oral toxicity.

Dosage group (mg·kg ⁻¹ ·d ⁻¹)		Treatment phase				Final Mortality *
		≤1 week	≤4 week	≤8 week	≤13 week	
Male	0	0	0	0	0	0/10
	500	0	0	0	0	0/10
	1000	0	0	0	0	0/10
	2000	0	0	0	0	0/10
Female	0	0	0	0	0	0/10
	500	0	0	0	0	0/10
	1000	0	0	0	0	0/10
	2000	0	0	0	0	0/10

* Number of animals with dead animals / Total animal number

Table S4. Effects of chronic oral administration of Yeosinsan extract in relative organ weight (percent of body weight).

Dosage group (mg·kg ⁻¹ ·d ⁻¹)		0	500	1000	2000
Male	TBW (g)	546.1 ± 79.76	543.6 ± 42.11	551.0 ± 49.88	565.0 ± 42.3
	(ADRG) Adrenal glands	0.0114 ± 0.00084	0.0117 ± 0.00139	0.0118 ± 0.00193	0.0114 ± 0.00116
	(BRA) Brain	0.4009 ± 0.03915	0.4100 ± 0.04120	0.3971 ± 0.03391	0.3935 ± 0.02886
	(HT) Heart	0.3132 ± 0.01592	0.2920 ± 0.01696	0.2986 ± 0.01851	0.2978 ± 0.01721
	(KID) Kidneys	0.6697 ± 0.06812	0.7311 ± 0.07892	0.7378 ± 0.05424	0.7574 ± 0.04892 *
	(LIV) Liver	2.8097 ± 0.29011	2.9097 ± 0.23430	2.8389 ± 0.16781	2.9352 ± 0.12050
	(PITG) Pituitary glands	0.0026 ± 0.00034	0.0027 ± 0.00047	0.0025 ± 0.00043	0.0023 ± 0.00033
	(SPL) Spleen	0.1672 ± 0.02193	0.1660 ± 0.01391	0.1673 ± 0.01904	0.1881 ± 0.03440
	(TES) Testes	0.6530 ± 0.09203	0.6483 ± 0.05873	0.6410 ± 0.05069	0.5896 ± 0.12706
	(THY) Thymus	0.0878 ± 0.01699	0.0815 ± 0.01821	0.0814 ± 0.01121	0.0811 ± 0.01831
	(EPI) Epididymis	0.2974 ± 0.03916	0.2972 ± 0.02440	0.2775 ± 0.02408	0.2578 ± 0.03942 *
	(LUN) Lung	0.3179 ± 0.03295	0.3272 ± 0.02489	0.3136 ± 0.03368	0.3258 ± 0.01546
	(THPA) Thyroid and parathyroid glands	0.0045 ± 0.00111	0.0051 ± 0.00110	0.0042 ± 0.00050	0.0044 ± 0.00080
	(SVCG) Seminal vesicles with coagulating gland	0.3658 ± 0.07572	0.3451 ± 0.06769	0.3309 ± 0.06510	0.3037 ± 0.06724
	(PROS) Prostate	0.1130 ± 0.02919	0.1129 ± 0.02694	0.1054 ± 0.02930	0.0114 ± 0.03132
Fe-male	TBW (g)	309.4 ± 26.33	300.5 ± 20.04	292.2 ± 19.22	290.4 ± 29.27
	(ADRG) Adrenal glands	0.0262 ± 0.00225	0.0274 ± 0.00481	0.0268 ± 0.00285	0.0268 ± 0.00589
	(BRA) Brain	0.6489 ± 0.04490	0.6745 ± 0.05233	0.6831 ± 0.05653	0.6836 ± 0.06319
	(HT) Heart	0.3384 ± 0.02245	0.3517 ± 0.03004	0.3337 ± 0.02633	0.3336 ± 0.03162
	(KID) Kidneys	0.7515 ± 0.05716	0.7694 ± 0.08297	0.7714 ± 0.06758	0.7933 ± 0.08546
	(LIV) Liver	2.8163 ± 0.18902	2.8114 ± 0.20877	2.8737 ± 0.18429	2.9696 ± 0.20901
	(OVA) Ovaries	0.0317 ± 0.00769	0.0315 ± 0.00434	0.0286 ± 0.00420	0.0319 ± 0.00620

(PITG) Pituitary glands	0.0069 ±	0.0059 ±	0.0066 ±	0.0068 ±
	0.00120	0.00113	0.00120	0.00115
(SPL) Spleen	0.1870 ±	0.2032 ±	0.2243 ±	0.2279 ±
	0.02320	0.03088	0.01930 **	0.03152 **
(THY) Thymus	0.1112 ±	0.1092 ±	0.1132 ±	0.1178 ±
	0.01727	0.01902	0.01450	0.02298
(SALG) Salivary glands	0.1508 ±	0.1530 ±	0.1541 ±	0.1630 ±
	0.01884	0.01766	0.01553	0.01447
(LUN) Lung	0.4375 ±	0.4504 ±	0.4554 ±	0.4640 ±
	0.05100	0.04816	0.02285	0.03459
(THPA) Thyroid and parathyroid glands	0.0061 ±	0.0067 ±	0.0064 ±	0.0064 ±
	0.00104	0.00124	0.00105	0.00099
(UTEC) Uterus/cervix	0.2371 ±	0.3017 ±	0.2826 ±	0.2587 ±
	0.06294	0.15211	0.11341	0.12401

Data were expressed as Mean ± SD, n = 10 animals per group. * P<0.05, ** P<0.01 according to Dunnett's LSD test.

Table S5. Summary of ophthalmology of chronic oral toxicity.

Dosage group (mg·kg ⁻¹ ·d ⁻¹)			0	500	1000	2000
Male	No abnormalities detected	Number of animals examined	10	10	10	10
		Number of animals not affected	10	10	10	10
		Mean number of animal days with no clinical sign	1	1	1	1
Fe-male	No abnormalities detected	Number of animals examined	10	10	10	10
		Number of animals not affected	10	10	10	10
		Mean number of animal days with no clinical sign	1	1	1	1

Table S6. Effects of chronic oral administration of Yeosinsan extract in urinalysis.

Dosage group (mg·kg ⁻¹ ·d ⁻¹)		0	500	1000	2000
Male	VOL (mL)	21.2 ± 7.90	15.6 ± 4.40	19.2 ± 8.95	27.0 ± 10.76
	SG	1.011 ± 0.0032	1.013 ± 0.0026	1.011 ± 0.0044	1.012 ± 0.0041
	pH	7.0 ± 0.00	6.9 ± 0.21	6.9 ± 0.21	6.9 ± 0.24
	U-K (mmol/L)	100.21 ± 32.227	118.26 ± 29.950	94.99 ± 28.221	93.26 ± 38.497
	U-Cl	33.9 ± 10.52	34.6 ± 9.41	32.3 ± 6.55	32.0 ± 11.33
	U-Na	33.9 ± 16.24	28.1 ± 9.33	30.1 ± 10.02	29.4 ± 17.37
Female	VOL (mL)	12.6 ± 4.33	14.1 ± 5.55	12.4 ± 3.37	16.0 ± 8.00
	SG	1.015 ± 0.0033	1.015 ± 0.0064	1.016 ± 0.0037	1.014 ± 0.0041
	pH	6.7 ± 0.35	6.8 ± 0.63	6.6 ± 0.28	6.8 ± 0.26
	U-K (mmol/L)	106.69 ± 25.914	135.38 ± 119.796	104.33 ± 25.166	85.27 ± 40.315
	U-Cl	43.4 ± 10.07	66.4 ± 66.58	44.7 ± 12.73	36.1 ± 13.89
	U-Na	42.2 ± 14.84	64.8 ± 60.47	41.2 ± 21.93	27.0 ± 13.88

Data were expressed as Mean ± SD, n = 10 animals per group.