

Acute and Subchronic Toxicity of Tri-sa-maw Recipe in Rats

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Background: Tri-sa-maw recipe is a botanical preparation comprised of equal proportions of the three herbal fruits, namely *Terminalia chebula* Retz., *Terminalia sp.* and *Terminalia bellirica* Roxb. This recipe is used for antipyretic, expectorant, periodic maintenance, and relieving stomach tightness(1). However, little toxicological information is available regarding its safety.

Objective: To evaluate the acute and subchronic toxicities of Tri-sa-maw water extract in rats.

Methods: In acute toxicity study(2), Tri-sa-maw water extract was administered by oral gavage to Sprague-Dawley (SD) rats (10 males, 10 females) at single dose of 5,000 mg/kg body weight while the control group received water vehicle. In subchronic toxicity study(2), the extract was administered orally at doses of 600, 1,200 and 2,400 mg/kg/day for 90 days to male and female SD rats respectively. General behavior, adverse effects and mortality were determined throughout the experimental period. Hematological and blood chemistry parameters, relative organ weights and histopathology were evaluated at the end of the experiment. Statistical significance was determined by one-way analysis of variance(ANOVA) and Dunnett's test. *P* values less than 0.05 were considered significant

Results: There were no mortality and signs of toxicity in acute and subchronic toxicity studies. In the single dose acute toxicity and repeated dose 90 days subchronic toxicity studies, there were no significant difference in body and organ weights, blood chemistry, hematological parameters, necropsy and histopathology between control and treatment groups. The hematological values reflect any toxic effects on function of bone marrow. The hematological values(Table 1,2) of female and male treatment rat were not significantly different from those of the control.

Table 1 :Effect of Tri-sa-maw recipe extract on hematological values of female rats in subchronic toxicity study

Control	Tri-sa-maw recipe (mg/kg)			
	600	1200	2400	Satellite

Red blood cell (x10 ⁶ /μl)	7.23 ± 0.09	7.13 ± 0.07	7.24 ± 0.12	7.14 ± 0.06	6.81 ± 0.12
Hemoglobin (g/dl)	14.45 ± 0.12	14.16 ± 0.12	14.24 ± 0.20	14.10 ± 0.17	13.81 ± 0.19
Hematocrit (%)	41.40 ± 0.40	40.50 ± 0.45	41.20 ± 0.65	40.80 ± 0.33	39.70 ± 0.65
Mean corpuscular volume (fl)	57.27 ± 0.44	56.81 ± 0.18	56.90 ± 0.27	56.91 ± 0.26	58.37 ± 0.44
Mean corpuscular hemoglobin (pg)	20.01 ± 0.17	19.86 ± 0.08	19.67 ± 0.09	19.86 ± 0.10	20.30 ± 0.14
Mean corpuscular hemoglobin concentration (g/dl)	34.91 ± 0.18	34.95 ± 0.16	34.58 ± 0.17	34.65 ± 0.08	34.76 ± 0.19
Platelet (x10 ⁵ /μl)	6.41 ± 0.16	6.55 ± 0.16	6.09 ± 0.33	5.62 ± 0.45	6.61 ± 0.18

Values are expressed as mean ± S.E.M., n = 10

*Significantly different from control, *P*<0.05.

Table 2: Effect of Tri-sa-maw recipe extract on hematological values of male rats in subchronic toxicity study

	Control	Tri-sa-maw recipe (mg/kg)			
		600	1200	2400	Satellite
Red blood cell (x10 ⁶ /μl)	7.79 ± 0.13	7.58 ± 0.10	7.59 ± 0.07	7.61 ± 0.08	7.72 ± 0.12
Hemoglobin (g/dl)	15.13 ± 0.20	14.84 ± 0.14	14.74 ± 0.14	14.77 ± 0.17	15.03 ± 0.13
Hematocrit (%)	43.00 ± 0.71	41.90 ± 0.55	41.70 ± 0.45	41.70 ± 0.30	43.10 ± 0.46
Mean corpuscular volume (fl)	54.98 ± 0.24	55.17 ± 0.19	55.90 ± 1.05	55.49 ± 0.42	55.74 ± 0.42
Mean corpuscular hemoglobin (pg)	19.44 ± 0.17	19.59 ± 0.12	19.43 ± 0.11	19.42 ± 0.16	19.49 ± 0.22
Mean corpuscular hemoglobin concentration (g/dl)	35.35 ± 0.27	35.50 ± 0.20	35.24 ± 0.19	35.00 ± 0.33	35.00 ± 0.22

concentration (g/dl)

Platelet ($\times 10^5/\mu\text{l}$)	6.78	\pm	7.59	\pm	7.15 \pm	7.00	\pm	7.72 \pm 0.72
	0.44		0.25		0.19	0.35		

Values are expressed as mean \pm S.E.M., n = 10

*Significantly different from control, $P < 0.05$.

Conclusion: Tri-sa-maw recipe extract did not produce both acute and subchronic oral toxicities in either female or male rats. These data confirm that this Tri-sa-maw recipe is safe for the experimental animals. Further study regarding toxicology of this extract should be carried out in non-rodent or human in order to increase the confidence in their safety for the development of pharmaceutical products in the future.

Keywords: Tri-sa-maw recipe, Acute toxicity, Subchronic toxicity

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- (2) World Health Organization (2000). General guidelines for methodologies on research and evaluation of traditional medicine. Switzerland.