

**Fasiglifam (TAK-875) Inhibits Hepatobiliary Transporters: A Possible Factor Contributing to Fasiglifam-induced Liver Injury**

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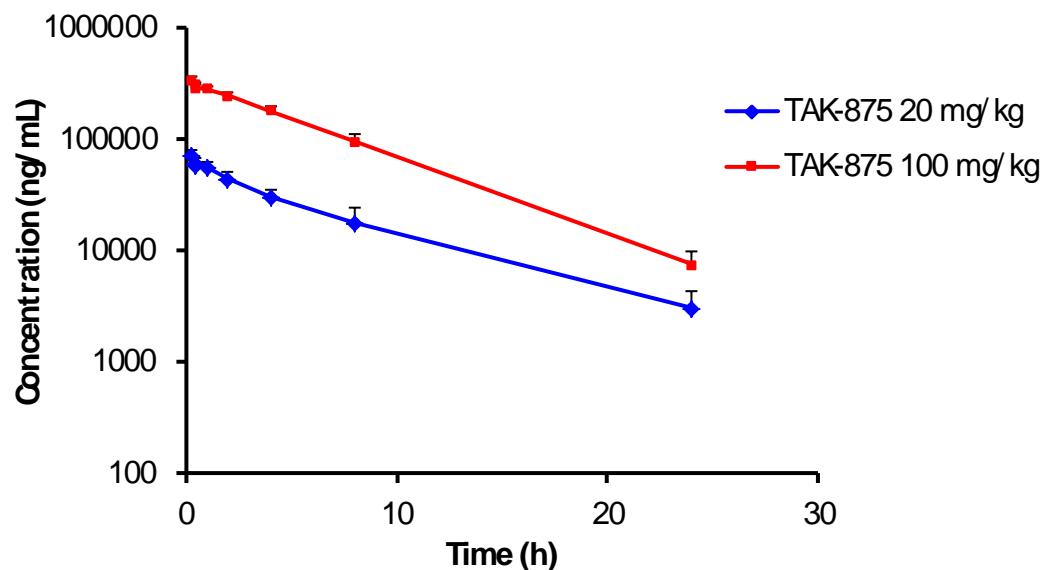
**Drug Metabolism and Disposition**

**Figure legends**

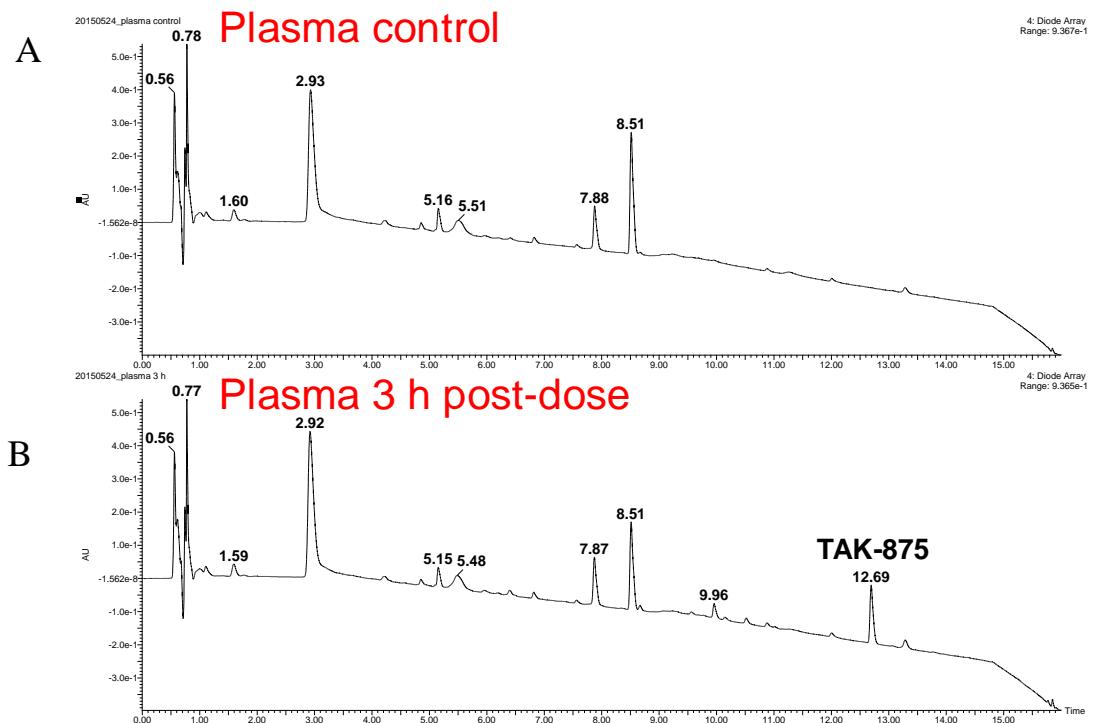
Supplemental Fig. 1. Time profiles of plasma concentration of TAK-875 after an intravenous dose of 20 or 100 mg/kg of TAK-875 to SD rats.

Supplemental Fig. 2. UPLC-UV chromatograms of pooled rat plasma 3 h after intravenous administration of 5 mg/kg TAK-875 (A) Control plasma; (B) Plasma at 3 h post-dose.

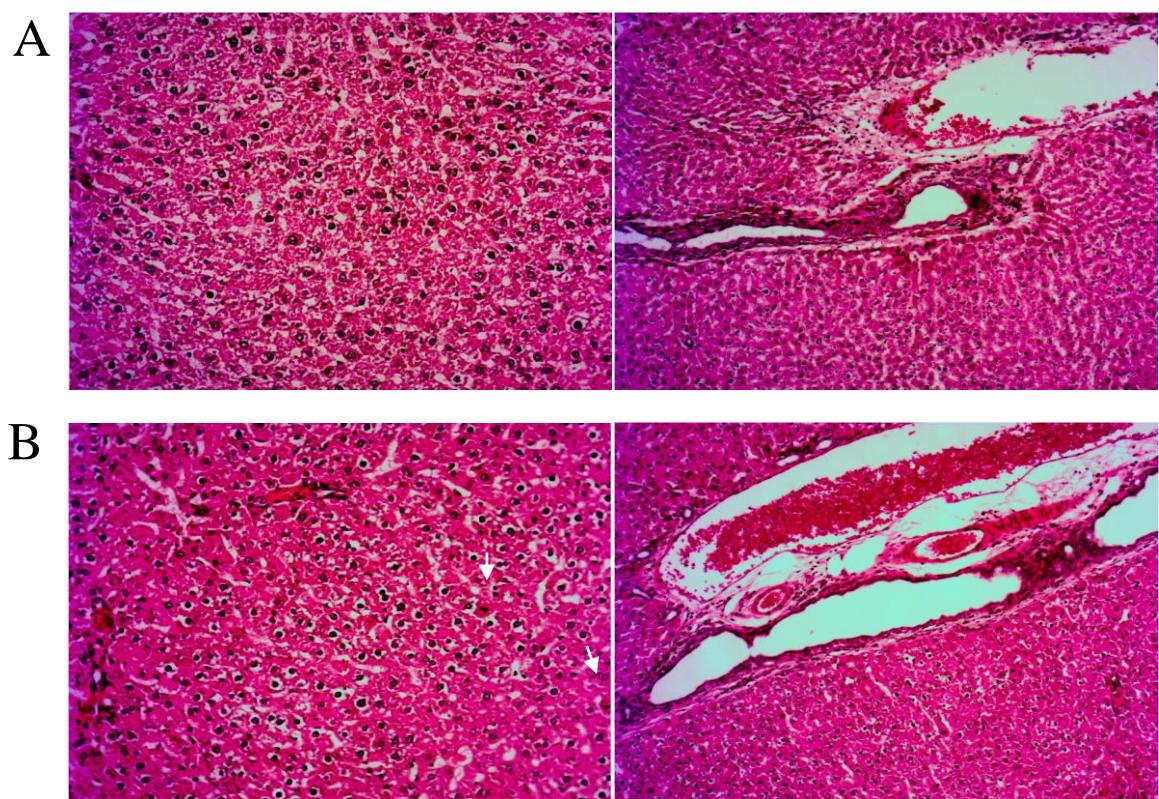
Supplemental Fig. 3. Effects of a single intravenous dose of TAK-875 (100 mg/kg) on the rats liver tissue at 24 h postdose. (A) Control group, (B) TAK-875 group.



**Supplemental Fig. 1**



Supplemental Fig. 2



**Supplemental Fig. 3**

Supplemental Table 1. Pharmacokinetic parameters of TAK-875 after an intravenous dose of 20 or 100 mg/kg of TAK-875 to SD rats. (Data are shown as the mean  $\pm$  SD)

TAK-875	T <sub>1/2</sub>	AUC <sub>0-t</sub>	AUC <sub>0-∞</sub>	V <sub>ss</sub>	CL	MRT	C <sub>0</sub>
	h	h*μg/mL	h*μg/mL	mL/kg	mL/h/kg	h	μg/mL
20 mg/kg	5.96 $\pm$ 0.66	413 $\pm$ 95	439 $\pm$ 107	371 $\pm$ 68	48.0 $\pm$ 12.3	7.89 $\pm$ 1.11	81.5 $\pm$ 11.4
100 mg/kg	4.32 $\pm$ 0.36	2094 $\pm$ 231	2142 $\pm$ 243	292 $\pm$ 19	47.2 $\pm$ 5.8	6.23 $\pm$ 0.50	385 $\pm$ 18