

Supplemental data for

Absorption, distribution, metabolism, and excretion of [¹⁴C]TPN729 after oral administration to rats

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Supplemental Table 1 AUC_{0-48h} of radioactivity in tissues and plasma of rats and their ratio to plasma following a single oral administration of [¹⁴C]TPN729 at 25 mg/kg (150 μCi/kg).

Tissue	Male (n=3)							Female (n=3)						
	Concentration (ng eq./g)				AUC _{0-48 h} (ng eq./g×h)	R	P	Concentration (ng eq./g)				AUC _{0-48 h} (ng eq./g×h)	R	P
	1 h	4 h	8 h	48 h				1 h	4 h	8 h	48 h			
Stomach	43978	15356	1819	583	193385	16.18	1.33%	213814	14754	6098	642	626271	43.81	0.30%
Small Intestine	76161	28461	1793	504	301478	25.23	0.66%	35507	20396	6241	468	289061	20.22	1.32%
Liver	54097	16211	3064	490	242142	20.26	0.91%	40202	23813	6018	633	308808	21.60	1.58%
Skin	4669	2782	656	180	37109	3.11	3.86%	3668	4476	948	125	46364	3.24	3.41%
Kidney	19617	7577	946	179	90155	7.54	0.91%	24939	15161	2941	151	170666	11.94	0.60%
Large Intestine	10588	11954	6186	299	205084	17.16	2.50%	11839	11235	15495	439	412661	28.87	2.83%
Pancreas	15443	4491	677	122	63920	5.35	0.79%	16805	10136	2571	99	127609	8.93	0.59%
Heart	6135	1998	471	144	32513	2.72	2.35%	15397	4035	1160	292	76262	5.34	1.89%
Lung	61735	15346	1778	157	219435	18.36	0.25%	64291	43789	5888	164	414655	29.01	0.26%
Spleen	22900	6447	1354	196	102071	8.54	0.86%	32072	22210	5004	154	255062	17.84	0.48%
Plasma	2831	797	121	42	11951	1.00	1.50%	1666	1208	263	48	14294	1.00	2.87%
Muscle	4687	1555	524	112	28592	2.39	2.39%	4866	3276	811	57	40191	2.81	1.17%
Blood	2050	684	130	60	10565	0.88	2.93%	1601	1047	271	78	14385	1.01	4.88%
Fat	3517	1844	620	757	42263	3.54	21.53%	2703	1903	611	109	27702	1.94	4.04%
Eye	12721	15455	12941	15972	683667	57.20	103.34%	18137	34334	30319	15702	1137503	79.58	45.73%
Brain	485	176	89	267	8886	0.74	55.16%	425	274	108	114	6476	0.45	26.91%
Bladder	14817	5404	878	87	69598	5.82	0.58%	7902	6822	1617	64	76539	5.35	0.81%
Adrenal gland	20592	7481	2502	485	132113	11.05	2.36%	20863	15660	3284	223	173242	12.12	1.07%
Testis	1588	1217	750	489	33714	2.82	30.77%	-	-	-	-	-	-	-
Ovary	-	-	-	-	-	-	-	10355	6457	1340	115	75078	5.25	1.11%
Womb	-	-	-	-	-	-	-	7705	7013	1269	128	70450	4.93	1.67%

AUC_{0-48h}, Area under the tissue concentration-time curve from time 0 to 48 h; R, The ratio of AUC_{0-48 h} in tissue to that in plasma. P, The ratio of concentration at 48 h to C_{max} in tissue; -, no sample collected.

Supplemental Table 2 Radioactivity distribution of TPN729 and metabolites in pooled plasma, urine, feces, and bile samples of rats.

ID	Pathway	Male					Female				
		Plasma		Urine 16.47% of Dose	Feces 76.52% of Dose	Bile 33.29% of Dose	Plasma		Urine 18.52% of Dose	Feces 72.75% of Dose	Bile 28.45% of Dose
		%(1 h)	%(4 h)	%Dose	%Dose	%Dose	%(1 h)	%(4 h)	%Dose	%Dose	%Dose
TPN729	Parent	11.46	13.01	1.79	4.04	1.32	19.65	9.94	1.64	6.34	0.81
M564-1	3[O]	-	-	-	-	-	-	-	-	16.87	-
M548-1	2[O]	-	-	0.33	6.22	1.36*	-	1.52	-	1.19	1.68*
M548-2	2[O]	-	1.94	0.48	7.77	2.58*	-	3.71	0.84	1.99	4.65*
M564-3	3[O]	-	-	-	2.67	-	-	-	-	3.46	-
M532-2	[O]	-	2.52	0.97	-	2.36	4.97	6.99	1.86	-	1.10
M532-3	[O]	-	-	-	4.37	-	-	-	-	-	-
M532-4	[O]	8.71	9.11	3.86	-	1.91*	15.30	10.73	5.48	9.04*	1.99
M530-1	[O]+[-2H]	-	-	1.64*	-	1.55	9.36	6.27	3.09	-	1.75
M548-4	2[O]	-	-	0.56	9.89	4.23	-	2.81	-	9.78	4.03
M421-1	TPN729M3+[-CH ₂]+[O]	-	5.45	0.92*	3.60*	1.36*	-	2.96	0.81	1.94*	0.33
M435-2	TPN729M3+[O]	5.59	8.27	1.28	2.05	0.56	1.34	7.53*	0.58	1.48	1.00*
M479-2	M463-2+[O]										
M435-4	TPN729M3+[O]	3.54	3.42	1.22	4.72*	0.21	4.25	2.97	0.93	1.42	0.42*
M435-5	TPN729M3+[O]	4.38	5.34			-		4.32	-	-	-
M405-2	TPN729M3+[-CH ₂]	12.14	11.17	-	-	-	3.62	7.05	-	-	0.27
M463-2	[-C ₄ H ₇ N]+ [O]	4.10*	3.02*	-	-	-	5.44	2.99	-	-	-
M477	[-C ₄ H ₉ N]+2[O]	-	-	-	3.41	1.22	-	-	-	1.31	0.44
TPN729M3	[-C ₆ H ₁₁ N]	22.66	8.02	-	-	0.14	8.43	7.97	-	-	-
Other metabolites [#]	NA	9.85	10.24	3.42	27.78	14.49	5.34	8.88	3.29	17.93	9.98

Note: -, Not detected in radio chromatography; *:co-eluted with other metabolite; [#]: The metabolites with the percentage $\geq 3\%$ were shown in the table above, and the total percentage of other metabolites was shown in the “Other metabolites” line; NA: Not applicable