

Electronic Supplementary Information for

**LC–MS/MS Method for Simultaneous Determination of Linarin and its
Metabolites in Rat Plasma and Liver Tissue Samples: Application to
Pharmacokinetic and Liver Tissue Distribution Study After Oral
Administration of Linarin**

Yang Li^{a,b}, Chenxi Guang^{a,b}, Na Zhao^{a,b}, Xinchu Feng^{a,*} and Feng Qiu^{a,b,*}

^a School of Chinese Materia Medica, Tianjin University of Traditional Chinese Medicine, Tianjin 300193, China

^b Tianjin State Key Laboratory of Modern Chinese Medicine, Tianjin University of Traditional Chinese Medicine, Tianjin 300193, China

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Table S1 Plasma concentrations of apigenin after oral administration of linarin in rats.

Groups	Time (h)	Concentration (ng/mL)								Mean $\pm$ SD
		NO.1	NO.2	NO.3	NO.4	NO.5	NO.6	NO.7	NO.8	
Normal rats	0.03	N.D.	N.D.	N.D.	1.37	10.20	N.D.	N.D.	1.30	1.61 $\pm$ 3.52
	0.08	1.11	4.92	1.34	N.D.	N.D.	2.81	N.D.	3.18	1.67 $\pm$ 1.81
	0.17	N.D.	1.07	N.D.	4.77	N.D.	N.D.	1.43	1.66	1.12 $\pm$ 1.64
	0.33	3.08	N.D.	2.15	1.02	1.90	2.06	5.64	1.54	2.17 $\pm$ 1.66
	1	1.09	N.D.	N.D.	2.12	1.24	2.34	1.17	1.93	1.24 $\pm$ 0.89
	2	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	0.00 $\pm$ 0.00
	4	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	0.00 $\pm$ 0.00
	6	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	0.00 $\pm$ 0.00
	8	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	0.00 $\pm$ 0.00
	12	3.44	N.D.	N.D.	N.D.	2.61	N.D.	N.D.	N.D.	0.76 $\pm$ 1.62
	24	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	0.00 $\pm$ 0.00
	36	N.D.	N.D.	1.04	N.D.	N.D.	N.D.	N.D.	N.D.	0.13 $\pm$ 0.37
	48	N.D.	N.D.	1.67	N.D.	N.D.	N.D.	N.D.	N.D.	0.21 $\pm$ 0.59
	60	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	0.00 $\pm$ 0.00
	72	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	0.00 $\pm$ 0.00

Model rats	0.03	N.D.	N.D.	1.41	N.D.	3.48	1.88	N.D.	1.81	1.07 ± 1.29
	0.08	N.D.	1.47	N.D.	N.D.	4.77	1.26	N.D.	N.D.	0.94 ± 1.67
	0.17	3.79	N.D.	2.24	N.D.	1.03	N.D.	N.D.	N.D.	0.88 ± 1.42
	0.33	N.D.	N.D.	3.97	N.D.	1.13	N.D.	N.D.	N.D.	0.64 ± 1.40
	1	N.D.	N.D.	N.D.	N.D.	N.D.	2.33	N.D.	N.D.	0.29 ± 0.82
	2	N.D.	N.D.	N.D.	3.13	N.D.	4.78	N.D.	N.D.	0.99 ± 1.88
	4	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	0.00 ± 0.00
	6	N.D.	N.D.	N.D.	4.15	N.D.	N.D.	N.D.	N.D.	0.52 ± 1.47
	8	N.D.	N.D.	1.38	5.85	N.D.	1.17	N.D.	N.D.	1.05 ± 2.02
	12	34.20	4.36	N.D.	2.91	2.37	1.05	1.20	N.D.	5.76 ± 11.59
	24	7.88	1.22	N.D.	N.D.	N.D.	1.32	N.D.	N.D.	1.30 ± 2.72
	36	2.76	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	0.35 ± 0.98
	48	N.D.	N.D.	N.D.	N.D.	1.09	2.20	N.D.	N.D.	0.41 ± 0.82
	60	N.D.	1.29	N.D.	6.91	N.D.	N.D.	N.D.	N.D.	1.03 ± 2.42
	72	N.D.	N.D.	N.D.	1.05	N.D.	N.D.	7.17	N.D.	1.03 ± 2.51

Footnote: N.D. = not detected; SD = standard deviation.

Table S2 Plasma concentrations of *p*-hydroxy benzaldehyde after oral administration of linarin in rats.

Groups	Time (h)	Concentration (ng/mL)								Mean $\pm$ SD
		NO.1	NO.2	NO.3	NO.4	NO.5	NO.6	NO.7	NO.8	
Normal rats	0.03	N.D.	N.D.	N.D.	11.10	11.80	2.90	10.20	N.D.	4.50 $\pm$ 5.51
	0.08	19.90	N.D.	N.D.	N.D.	N.D.	14.10	N.D.	N.D.	4.25 $\pm$ 8.02
	0.17	N.D.	N.D.	N.D.	9.18	N.D.	N.D.	N.D.	N.D.	1.15 $\pm$ 3.25
	0.33	27.70	N.D.	N.D.	1.05	N.D.	N.D.	3.33	N.D.	4.01 $\pm$ 9.64
	1	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	15.10	N.D.	1.89 $\pm$ 5.34
	2	6.63	2.39	4.02	4.84	6.85	2.79	7.79	2.71	4.75 $\pm$ 2.11
	4	4.83	5.50	5.58	7.29	2.97	1.32	7.42	2.72	4.70 $\pm$ 2.20
	6	3.14	3.20	2.58	7.88	3.49	2.74	9.74	9.05	5.23 $\pm$ 3.09
	8	5.62	3.23	3.28	3.52	6.29	6.52	5.41	3.61	4.69 $\pm$ 1.40
	12	3.55	2.53	N.D.	2.68	3.14	3.12	N.D.	3.59	2.33 $\pm$ 1.48
	24	1.34	2.11	2.35	1.86	N.D.	3.20	1.89	1.76	1.81 $\pm$ 0.91
	36	1.74	N.D.	3.19	N.D.	1.04	N.D.	2.51	N.D.	1.06 $\pm$ 1.29
	48	1.05	N.D.	2.69	N.D.	N.D.	2.10	2.60	1.01	1.18 $\pm$ 1.16
	60	1.13	N.D.	3.59	N.D.	N.D.	2.99	N.D.	N.D.	0.96 $\pm$ 1.50
	72	1.56	7.30	13.50	N.D.	1.13	2.04	2.49	1.69	3.71 $\pm$ 4.51

Model rats	0.03	N.D.	10.80	11.40	N.D.	29.60	15.40	1.42	N.D.	8.58 ± 10.51
	0.08	5.88	N.D.	1.77	N.D.	25.70	22.90	N.D.	7.82	8.01 ± 10.49
	0.17	31.90	N.D.	N.D.	5.94	11.00	N.D.	8.26	8.42	8.19 ± 10.53
	0.33	2.81	18.30	14.20	N.D.	15.80	N.D.	6.47	7.04	8.08 ± 7.21
	1	3.25	N.D.	N.D.	2.90	N.D.	7.37	6.18	4.43	3.02 ± 2.89
	2	N.D.	7.24	N.D.	N.D.	N.D.	3.18	18.60	7.77	4.60 ± 6.54
	4	N.D.	N.D.	N.D.	N.D.	N.D.	7.23	6.67	3.19	2.14 ± 3.17
	6	N.D.	6.23	N.D.	N.D.	N.D.	3.06	N.D.	6.73	2.00 ± 2.96
	8	4.21	N.D.	N.D.	N.D.	N.D.	N.D.	3.07	3.99	1.41 ± 1.97
	12	85.80	16.70	N.D.	N.D.	N.D.	5.02	12.50	6.68	15.84 ± 28.93
	24	99.90	N.D.	6.50	12.20	24.40	5.03	39.70	1.84	23.70 ± 33.55
	36	37.90	N.D.	N.D.	N.D.	N.D.	N.D.	9.08	N.D.	5.87 ± 13.33
	48	61.40	N.D.	N.D.	N.D.	4.53	12.20	31.90	N.D.	13.75 ± 22.18
	60	27.80	4.19	N.D.	15.10	N.D.	N.D.	31.00	N.D.	9.76 ± 13.19
	72	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	19.60	N.D.	2.45 ± 6.93

Footnote: N.D. = not detected; SD = standard deviation.