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Supporting Information to

Simultaneous Determination and Pharmacokinetic Study of Losartan, Losartan Carboxylic Acid, Ramipril, Ramiprilat, and Hydrochlorothiazide in Rat Plasma by a Liquid Chromatography/Tandem Mass Spectrometry Method

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Tab. S1. Results of recovery and matrix effect of LOS, LCA, RAM, RPT, HCZ, and ISs in rat plasma (n = 6)

Analyte	Nominal conc. (ng/mL)	Recovery (%)		Matrix effect (%)	
		Mean ± SD	%RSD	Mean ± SD	RSD (%)
LOS	3.00	75 .33 ± 4.11	8.12	93.22 ± 3.50	6.55
	9.00	78.14 ± 3.80	5.11	94.50 ± 3.10	6.52
	600	82.15 ± 3.52	6.35	94.25 ± 4.20	3.99
	2700	88.88 ± 6.50	5.68	97.22 ± 1.80	4.25
LCA	3.00	75 .33 ± 4.11	7.41	92.50 ± 5.50	7.10
	9.00	72.21 ± 5.50	6.22	93.33 ± 3.80	6.41
	600	81.23 ± 4.21	3.85	93.31 ± 3.42	5.27
	2700	84. 23± 3.55	4.11	95.54 ± 2.21	4..51
RAM	0.1	81.27 ± 4.21	6.23	98.15 ± 2.03	3.30
	0.3	87.15 ± 4.20	8.51	98.14 ± 2.99	7.95
	15	87.25 ± 3.20	7.99	99.41 ± 4.50	8.80
	180	90.10 ± 2.14	6.25	97.58 ± 2.31	5.21
RPT	0.1	80.99 ± 2.65	5.66	95.21 ± 3.65	6.40
	0.3	84.22 ± 3.41	6.10	94.21 ± 3.80	3.80
	15	81.89 ± 6.20	3.30	91.38 ± 4.80	6.10
	180	86.97 ± 3.30	3.56	99.64 ± 3.14	4.60
HCZ	1	89.65 ± 3.50	4.50	90.14 ± 4.86	5.60
	3	86.35 ± 5.14	5.26	88.99 ± 6.20	4.21
	90	88.42 ± 3.80	3.27	92.16 ± 3.88	6.32
	1200	90.50 ± 4.20	3.80	91.45 ± 4.50	3.99
IS (IBS)	100	88.20 ± 6.20	2.97	99.32 ± 2.89	4.51
IS(MET)	100	90.34 ± 5.35	3.45	98.45 ± 3.80	6.42

Tab. S2. Stability of LOS, LCA, RAM, RPT, HCZ, and ISs after storage under indicated conditions (n=3); Concentrations in ng/mL (± SD).

Ana-lyte	Nominal Conc.	Benchtop stability at 24°Cfor 12 h		Long-term stability at −80°C (90 d)		Autosampler stability at 4°C (24 h)		Freeze-thaw stability (from −80°C to 24ºC)		Stock solution stability 4–8°C (7 d)	
		Conc. Found	CV (%)	Conc. Found	CV (%)	Conc. Found	CV (%)	Conc. Found	CV (%)	Conc. Found	CV (%)
LOS	9	9 ± 0.32	3.99	8.55 ± 1.40	5.55	9 ± 0.85	3.69	9 ± 0.20	4.20	9 ± 1.10	2.87
	600	594 ± 3.80	5.99	589.99 ± 3.66	3.60	595.66 ± 3.15	4.60	589.48 ± 4.88	6.88	591.55 ± 6.10	6.33
	2700	2686 ± 6.25	4.10	2614.00 ± 8.82	4.88	2688 ± 6.80	3.17	2681.74 ± 5.50	3.81	2691.22 ± 7.40	5.55
LCA	9	8.70 ± 0.25	3.84	8.39 ± 1.98	6.99	8.80 ± 0.15	3.65	8.41 ± 0.41	4.47	8.88 ± 0.18	4.96
	600	590.10 ± 4.71	6.89	583.41 ± 4.87	5.84	592 ± 2.88	3.41	584.32 ± 3.43	6.18	589.14 ± 4.79	5.57
	2700	2681.50 ± 8.28	3.89	2678.33 ± 9.28	4.14	2685.20 ± 5.0	4.47	2683.12 ± 9.84	5.14	2684.90 ± 7.33	3.10
LCA	9	8.70 ± 0.25	3.84	8.39 ± 1.98	6.99	8.80 ± 0.15	3.65	8.41 ± 0.41	4.47	8.88 ± 0.18	4.96
	600	590.10 ± 4.71	6.89	583.41 ± 4.87	5.84	592 ± 2.88	3.41	584.32 ± 3.43	6.18	589.14 ± 4.79	5.57
	2700	2681.50 ± 8.28	3.89	2678.33 ± 9.28	4.14	2685.20 ± 5.0	4.47	2683.12 ± 9.84	5.14	2684.90 ± 7.33	3.10
RAM	0.3	0.30 ± 1.14	3.88	0.30 ± 1.44	3.33	0.30 ± 1.01	5.55	0.30 ± 1.24	5.65	0.30 ± 0.98	4.10
	15	14.15 ± 3.25	4.19	13.95 ± 1.14	4.23	14.85 ± 2.50	6.66	14.15 ± 1.50	4.14	14.23 ± 3.66	3.89
	180	174.89 ± 6.80	8.80	173.14 ± 5.55	3.74	175.00 ± 3.50	6.45	175.99 ± 4.20	3.11	176.10 ± 4.44	6.82
RPT	0.3	0.30 ± 1.18	4.19	0.30 ± 1.80	4.10	0.30 ± 1.21	4.20	0.30 ± 1.80	3.99	0.30 ± 1.90	4.40
	15	14.09 ± 2.14	5.55	13.88 ± 1.17	6.41	14.20 ± 0.80	3.87	14.14 ± 0.40	4.23	14.22 ± 1.18	3.10
	180	174.15 ± 6.20	4.88	172 ± 6.77	4.77	175.55 ±8.89	3.77	173.29 ± 4.30	5.71	175.10 ± 8.51	7.05
HCZ	3	2.89 ± 1.10	6.88	2.80 ± 0.89	5.26	2.89 ± 1.28	5.32	2.84 ± 0.57	4.68	2.86 ± 0.88	6.66
	90	86.99 ± 3.36	4.41	85.41 ± 5.17	4.48	87.10 ± 3.28	4.89	85.12 ± 4.99	3.66	87.01 ± 2.84	4.68
	1200	1189.88 ± 8.80	6.66	1180.36 ± 12.45	6.30	1191.89 ± 8.50	5.11	1183.66 ± 8.50	4.48	1189.10 ± 10.54	5.02
IS (IBS)	180	176.75 ± 8.11	3.80	173 ± 6.45	4.85	175.06 ± 4.08	3.66	174.11 ± 6.03	4.45	176.66 ± 5.04	5.20
IS (RPT)	180	175.85 ± 4.88	4.10	173.90 ± 4.45	3.37	176.11 ± 4.98	6.66	175.11 ± 5.10	4.11	175.38 ± 3.54	5.14