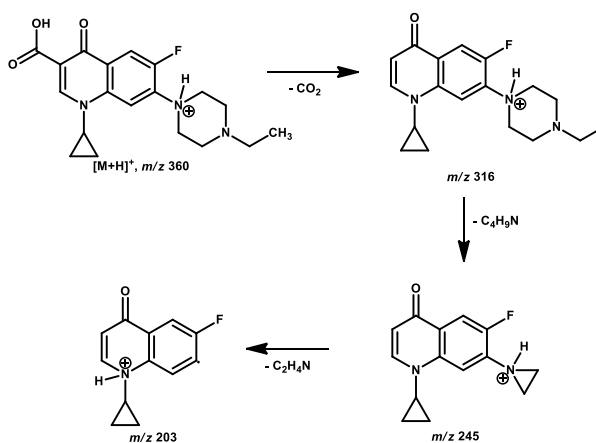
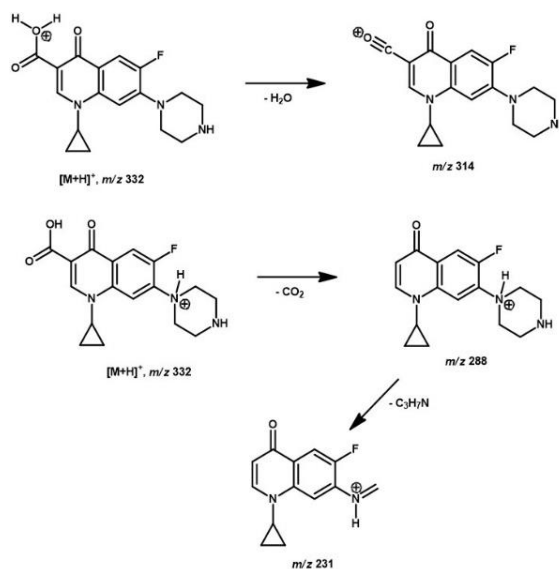


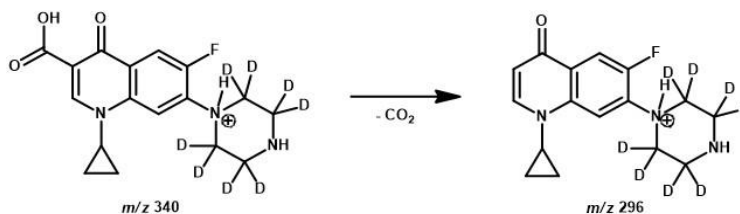
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Scheme 1S. Proposed fragmentation mechanism of for protonated $[M + H]^+$ of m/z 360 (ENR). Note that to form the fragment ion of m/z 203 loss of a neutral molecule of C_3H_6 (42 Da) composition could also be proposed.



Scheme 2S. Proposed fragmentation mechanisms for protonated $[M + H]^+$ of m/z 332 (CIP).



Scheme 3S. Proposed fragmentation mechanism for CO_2 loss from protonated CIP-d8 of m/z 340.

Table 1S. Method performance for ENR by LC-MS/MS.

Plasma ENR (ng mL ⁻¹)	Intra (n = 3)			Inter (n = 6)		
	mean + s (ng mL ⁻¹)	CV (%)	Recovery (%)	mean + s (ng mL ⁻¹)	CV (%)	Recovery (%)
6.000	6.440 ± 0.530	8.22	93.0	6.670 ± 0.730	10.9	111
100.0	99.09 ± 6.08	6.13	99.0	105.0 ± 5.76	5.48	105
290.0	270.4 ± 8.18	3.02	93.0	288.0 ± 8.76	3.04	99.0
2600	2588 ± 76.3	2.95	99.0	2590 ± 93.7	3.62	99.0
Liver ENR (ng g ⁻¹)	Intra (n = 3)			Inter (n = 6)		
	mean + s (ng g ⁻¹)	CV (%)	Recovery (%)	mean + s (ng g ⁻¹)	CV (%)	Recovery (%)
6.000	6.100 ± 0.701	2.83	98.0	6.760 ± 0.792	11.7	113
180.0	188.8 ± 2.65	1.40	105	193.0 ± 5.81	3.00	107
290.0	295.2 ± 4.65	1.58	102	298.2 ± 6.75	2.27	103
4000	4008.9 ± 11.0	0.271	101	4033 ± 102.1	2.53	101
Kidney ENR (ng g ⁻¹)	Intra (n = 3)			Inter (n = 6)		
	mean + s (ng g ⁻¹)	CV (%)	Recovery (%)	mean + s (ng g ⁻¹)	CV (%)	Recovery (%)
6.000	6.300 ± 0.531	8.59	105	6.880 ± 0.880	12.8	114
120.0	124.5 ± 6.08	4.88	103	127.8 ± 7.76	6.07	107
290.0	295.3 ± 8.08	2.73	102	298.3 ± 9.08	3.04	103
6000	6021 ± 116	1.93	100	6050 ± 223	3.68	101
Muscle ENR (ng g ⁻¹)	Intra (n = 3)			Inter (n = 6)		
	mean + s (ng g ⁻¹)	CV (%)	Recovery (%)	mean + s (ng g ⁻¹)	CV (%)	Recovery (%)
3.000	3.100 ± 0.151	4.83	103	3.400 ± 0.230	6.76	113
45.00	44.80 ± 2.65	5.92	99.0	46.8 0± 3.80	8.12	104
90.00	92.60 ± 3.63	3.92	102	95.60 ± 5.63	5.89	106
2600	2580 ± 50.14	1.92	99.0	2677 ± 96.4	3.60	103
Skin/fat ENR (ng g ⁻¹)	Intra (n = 3)			Inter (n = 6)		
	mean + s (ng g ⁻¹)	CV (%)	Recovery (%)	mean + s (ng g ⁻¹)	CV (%)	Recovery (%)
6.000	5.880 ± 0.531	9.01	98.0	6.070 ± 0.731	12.0	102
100.0	97.50 ± 6.08	6.23	98.0	103.0 ± 4.38	4.25	103
290.0	288 .0 ± 8.18	2.84	99.0	292.0 ± 3.66	1.25	101
2600	2605 ± 76.3	2.93	100	2630 ± 98.4	3.74	101

Table 2S. Method performance for CIP by LC-MS/MS.

Plasma CIP (ng mL ⁻¹)	Intra (n = 3)			Inter (n = 6)		
	mean + s (ng mL ⁻¹)	CV (%)	Recovery (%)	mean + s (ng mL ⁻¹)	CV (%)	Recovery (%)
6.000	6.300 ± 0.480	7.62	105	6.800 ± 0.681	10.0	113
100.0	105.6 ± 8.63	8.17	106	107.0 ± 10.4	9.71	107
290.0	298.6 ± 6.63	2.22	103	297.0 ± 8.40	2.82	102
2600	2659 ± 35.3	1.33	102	2677 ± 63.7	2.38	103
Liver CIP (ng g ⁻¹)	Intra (n = 3)			Inter (n = 6)		
	mean + s (ng g ⁻¹)	CV (%)	Recovery (%)	mean + s (ng g ⁻¹)	CV (%)	Recovery (%)
6.000	6.300 ± 0.341	5.40	105	6.450 ± 0.781	12.1	108
180.0	182.5 ± 7.97	4.36	101	185.0 ± 11.4	6.16	103
290.0	298.3 ± 6.34	2.12	103	300.3 ± 8.34	1.28	103
4000	4058 ± 81.2	2.00	101	4088 ± 109	2.65	102
Kidney CIP (ng g ⁻¹)	Intra (n = 3)			Inter (n = 6)		
	mean + s (ng g ⁻¹)	CV (%)	Recovery (%)	mean + s (ng g ⁻¹)	CV (%)	Recovery (%)
6.000	6.800 ± 0.481	7.05	113	6.900 ± 0.661	9.56	115
120.0	119.6 ± 10.6	8.88	99.0	122.8 ± 11.4	9.28	102
290.0	288.6 ± 8.63	2.99	99.0	298.6 ± 10.6	3.54	103
3000	3055 ± 25.3	0.821	102	3078 ± 86.7	2.81	103
Muscle CIP (ng g ⁻¹)	Intra (n = 3)			Inter (n = 6)		
	mean + s (ng g ⁻¹)	CV (%)	Recovery (%)	mean + s (ng g ⁻¹)	CV (%)	Recovery (%)
3.000	3.100 ± 0.341	11.0	103	3.200 ± 0.451	14.0	106
45.00	43.50 ± 1.97	4.52	97.0	48.40 ± 4.40	9.09	107
90.00	94.60 ± 3.63	3.83	105	96.60 ± 4.63	4.80	107
2600	2595 ± 80.3	3.10	99.0	2680 ± 100	3.73	103
Skin/fat CIP (ng g ⁻¹)	Intra (n = 3)			Inter (n = 6)		
	mean + s (ng g ⁻¹)	CV (%)	Recovery (%)	mean + s (ng g ⁻¹)	CV (%)	Recovery (%)
6.000	6.100 ± 0.452	9.20	102	6.500 ± 0.860	13.2	108
100.0	102.4 ± 7.62	7.44	102	105.0 ± 10.4	9.90	105
290.0	290.1 ± 7.43	2.56	100	297.0 ± 9.33	3.14	102
2600	2559 ± 38.3	1.50	98.0	2677 ± 79.6	2.97	103