Electronic Supplementary Information (ESI)

Herb-herb pharmacokinetic interaction between Glehniae Radix and Ophiopogonis Radix in rats based on superimposed multiple product ions (SMPI) LC-HR-MS/MS

Xiaowei Shi,†[a] Shuang Wang,†[a] Qi Qian,[a] Na Zhou,[a] Pengcheng Qi,[a] Xiyan Mu[a] and Qiao Wang*[ab]

a. Department of Pharmaceutical Analysis, School of Pharmaceutical Sciences, Hebei Medical University, Shijiazhuang, 050017, P. R. China

b. Institute of Chinese Integrative Medicine, Hebei Medical University, Shijiazhuang, 050017, P. R. China

† These authors contributed equally to this work.

Table S1 The LC-MS/MS transitions of nine constituents in GR and OR.

ESI mode	Compounds	MS (*m/z*)	MS/MS (*m/z*)	DP (V)	CE (eV)
Positive for GR	xanthotoxin	217.1	174.1	55	38
	bergapten	217.1	202.0	58	29
	isoimpinellin	247.1	217.1	61	33
	imperatorin	271.1	203.1	25	15
	psoralen	187.1	131.1	62	34
Negative for OR	ophiopogonin D	913.4	853.5	-50	-52
	methylophiopogonanone A	341.1	178.1	-69	-41
	methylophiopogonanone B	327.1	178.1	-61	-41
	methylophiopogonone A	339.1	131.1	-74	-46

Table S2 The intra- and inter-batch accuracies and precisions of the analytes in rat plasma (*n*=6)

Compounds	Intra-batch (*n*=6)			Inter-batch (*n*=6)		
Spiked conc. (ng/ mL)	Measured conc. (ng/ mL)	Accuracy (%)	Precision (%)	Measured conc. (ng/ mL)	Accuracy (%)	Precision (%)
xanthotoxin						
0.04	0.0422	5.5	10.1	0.0416	4.0	12.3
0.10	0.105	5.0	4.9	0.103	3.0	7.1
1.00	0.980	-2.0	5.5	1.01	1.0	6.1
16.0	16.3	1.9	1.6	16.1	0.6	4.7
bergapten						
0.04	0.0425	6.2	13.7	0.0419	4.8	11.8
0.10	0.0980	-2.0	1.2	0.101	1.0	1.6
1.00	1.06	6.0	3.1	1.04	4.0	4.7
16.0	16.1	0.6	2.1	15.9	-0.6	3.4
isopimpinellin						
0.04	0.0373	-6.8	12.5	0.0404	1.0	10.4
0.10	0.104	4.0	1.3	0.101	1.0	4.6
1.00	1.04	4.0	4.0	1.02	2.0	7.2
16.0	16.77	4.8	1.8	15.92	-0.5	3.3
imperatorin						
0.06	0.0674	12.3	15.0	0.0625	4.2	8.9
0.15	0.163	8.7	4.0	0.154	2.7	8.9
1.50	1.47	-2.0	1.7	1.51	0.7	2.6
24.0	24.1	0.4	2.4	23.5	-2.1	3.7
psoralen						
0.06	0.0651	8.5	14.4	0.0620	3.3	8.9
0.15	0.145	-3.3	5.1	0.148	-1.3	3.8
1.50	1.56	4.0	2.7	1.47	-2.0	5.9
24.0	24.82	3.4	2.0	23.85	-0.6	6.8
ophiopogonin D						
0.8	0.742	-7.2	16.4	0.808	4.8	9.8
1.60	1.57	-1.9	3.1	1.62	1.3	5.0
20.0	21.2	6.0	0.2	20.7	3.5	0.2
160	154	-3.8	3.7	161	0.6	5.2
methylophiopogonanone A						
0.30	0.294	-2.0	15.2	0.321	7.0	10.1
0.60	0.631	5.0	2.1	0.590	-1.7	4.7
7.50	7.27	-3.1	2.2	7.34	-2.1	7.4
60.0	62.1	3.5	7.2	60.3	0.5	10.1
methylophiopogonanone B						
0.30	0.299	-0.4	12.3	0.316	5.4	10.2
0.60	0.580	-3.3	3.2	0.629	5.0	4.8
7.50	7.43	-0.9	4.5	7.48	-0.3	6.7
60.0						

	64.2	7.0	4.5	61.7	2.8	7.9
methylophiopogonone A						
0.30	0.348	16.1	12.7	0.317	5.7	9.1
0.60	0.62	3.3	2.7	0.57	-5.0	5.7
7.50	7.14	-4.8	5.9	7.40	-1.3	9.1
60.0	61.7	2.8	2.6	61.0	1.7	3.3

Table S3 The mean extraction recoveries and matrix effect of the analytes in rat plasma (n = 6)

Components	Spiked conc. (ng/mL)	Extraction recovery (%)	RSD (%)	Matrix effect (%)	RSD (%)
xanthotoxin	0.10	99.7	7.1	107.3	6.2
	1.00	97.9	5.0	112.5	3.3
	16.0	97.2	2.2	103.6	7.6
bergapten	0.10	89.7	10.9	104.2	7.8
	1.00	105.3	4.2	91.0	7.8
	16.0	100.1	2.0	90.3	5.9
isopimpinellin	0.10	105.5	8.7	93.6	8.2
	1.00	103.5	3.4	100.7	5.8
	16.0	99.1	1.1	96.0	4.4
imperatorin	0.15	101.8	5.5	101.9	7.2
	1.50	84.7	5.5	96.9	5.4
	24.0	97.6	3.8	94.8	3.1
psoralen	0.15	97.9	6.6	90.8	2.7
	1.50	97.8	3.8	93.2	9.5
	24.0	100.6	0.8	92.1	5.6
pimpinellin, IS	14.0	96.3	3.3	88.1	8.2
ophiopogonin D	1.60	100.5	6.8	104.3	2.9
	20.0	96.3	4.5	107.9	9.3
	160	91.9	6.9	97.3	3.4
methylophiopogonanone A	0.60	86.5	7.9	98.0	4.0
	7.50	97.1	4.9	107.5	2.2
	60.0	94.0	1.4	104.1	7.6
methylophiopogonanone B	0.60	87.1	7.7	93.5	8.3
	7.50	88.6	5.5	104.5	6.0
	60.0	85.0	3.0	97.6	4.3
methylophiopogonone A	0.60	83.2	7.0	97.3	9.4
	7.50	87.4	5.8	109.0	5.2
	60.0	87.1	2.7	105.4	2.5
pectolinarigenin, IS	10.0	91.6	6.3	91.8	2.4

Table S4 Stability of the analytes in rat plasma (n = 6)

Compound	At room temperature for 6 h in plasma		After three freeze-thaw cycles in plasma		At −80 °C for 30 days in plasma		In autosampler for 6 h		At −40 °C for 12 h in processed plasma	
Spiked conc. (ng/mL)	Measured conc. (ng/mL)	Accuracy (%)	Measured conc. (ng/mL)	Accuracy (%)	Measured conc. (ng/mL)	Accuracy (%)	Measured conc. (ng/mL)	Accuracy (%)	Measured conc. (ng/mL)	Accuracy (%)
xanthotoxin										
0.10	0.098±0.009	98.0	0.097±0.008	97.4	0.105±0.005	94.6	0.103±0.001	103.1	0.093±0.002	93.0
1.00	1.095±0.007	109.5	1.073±0.046	107.3	1.051±0.044	105.1	1.009±0.016	100.9	0.961±0.039	96.1
16.0	14.67±0.331	91.7	14.640±0.276	91.5	14.784±0.308	92.4	17.420±0.256	108.9	14.470±0.369	90.4
bergapten										
0.10	0.107±0.002	106.6	0.097±0.003	96.8	0.096±0.004	95.6	0.107±0.004	107.4	0.097±0.005	96.6
1.00	0.880±0.034	88.0	0.965±0.030	96.5	1.051±0.053	105.1	1.020±0.093	102.0	0.942±0.047	94.2
16.0	14.533±0.359	90.8	13.907±0.136	86.9	14.784±0.467	92.4	16.540±0.962	103.4	16.153±0.412	101.0
isopimpinellin										
0.10	0.096±0.002	95.5	0.108±0.003	108.3	0.091±0.003	90.7	0.104±0.004	104.0	0.095±0.008	95.0
1.00	0.831±0.029	83.1	0.928±0.045	92.8	0.981±0.055	98.1	1.077±0.087	107.7	0.871±0.052	87.1
16.0	14.160±0.140	88.5	14.087±0.653	88.0	15.344±0.551	95.9	17.353±1.136	108.5	14.057±0.276	87.9
imperatorin										
0.15	0.142±0.002	94.7	0.160±0.009	106.7	0.158±0.007	105.6	0.159±0.006	106.1	0.132±0.011	88.0
1.50	1.623±0.085	108.2	1.578±0.057	105.2	1.458±0.076	97.2	1.495±0.024	99.7	1.544±0.139	102.9
24.0	22.060±0.642	91.9	24.320±0.713	101.3	25.104±0.858	1.046	21.813±1.450	90.9	23.140±0.627	96.4
psoralen										
0.15	0.148±0.009	98.7	0.163±0.008	108.7	0.154±0.011	102.4	0.151±0.015	100.7	0.146±0.012	97.2
1.50	1.513±0.031	100.9	1.386±0.034	92.4	1.385±0.058	92.3	1.491±0.083	99.4	1.450±0.084	96.7
24.0	23.840±0.929	99.3	25.180±1.471	104.9	22.296±0.898	92.9	24.900±0.849	103.8	24.003±0.345	100.0

ophiopogonin D										
1.60	1.656±0.089	103.5	1.481±0.067	92.6	1.579±0.093	98.7	1.554±0.110	97.1	1.438±0.054	89.9
20.0	20.466±0.974	102.3	18.826±1.321	94.1	19.342±1.183	96.7	20.108±0.733	100.5	20.684±0.839	103.4
160	156.704±9.372	97.9	154.080±12.107	96.3	158.637±9.382	99.1	147.500±7.649	92.2	168.336±5.899	105.2
methylophiopogonanone A										
0.60	0.639±0.027	106.5	0.650±0.043	108.4	0.628±0.037	104.7	0.649±0.039	108.2	0.623±0.028	108.4
7.50	7.335±0.425	97.8	6.842±0.376	91.2	7.658±0.355	102.1	7.605±0.513	101.4	7.898±0.631	91.2
60.0	53.646±3.164	89.4	59.484±2.719	99.1	59.026±3.011	98.4	58.698±2.407	97.8	58.872±3.850	99.1
methylophiopogonanone B										
0.60	0.553±0.037	92.1	0.541±0.029	90.2	0.572±0.033	95.4	0.564±0.018	94.1	0.640±0.040	90.2
7.50	7.080±0.529	94.4	6.908±0.378	92.1	6.956±0.409	92.7	7.615±0.392	101.5	7.605±0.413	92.1
60.0	62.322±2.449	103.9	64.086±3.705	106.8	57.989±4.332	96.6	56.491±2.714	94.2	56.778±3.082	106.8
methylophiopogonone A										
0.60	0.547±0.027	91.1	0.602±0.033	100.3	0.560±0.018	93.4	0.537±0.027	89.5	0.622±0.39	100.3
7.50	7.335±0.362	97.8	7.028±0.419	93.7	7.072±0.522	94.3	7.410±0.317	98.8	7.467±0.299	93.7
60.0	57.198±4.093	95.3	62.718±1.575	104.5	61.266±4.781	102.1	65.080±3.005	108.5	58.490±2.948	104.5