

1 **Electronic supplementary information**

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3 **Study on the therapeutic material basis and effect of Acanthopanax**  
4 **senticosus leaves in the treatment of ischemic stroke by PK-PD analysis**  
5 **based on online microdialysis-LC-MS/MS method**

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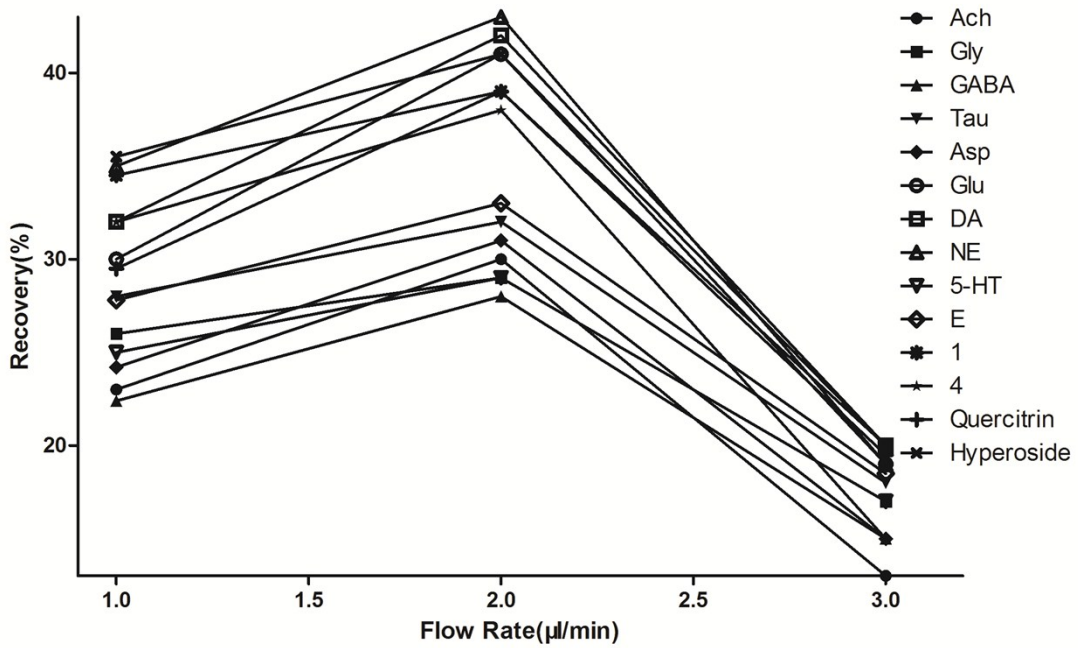
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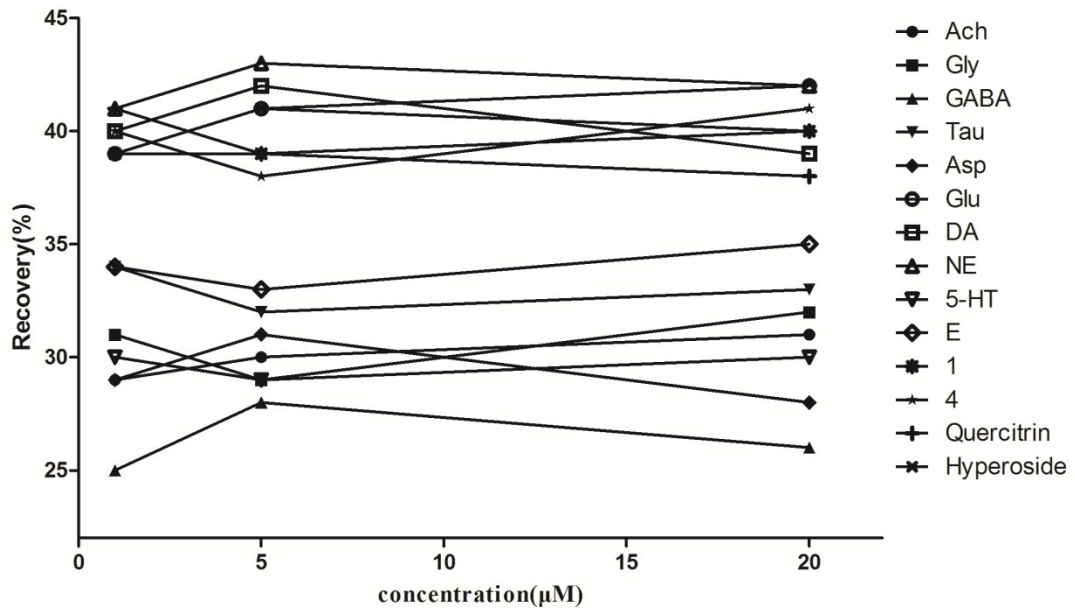
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26 Figure S.1 Comparison of blood probe recoveries of 14 analytes at different perfusion rates and at a concentration of 5.0  $\mu\text{M}$



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28 Figure S.2 Comparison of blood probe recoveries of 14 analytes at different concentration and at a perfusion rate of 2.0  
29  $\mu\text{L}/\text{min}$

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Table S.1 MRM parameters for 16 analytes

Analytes	Parent ion ( <i>m/z</i> )	Cone voltage (V)	Daughter ion ( <i>m/z</i> )	Collision energy (eV)
DA	153.97	12	137.00	10
			91.08	22
Ach	146.03	22	87.04	12
			60.11	10
Asp	133.97	12	74.03	14
			88.07	10
GABA	103.97	14	86.99	10
			68.03	14
Glu	147.97	14	84.11	16
			130.03	8
Gly	75.97	14	30.19	8
			48.14	6
5-HT	176.97	10	160.02	8
			132.06	20
Tau	125.90	22	108.02	12
			44.19	14
E	183.97	12	166.04	6
			107.06	24
NE	169.97	6	152.04	8
			107.03	18
Rutin	609.16	42	300.06	36
			270.94	48
Hyperoside	463.03	36	300.06	28
			270.94	42
Quercitrin	447.10	36	300.12	28
			270.94	44
Isoquercitrin	463.10	40	270.94	38
			254.95	36
1,3-diCQA	515.10	18	191.04	32
			353.04	16
4,5-diCQA	514.86	25	352.91	17
			172.90	21

Table S.2 Linearity, LOD and LOQ for 14 analytes

Analytes	R <sup>2</sup>	Regression equation	Dynamic range (μM)	LOD (μM)	LOQ (μM)
Ach	0.9944	y=0.8154x+3.8703	1.0000~20.00	0.1000	0.5000
Gly	0.9962	y=0.0036x+0.0254	2.500~20.00	0.2500	0.7500
GABA	0.9810	y=0.2189x+0.5520	2.500~20.00	0.2500	0.7500
Tau	0.9963	y=0.0119x+0.0390	1.000~20.00	0.1000	0.5000
Asp	0.9918	y=0.0393x+0.0996	1.000~20.00	0.1000	0.5000
Glu	0.9815	y=0.2075x+0.0968	0.5000~20.00	0.0500	0.2500
DA	0.9919	y=0.2410x+0.3998	1.000~20.00	0.0500	0.2500
NE	0.9999	y=0.1886x+1.1022	2.500~20.00	0.0500	0.2500
5-HT	0.9858	y=0.0773x+0.2107	2.500~20.00	0.0250	0.1250
E	0.9938	y=0.3218x-0.9894	2.500~20.00	0.0250	0.1250
1,3-diCOQ	0.9974	y=5715.32x+6173.52	0.5000~20.00	0.0250	0.1250
4,5-diCOQ	0.9986	y=1592.85x+496.721	0.5000~20.00	0.0250	0.1250
Quercitrin	0.9935	y=27302.7x-346.295	0.1000~100.0	0.0010	0.0050
Hyperoside	0.9960	y=29461.3x+60180.6	1.000~100.0	0.05000	0.2500

Table S.3 The precision and accuracy for 14 analytes

Analytes	Added ( $\mu\text{M}$ )	inter-day(n=5)			intra-day(n=5)		
		Observed	Precision(RSD,%)	Accuracy(RE,%)	Observed	Precision (RSD,%)	Accuracy(RE,%)
Ach	1	0.9800 $\pm$ 0.0200	-1.630	-2.000	1.030 $\pm$ 0.0200	1.940	3.020
	5	5.080 $\pm$ 0.5600	11.02	1.600	5.050 $\pm$ 0.7200	14.25	1.010
	20	20.22 $\pm$ 0.3400	1.680	1.100	19.94 $\pm$ 1.560	7.820	0.300
Gly	1	0.8700 $\pm$ 0.1300	-14.94	-1.300	0.910 $\pm$ 0.090	-9.900	9.000
	5	4.880 $\pm$ 0.1700	-3.480	-2.400	5.110 $\pm$ 0.4500	8.800	2.200
	20	21.09 $\pm$ 2.1700	10.29	5.450	22.80 $\pm$ 1.290	5.450	14.00
GABA	1	0.8800 $\pm$ 0.0900	-10.22	-12.00	0.9300 $\pm$ 0.1100	11.83	7.000
	5	4.830 $\pm$ 0.5900	-12.22	-3.400	5.180 $\pm$ 0.6600	12.74	3.600
	20	18.61 $\pm$ 1.380	-7.420	-6.950	19.18 $\pm$ 2.410	-12.57	-4.100
Tau	1	1.090 $\pm$ 0.1500	13.76	9.010	0.8700 $\pm$ 0.1300	-14.94	-13.00
	5	5.330 $\pm$ 0.6800	12.76	6.600	5.200 $\pm$ 0.4900	9.420	4.000
	20	22.08 $\pm$ 2.130	9.650	10.40	21.37 $\pm$ 2.050	9.590	6.850
Asp	1	0.8900 $\pm$ 0.0900	-10.11	-10.98	0.8700 $\pm$ 0.1200	-13.79	13.01
	5	4.780 $\pm$ 0.6900	-14.44	-4.400	5.140 $\pm$ 0.5500	10.70	2.800
	20	22.44 $\pm$ 3.010	13.41	12.20	21.39 $\pm$ 1.990	9.300	6.950
Glu	1	1.120 $\pm$ 0.1300	11.61	12.02	1.020 $\pm$ 0.0900	8.820	2.030
	5	4.770 $\pm$ 0.4900	-10.27	-4.610	5.130 $\pm$ 0.3200	6.240	2.600
	20	21.93 $\pm$ 2.870	13.09	9.650	22.09 $\pm$ 2.660	12.04	10.45
DA	1	0.8700 $\pm$ 0.1100	-12.64	-13.02	1.090 $\pm$ 0.1400	12.84	9.010
	5	4.8900 $\pm$ 0.5700	-11.66	-2.230	5.230 $\pm$ 0.7300	13.96	4.600
	20	21.49 $\pm$ 2.710	12.61	7.450	22.85 $\pm$ 2.950	12.91	14.25
NE	1	0.8800 $\pm$ 0.0800	-9.090	-12.01	0.8600 $\pm$ 0.080	-9.300	-14.02
	5	5.240 $\pm$ 0.5500	10.50	4.800	4.770 $\pm$ 0.6800	-14.26	-4.600
	20	18.75 $\pm$ 1.970	-10.51	-6.250	22.31 $\pm$ 2.180	9.770	11.55
5-HT	1	0.8900 $\pm$ 0.1300	-14.61	-11.02	0.9700 $\pm$ 0.1100	-11.34	-3.000
	5	4.830 $\pm$ 0.6700	-13.87	-3.400	5.230 $\pm$ 0.7100	13.58	4.600
	20	22.18 $\pm$ 2.660	11.99	10.90	22.39 $\pm$ 1.990	8.890	11.95
E	1	1.130 $\pm$ 0.0300	2.650	13.00	1.140 $\pm$ 0.1500	13.16	14.04
	5	5.240 $\pm$ 0.4800	9.160	4.800	4.870 $\pm$ 0.7200	-14.78	-2.610
	20	22.78 $\pm$ 1.940	8.520	13.90	21.32 $\pm$ 2.100	9.850	6.600
1,3-diCOQ	0.5	0.5100 $\pm$ 0.0600	11.86	1.200	0.4600 $\pm$ 0.0400	-8.700	-8.000
	5	4.880 $\pm$ 0.7200	-14.75	-2.400	4.790 $\pm$ 0.5600	-11.69	-4.200
	20	21.53 $\pm$ 1.880	8.730	7.650	22.91 $\pm$ 2.340	10.21	14.55
4,5-diCOQ	0.5	0.5100 $\pm$ 0.0700	13.73	14.00	0.5100 $\pm$ 0.0600	11.02	14.00
	5	5.200 $\pm$ 0.6500	12.50	4.000	5.1300 $\pm$ 0.2600	5.070	2.610
	20	18.33 $\pm$ 1.290	-7.040	-8.350	21.10 $\pm$ 2.410	11.42	5.500
Quercitrin	0.5	0.4700 $\pm$ 0.0500	-10.64	-6.020	0.4500 $\pm$ 0.0600	-13.33	-10.01
	10	11.13 $\pm$ 1.430	12.65	11.10	13.10 $\pm$ 1.290	9.850	13.10
	100	108.20 $\pm$ 12.88	11.90	8.200	92.29 $\pm$ 9.940	-10.77	-7.710

Analytes	Added ( $\mu\text{M}$ )	inter-day(n=5)			intra-day(n=5)		
		Observed	Precision(RSD,%)	Accuracy(RE,%)	Observed	Precision (RSD,%)	Accuracy(RE,%)
Hyperoside	1	1.120 $\pm$ 0.1300	11.61	12.01	0.8700 $\pm$ 0.0900	-10.34	-13.02
	10	8.940 $\pm$ 1.180	-13.20	-10.60	9.120 $\pm$ 1.350	-14.80	-8.800
	100	106.72 $\pm$ 10.39	9.740	6.720	113.2 $\pm$ 8.480	7.490	13.20

Table S.4 The matrix effect for 14 analytes

Analytes	Added( $\mu$ M)	The blood micro-dialysis (ME, %)	The hippocampal micro-dialysis (ME,%)
Ach	1	-14.90	10.30
	5	13.20	-9.39
	20	6.88	-14.02
Gly	1	-13.28	12.92
	5	-10.25	-3.98
	20	5.33	-7.89
GABA	1	14.00	14.83
	5	-9.08	-3.49
	20	5.66	8.09
Tau	1	-13.18	-12.96
	5	-9.88	11.32
	20	8.90	-12.35
Asp	1	-13.99	10.25
	5	4.24	-8.90
	20	7.99	12.00
Glu	1	12.93	-14.00
	5	-8.90	10.39
	20	5.64	-8.39
DA	1	-13.17	14.91
	5	-10.23	-10.82
	20	8.34	6.93
NE	1	14.03	12.93
	5	-8.99	3.29
	20	-4.98	5.66
5-HT	1	-13.79	-13.02
	5	14.54	-3.27
	20	1.09	9.94
E	1	13.95	-12.58
	5	-10.43	-9.00
	20	5.65	12.54
1,3-diCOQ	0.5	-14.45	13.98
	5	8.79	-6.67
	20	5.45	-12.89
4,5-diCOQ	0.5	13.39	14.28
	5	-13.09	14.30
	20	-3.66	-9.83
Quercitrin	0.5	-14.20	-13.98
	10	10.41	8.35
	100	-3.99	10.26

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Analytes	Added( $\mu$ M)	The blood micro-dialysis (ME, %)	The hippocampal micro-dialysis (ME,%)
	1	14.39	11.52
Hyperoside	10	-5.35	-6.77
	100	9.09	12.04

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