# An integrated strategy using LC-MS/MS combined with *in vivo* microdialysis for simultaneous determination of lignans of *Schisandra chinensis* (Turcz.) Baill. Fructus and endogenous neurotransmitters: Application to pharmacokinetic and pharmacodynamic study

Jun Fu[a,b], Hongxu Zhang[a,b], Shu Liu[b], Jiajie Wu[a,b], Yuying Zhang[a,b], Yang Gao[a,b], Fengrui Song[b], Yuhua Qin[c], Xiuli Hu[a], Zhongying Liu[a*]

**Affiliation**

[a] *School of Pharmaceutical Sciences, Jilin University, Changchun 130021, China.*

[b] *National Center of Mass Spectrometry in Changchun & Jilin Provincial Key Laboratory of Chinese Medicine Chemistry and Mass Spectrometry, Changchun Institute of Applied Chemistry, Chinese Academy of Sciences, Changchun, 130022, China.*

[C] *Hainan Tropical Marine University, Sanya, 572022*

* Corresponding author: Zhongying Liu, School of Pharmaceutical Sciences, Jilin University, Changchun 130021, China.

E-mail address: liuzy@jlu.edu.cn

**Table of contents**

Table S1 The *in vitro* recoveries for all analytes determined by gain method (n=3)

| Comp | Con (ng/mL) | Blood prob Flow rate (μL/min) | | | | | Brain prob Flow rate (μL/min) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1.0 | 1.5 | 2.0 | 2.5 | 3.0 | 1.0 | 1.5 | 2.0 | 2.5 | 3.0 |
| Gomisin A | 10 | 31.52±2.20 | 30.82±8.81 | 27.22±3.21 | 23.60±3.84 | 19.75±6.77 | 30.35±3.78 | 27.79±1.33 | 25.49±4.01 | 18.83±2.07 | 12.69±5.38 |
| | 200 | 32.58±5.37 | 30.17±3.03 | 28.73±3.67 | 24.35±7.79 | 20.31±5.71 | 30.90±7.58 | 28.06±5.05 | 25.78±5.69 | 18.73±5.35 | 12.03±5.96 |
| | 400 | 32.21±5.23 | 30.41±5.69 | 27.47±6.93 | 23.73±8.86 | 20.15±8.80 | 30.82±7.83 | 28.17±3.84 | 24.55±5.75 | 19.10±5.82 | 12.42±5.01 |
| Gomisin D | 2 | 31.21±3.81 | 29.76±8.64 | 27.59±6.65 | 24.79±4.56 | 20.23±5.02 | 29.88±9.54 | 25.55±1.07 | 23.93±3.77 | 16.41±3.07 | 10.69±5.57 |
| | 200 | 32.33±5.65 | 31.82±1.61 | 27.66±4.48 | 25.26±5.87 | 21.76±3.84 | 30.18±7.68 | 25.19±2.27 | 23.44±5.65 | 15.26±1.47 | 11.76±1.20 |
| | 400 | 31.81±2.61 | 30.43±5.44 | 26.08±3.29 | 25.08±4.92 | 20.62±5.71 | 29.75±4.79 | 25.97±3.50 | 24.45±5.49 | 16.85±5.46 | 11.71±3.66 |
| Gomisin E | 2 | 34.55±2.04 | 30.26±2.61 | 25.84±5.10 | 24.18±8.04 | 20.13±5.42 | 31.79±7.90 | 27.57±3.88 | 24.75±4.07 | 17.71±3.92 | 11.69±1.99 |
| | 200 | 34.70±5.05 | 30.24±7.53 | 26.69±5.17 | 24.73±3.89 | 20.70±6.73 | 31.32±6.41 | 27.19±4.95 | 24.56±3.78 | 16.75±1.57 | 11.65±2.03 |
| | 400 | 33.21±6.50 | 30.33±1.74 | 26.35±4.47 | 23.96±3.61 | 19.95±7.12 | 31.24±3.84 | 28.01±5.17 | 24.40±4.78 | 18.15±4.38 | 12.16±5.52 |
| Gomisin G | 1 | 32.83±7.05 | 31.09±8.18 | 28.29±3.37 | 24.88±4.42 | 21.09±4.73 | 30.48±8.45 | 28.35±4.36 | 25.69±4.96 | 15.94±2.92 | 11.55±3.82 |
| | 200 | 33.28±2.99 | 31.56±5.22 | 28.25±4.77 | 25.11±8.93 | 21.87±5.32 | 30.17±5.39 | 28.51±5.87 | 25.29±5.96 | 15.83±4.46 | 11.51±1.31 |
| | 400 | 33.70±6.61 | 30.28±9.64 | 28.57±5.46 | 25.26±4.81 | 21.32±8.57 | 31.01±7.17 | 27.58±2.98 | 25.38±4.46 | 16.67±2.30 | 12.29±2.16 |
| Gomisin K1 | 1 | 33.74±2.90 | 30.15±3.39 | 27.05±6.85 | 24.27±6.60 | 21.09±4.49 | 32.89±3.68 | 28.16±2.30 | 23.86±2.01 | 19.34±2.40 | 11.83±3.99 |
| | 200 | 34.51±8.01 | 30.07±9.10 | 27.14±3.31 | 23.79±6.56 | 21.51±7.50 | 33.58±4.79 | 28.45±1.55 | 24.43±4.38 | 19.90±4.03 | 10.56±3.01 |
| | 400 | 34.20±5.99 | 30.21±3.46 | 27.43±3.81 | 23.63±5.58 | 20.82±6.44 | 33.18±7.90 | 27.81±2.08 | 23.47±4.37 | 18.84±3.14 | 12.02±3.21 |
| Benzoyl-gomisin-H | 0.5 | 34.35±5.45 | 30.55±4.33 | 27.66±4.63 | 22.46±7.80 | 20.42±8.31 | 32.95±6.41 | 25.11±2.88 | 21.19±4.60 | 15.86±3.65 | 11.73±5.21 |
| | 200 | 34.21±3.37 | 30.42±5.00 | 27.43±5.32 | 23.61±6.78 | 21.77±4.11 | 33.09±3.84 | 25.23±2.67 | 21.15±5.47 | 15.21±1.70 | 11.06±1.84 |
| | 400 | 35.09±7.85 | 31.38±6.49 | 27.54±5.18 | 23.59±5.36 | 21.10±4.68 | 33.25±8.45 | 24.75±3.12 | 20.53±1.53 | 15.70±5.26 | 10.50±1.77 |
| Angeloylgomisin Q | 2 | 33.32±3.31 | 30.74±1.42 | 26.78±4.75 | 24.13±7.70 | 20.98±3.27 | 29.92±5.39 | 27.54±1.51 | 24.12±3.61 | 18.88±2.10 | 12.48±4.81 |
| | 200 | 33.75±6.45 | 30.97±2.44 | 26.96±8.77 | 24.21±5.78 | 21.18±5.72 | 30.57±4.79 | 28.78±1.15 | 23.25±3.28 | 19.31±2.23 | 11.71±5.47 |
| | 400 | 32.64±8.60 | 30.61±3.86 | 27.19±3.57 | 23.88±6.66 | 21.52±6.65 | 30.20±4.38 | 28.86±3.91 | 23.35±3.24 | 19.42±2.18 | 12.22±4.83 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Schizandrin | 2 | 33.97±7.17 | 30.21±7.74 | 26.63±4.71 | 23.62±4.23 | 21.39±5.24 | 31.13±6.41 | 26.26±4.57 | 21.69±1.67 | 18.91±3.43 | 11.37±4.61 |
| | 200 | 35.12±2.17 | 30.32±3.06 | 27.93±4.04 | 24.49±4.65 | 21.30±3.70 | 31.19±3.84 | 25.75±1.21 | 20.98±3.76 | 17.63±2.19 | 11.79±1.89 |
| | 400 | 34.31±2.56 | 31.16±1.77 | 27.43±4.14 | 24.12±6.71 | 21.01±7.92 | 31.55±3.68 | 27.18±2.03 | 21.51±5.98 | 18.75±3.42 | 11.42±1.65 |
| Schisandrin A | 1 | 33.41±9.16 | 30.45±3.02 | 28.85±3.56 | 23.45±7.46 | 20.65±7.89 | 31.39±4.07 | 25.37±5.42 | 21.86±3.41 | 17.63±4.58 | 10.74±5.88 |
| | 200 | 34.36±4.96 | 30.70±2.84 | 28.38±6.53 | 23.22±7.48 | 21.27±4.62 | 31.71±6.20 | 25.47±5.12 | 22.26±4.75 | 17.65±5.92 | 10.77±2.97 |
| | 400 | 34.18±4.03 | 30.09±8.35 | 27.96±6.92 | 23.87±4.83 | 21.15±3.39 | 31.82±6.75 | 25.14±2.50 | 22.29±5.92 | 18.51±3.86 | 11.26±2.89 |
| Schisandrin B | 1 | 32.34±5.99 | 29.73±3.18 | 27.19±3.42 | 23.19±6.57 | 20.71±4.42 | 29.92±4.24 | 25.66±3.58 | 22.13±3.87 | 19.57±5.43 | 11.68±4.50 |
| | 200 | 32.49±4.14 | 30.15±4.14 | 27.02±3.25 | 23.27±5.72 | 21.43±7.42 | 30.20±3.92 | 25.85±3.26 | 21.52±5.97 | 19.55±3.56 | 11.47±4.51 |
| | 400 | 32.14±6.41 | 30.25±6.96 | 26.86±5.89 | 22.64±6.74 | 21.39±5.37 | 30.31±7.08 | 25.63±4.49 | 21.99±3.37 | 19.78±2.94 | 11.91±2.71 |
| NE | 50 | 34.18±4.75 | 30.59±3.64 | 27.48±3.90 | 25.36±7.29 | 20.74±4.72 | 32.64±3.22 | 27.51±1.62 | 22.53±1.01 | 18.25±2.84 | 12.14±1.69 |
| | 400 | 34.27±2.33 | 31.13±3.68 | 27.90±6.38 | 24.74±7.94 | 21.65±5.74 | 32.79±5.47 | 27.45±1.53 | 22.97±1.73 | 17.62±3.40 | 12.05±5.82 |
| | 800 | 33.91±2.73 | 30.83±3.93 | 26.92±4.49 | 25.18±6.83 | 21.17±6.24 | 31.96±3.83 | 27.15±1.28 | 23.22±5.80 | 18.19±3.77 | 11.61±3.73 |
| 5-HT | 2 | 35.79±5.38 | 31.97±5.57 | 29.37±4.37 | 25.81±4.38 | 19.54±4.35 | 32.77±5.47 | 27.73±2.66 | 22.79±1.80 | 14.66±3.51 | 11.03±1.92 |
| | 200 | 35.93±4.95 | 32.07±3.06 | 29.30±4.35 | 25.64±5.04 | 19.04±4.42 | 33.12±5.28 | 27.91±1.78 | 22.43±4.36 | 15.23±4.36 | 10.41±4.60 |
| | 400 | 35.57±1.80 | 32.12±9.43 | 28.94±8.73 | 25.59±5.05 | 19.97±5.31 | 33.19±5.96 | 28.07±1.98 | 21.87±4.43 | 14.71±2.13 | 10.84±1.26 |
| Ach | 20 | 34.92±7.90 | 30.32±5.94 | 25.95±7.82 | 22.24±4.96 | 19.32±5.68 | 31.68±7.35 | 27.65±2.29 | 21.48±2.38 | 18.54±4.48 | 10.78±2.96 |
| | 400 | 35.33±1.48 | 30.64±6.64 | 25.68±5.92 | 22.49±5.64 | 18.52±7.72 | 32.13±3.92 | 28.12±4.15 | 21.55±2.14 | 18.32±3.72 | 10.51±2.83 |
| | 800 | 35.21±3.14 | 30.61±1.58 | 26.17±7.89 | 21.65±6.07 | 19.28±5.92 | 32.26±3.66 | 28.24±3.07 | 21.16±4.58 | 19.22±5.73 | 11.22±5.24 |
| GABA | 5 | 34.95±5.04 | 31.02±5.45 | 28.39±8.48 | 23.57±7.54 | 19.58±5.57 | 30.54±5.30 | 27.07±4.45 | 23.95±2.18 | 17.59±1.29 | 11.77±5.32 |
| | 200 | 35.06±3.70 | 30.41±1.30 | 28.61±7.69 | 23.42±4.20 | 19.59±7.30 | 30.72±4.22 | 26.63±2.54 | 23.96±3.63 | 17.57±3.56 | 12.52±3.07 |
| | 400 | 34.73±6.52 | 30.92±1.54 | 28.41±7.14 | 23.75±4.99 | 19.84±4.76 | 29.62±2.80 | 26.96±2.13 | 23.77±2.19 | 18.22±3.18 | 12.17±1.01 |
| Asp | 20 | 33.66±7.82 | 30.45±3.92 | 25.95±5.81 | 22.74±3.84 | 20.31±8.96 | 31.53±6.65 | 27.46±1.85 | 20.48±3.79 | 16.06±4.17 | 12.96±4.88 |
| | 400 | 33.81±6.19 | 30.04±2.62 | 26.38±8.61 | 23.27±3.38 | 20.84±6.47 | 31.81±5.92 | 27.09±1.42 | 20.46±2.04 | 16.13±5.61 | 12.91±3.82 |
| | 800 | 33.72±7.71 | 30.56±4.21 | 26.29±3.47 | 23.26±8.41 | 21.24±6.35 | 31.69±5.20 | 27.18±1.75 | 20.93±2.47 | 16.29±3.32 | 12.32±1.88 |
| GLU | 20 | 35.68±5.64 | 30.81±4.94 | 27.82±3.27 | 23.85±4.81 | 20.72±8.84 | 33.63±4.49 | 28.16±3.21 | 24.94±2.82 | 19.69±1.27 | 12.56±3.12 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 400 | 35.40±9.45 | 31.19±7.79 | 27.56±8.82 | 23.61±6.26 | 20.35±5.04 | 34.82±8.03 | 28.02±4.77 | 25.09±4.66 | 18.94±3.70 | 12.41±2.82 |
| | 800 | 35.97±6.31 | 31.52±4.43 | 27.53±4.45 | 23.94±7.05 | 20.58±8.52 | 34.58±4.01 | 27.91±2.11 | 25.26±2.42 | 19.76±3.68 | 12.88±2.33 |
| GLY | 50 | 34.94±5.55 | 31.57±9.46 | 27.65±4.03 | 24.64±8.88 | 19.72±3.57 | 32.94±3.35 | 28.16±3.41 | 23.58±5.45 | 15.91±1.09 | 12.69±3.01 |
| | 400 | 34.71±5.68 | 31.96±6.63 | 27.71±6.22 | 24.50±5.11 | 19.90±8.46 | 32.97±3.98 | 28.57±3.38 | 23.97±2.55 | 16.24±3.95 | 12.62±4.94 |
| | 800 | 34.87±6.08 | 31.79±4.71 | 26.82±4.28 | 24.71±3.99 | 19.61±6.77 | 32.53±3.51 | 27.91±5.26 | 23.83±3.18 | 16.22±3.66 | 12.55±1.33 |