*Electronic Supplementary Information*

# Gaining insights into nutrient and metal element distributions in radix *Angelicae sinensis* by mass spectrometry

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*Electronic Supplementary Information*

**Table S1:** Regression equations, determination coefficients ($R^2$), and linear ranges in μg•mL$^{-1}$ of 24 standard chemicals for quantitative analysis.

| No | Compound | Regression equation | Determination coefficient | Linear range/μg•mL$^{-1}$ |
|---|---|---|---|---|
| 1 | ferulic acid | $y = 24835x - 2879.1$ | 0.9991 | 0–10.00 |
| 2 | isoferulic acid | $y = 34979x - 4469.8$ | 0.9992 | 0.05–10.00 |
| 3 | vanillic acid | $y = 20205x + 63599$ | 0.9942 | 0–50.00 |
| 4 | caffeic acid | $y = 3824x + 2525.4$ | 0.9912 | 0.005–0.20 |
| 5 | thymine | $y = 16997x + 228.94$ | 0.9995 | 0–1.00 |
| 6 | guanine | $y = 16912x + 92.645$ | 0.9989 | 0–10.00 |
| 7 | adenine | $y = 40789x + 554.02$ | 0.9999 | 0–2.00 |
| 8 | cytidine | $y = 81618x + 1310.3$ | 0.9997 | 0–0.20 |
| 9 | γ-aminobutyric acid | $y = 7926x + 778.9$ | 0.9995 | 0.08–8.00 |
| 10 | *L*-hydroxyproline | $y = 64.461x + 3803.3$ | 0.9967 | 0–800.00 |
| 11 | *L*-glutamine | $y = 600000x + 200000$ | 0.9961 | 0–3.00 |
| 12 | *L*-asparagine | $y = 25429x + 5844.7$ | 0.9960 | 0–5.00 |
| 13 | *Z*-ligustilide | $y = 657.48x + 1668.9$ | 0.9989 | 0–10.00 |
| 14 | senkyunolide I | $y = 81742x + 27863$ | 0.9990 | 0–5.00 |
| 15 | glutamic acid | $y = 41405x + 1927.1$ | 0.9985 | 0–3.00 |
| 16 | *L*-arginine | $y = 166380x + 282.62$ | 0.9998 | 0–8.00 |
| 17 | *L*-phenylalanine | $y = 154005x + 660.58$ | 0.9986 | 0–1.00 |
| 18 | *L*-proline | $y = 2490.6x + 59.458$ | 0.9984 | 0–8.00 |
| 19 | *L*-valine | $y = 125545x + 852.05$ | 0.9990 | 0–8.00 |
| 20 | *L*-alanine | $y = 22407x + 2126.1$ | 0.9999 | 0–5.00 |
| 21 | *L*-leucine | $y = 12884x + 330.02$ | 0.9986 | 0.008–5.00 |
| 22 | *L*-tyrosine | $y = 124919x + 1189.2$ | 0.9994 | 0.005–0.50 |
| 23 | *L*-tryptophan | $y = 107038x + 9287.3$ | 0.9973 | 0–5.00 |
| 24 | *L*-ornithine | $y = 75319x + 12207$ | 0.9979 | 0–50.00 |

**Table S2:** Precision, repeatability and stability of the UPLC-MS/MS analysis of 24 standard chemicals and five individual aqueous extracts of one exemplary radix *Angelicae sinensis* powder sample, with respect to the relative standard deviation (RSD) of the corresponding integrated peak areas in percentage (%).

| Compound | Intraday precision / % | Three-day stability / % | Sample repeatability / % |
|---|---|---|---|
| ferulic acid | 1.68 | 2.16 | 1.81 |
| isoferulic acid | 2.09 | 2.17 | 2.41 |
| vanillic acid | 2.41 | 2.21 | 2.47 |
| caffeic acid | 1.97 | 2.43 | 0.55 |
| thymine | 1.91 | 1.89 | 2.06 |
| guanine | 1.17 | 1.26 | 1.30 |
| adenine | 2.26 | 1.69 | 1.80 |
| cytidine | 2.41 | 2.33 | 2.20 |
| *γ*-aminobutyric acid | 1.75 | 0.99 | 0.78 |
| *L*-hydroxyproline | 2.24 | 2.32 | 2.43 |
| *L*-glutamine | 2.38 | 2.19 | 1.01 |
| *L*-asparagine | 2.08 | 1.06 | 1.07 |
| *Z*-ligustilide | 2.25 | 1.67 | 1.85 |
| senkyunolide I | 2.06 | 1.17 | 1.31 |
| glutamic acid | 2.49 | 1.34 | 0.86 |
| *L*-arginine | 1.50 | 1.73 | 1.87 |
| *L*-phenylalanine | 1.94 | 1.09 | 1.00 |
| *L*-proline | 1.87 | 1.72 | 1.25 |
| *L*-valine | 2.25 | 1.46 | 1.00 |
| *L*-alanine | 1.75 | 1.96 | 2.11 |
| *L*-leucine | 2.15 | 1.91 | 1.61 |
| *L*-tyrosine | 2.38 | 1.57 | 1.73 |
| *L*-tryptophan | 1.25 | 1.22 | 1.34 |
| *L*-ornithine | 1.60 | 1.59 | 1.29 |

To inspect the stability, reproducibility and repeatability of the UPLC-MS/MS analysis, the mixture solution of 24 standard chemicals in 2 μL was successively tested six times on one day using a single aliquot (*i.e.*, $n$=6). At the same time, over a three-day period fresh aliquots of the mixture solution were removed from cold storage, and continuously analyzed six times every day (*i.e.*, $n$=18). On the other hand, five powder aliquots were sampled from one exemplary RAS material (*i.e.*, sample #1 in sample set1) by weighing 5.0 g for each, and the aqueous extraction was followed. All of the mixture standard solution and the sample extracted solutions were sequentially loaded to the UPLC-MS/MS for measurement. The area under the chromatographic peak acquired at quantitative production ion was integrated for each compound after necessary baseline correction, and the relative standard deviation between the peak areas was accordingly calculated.

**Table S3:** Recovery of 24 standard chemicals concerning their concentrations in aqueous extract of powder sample, spiking solution, really measured value, and relative standard deviation (RSD) in percentage (%). Recovery = $(c_{measured} - c_{sample})/c_{spiking} \times 100\%$.

| Compound | Sample concentration ($c_{sample}$)/mg•g$^{-1}$ | Spiking concentration ($c_{spiking}$)/mg•g$^{-1}$ | Measured concentration ($c_{measured}$)/mg•g$^{-1}$ | Recovery / % | Averaged recovery / % | RSD / % |
|---|---|---|---|---|---|---|
| ferulic acid | 1.410 | 0.70 | 2.144 | 104.86 | 103.75 | 1.78 |
| | 1.403 | 1.40 | 2.870 | 104.79 | | |
| | 1.402 | 2.10 | 3.536 | 101.62 | | |
| isoferulic acid | 0.241 | 0.12 | 0.357 | 96.67 | 97.91 | 1.10 |
| | 0.236 | 0.20 | 0.433 | 98.50 | | |
| | 0.235 | 0.28 | 0.511 | 98.57 | | |
| vanillic acid | 4.810 | 2.50 | 7.275 | 98.60 | 98.56 | 2.08 |
| | 4.802 | 3.50 | 8.179 | 96.86 | | |
| | 4.815 | 4.50 | 9.342 | 100.60 | | |
| caffeic acid | 0.326 | 0.15 | 0.477 | 100.67 | 99.06 | 2.03 |
| | 0.329 | 0.25 | 0.571 | 96.80 | | |
| | 0.327 | 0.35 | 0.676 | 99.41 | | |
| thymine | 0.038 | 0.02 | 0.058 | 100.00 | 98.06 | 1.77 |
| | 0.039 | 0.03 | 0.068 | 96.67 | | |
| | 0.038 | 0.04 | 0.077 | 97.50 | | |
| guanine | 0.387 | 0.20 | 0.589 | 101.00 | 98.61 | 2.10 |
| | 0.388 | 0.40 | 0.778 | 97.50 | | |
| | 0.388 | 0.60 | 0.972 | 97.33 | | |
| adenine | 0.038 | 0.02 | 0.057 | 95.00 | 96.39 | 1.32 |
| | 0.039 | 0.03 | 0.068 | 96.67 | | |
| | 0.039 | 0.04 | 0.078 | 97.50 | | |
| cytidine | 0.008 | 0.004 | 0.012 | 102.50 | 100.28 | 2.09 |
| | 0.008 | 0.006 | 0.014 | 98.33 | | |
| | 0.008 | 0.008 | 0.016 | 100.00 | | |
| *γ*-aminobutyric acid | 1.096 | 0.50 | 1.641 | 109.00 | 107.82 | 1.95 |
| | 1.093 | 1.00 | 2.147 | 105.40 | | |
| | 1.098 | 1.50 | 2.734 | 109.07 | | |
| *L*-hydroxyproline | 4.847 | 2.50 | 7.267 | 96.80 | 98.98 | 1.91 |
| | 4.931 | 4.50 | 9.433 | 100.04 | | |
| | 4.764 | 6.50 | 11.271 | 100.11 | | |
| *L*-glutamine | 1.805 | 0.75 | 2.548 | 99.07 | 101.22 | 1.88 |
| | 1.803 | 1.50 | 3.332 | 101.93 | | |
| | 1.802 | 2.25 | 4.112 | 102.67 | | |
| *L*-asparagine | 0.140 | 0.07 | 0.211 | 101.43 | 100.23 | 2.06 |
| | 0.142 | 0.14 | 0.279 | 97.86 | | |
| | 0.141 | 0.21 | 0.354 | 101.43 | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| | 2.637 | 1.30 | 3.979 | 103.23 | | |
| *Z*-ligustilide | 2.630 | 2.60 | 5.355 | 104.81 | 102.75 | 2.27 |
| | 2.633 | 3.90 | 6.541 | 100.21 | | |
| | 0.565 | 0.30 | 0.853 | 96.00 | | |
| senkyunolide I | 0.561 | 0.60 | 1.151 | 98.33 | 97.67 | 1.49 |
| | 0.567 | 0.90 | 1.455 | 98.67 | | |
| | 0.122 | 0.06 | 0.183 | 101.67 | | |
| glutamic acid | 0.121 | 0.12 | 0.244 | 102.50 | 100.84 | 2.19 |
| | 0.122 | 0.18 | 0.299 | 98.33 | | |
| | 1.132 | 0.50 | 1.646 | 102.80 | | |
| *L*-arginine | 1.138 | 1.00 | 2.145 | 100.70 | 103.19 | 2.62 |
| | 1.113 | 1.50 | 2.704 | 106.07 | | |
| | 0.164 | 0.08 | 0.248 | 105.00 | | |
| *L*-phenylalanine | 0.164 | 0.16 | 0.328 | 102.50 | 103.75 | 1.20 |
| | 0.163 | 0.24 | 0.412 | 103.75 | | |
| | 0.576 | 0.30 | 0.873 | 99.00 | | |
| *L*-proline | 0.572 | 0.60 | 1.185 | 102.17 | 101.09 | 1.79 |
| | 0.577 | 0.90 | 1.496 | 102.11 | | |
| | 0.191 | 0.10 | 0.292 | 101.00 | | |
| *L*-valine | 0.192 | 0.20 | 0.391 | 99.50 | 100.94 | 1.40 |
| | 0.192 | 0.30 | 0.499 | 102.33 | | |
| | 2.070 | 1.00 | 3.102 | 103.20 | | |
| *L*-alanine | 2.090 | 2.00 | 4.175 | 104.25 | 102.51 | 2.12 |
| | 2.060 | 3.00 | 5.062 | 100.07 | | |
| | 0.198 | 0.10 | 0.299 | 101.00 | | |
| *L*-leucine | 0.197 | 0.20 | 0.403 | 103.00 | 101.89 | 1.00 |
| | 0.200 | 0.30 | 0.505 | 101.67 | | |
| | 0.064 | 0.03 | 0.095 | 103.33 | | |
| *L*-tyrosine | 0.063 | 0.06 | 0.124 | 101.67 | 102.78 | 0.94 |
| | 0.062 | 0.09 | 0.155 | 103.33 | | |
| | 0.568 | 0.25 | 0.815 | 98.80 | | |
| *L*-tryptophan | 0.566 | 0.50 | 1.078 | 102.40 | 99.91 | 2.16 |
| | 0.569 | 0.75 | 1.308 | 98.53 | | |
| | 1.534 | 0.75 | 2.304 | 102.67 | | |
| *L*-ornithine | 1.525 | 1.50 | 3.064 | 102.60 | 101.31 | 2.26 |
| | 1.533 | 2.25 | 3.753 | 98.67 | | |

To examine the recovery rate, a total of nine powder aliquots in three groups were first made from one single powder sample by weighing *ca*. 5.0 g for each. Each group was composed of three aliquots. Then, three different levels of each of 24 standard chemical solutions were individually spiked to the aliquots. Their aqueous solutions were prepared and tested for UPLC-MS/MS. The area under the chromatographic peak acquired at quantitative production ion was integrated after necessary baseline correction, and both the recoveries and relative standard deviations were accordingly calculated for each of 24 standard chemicals.

**Table S4:** ICP-MS instrumental operating parameters.

| Parameter | Value | Parameter | Value |
|---|---|---|---|
| Radio-frequency power/W | 1100 | Intercept the cone aperture/mm | 0.7 |
| Atomizing gas flow rate/(L•min$^{-1}$) | 0.9 | Sample depth/mm | 6.6 |
| Flow rate of plasma/(L•min$^{-1}$) | 11 | Pulsed voltage/V | 950 |
| Auxiliary gas flow/(L•min$^{-1}$) | 1 | Vacuum degree of analysis room/Pa | 0.00067 |
| Fog room | double access | Identify the valve | 15 |
| Atomizing chamber temperature/°C | 2 | Compensation standard for single bar | -17 |
| Sampling cone aperture/mm | 1.1 | Compensation standard for four-stage rods | 0 |

**Table S5:** AAS instrumental operating parameters.

| Element | Lamp current / mA | λ / nm | Pass band / nm | Flame type | Acetylene flow / L•min$^{-1}$ | Oxygen flow / L•min$^{-1}$ |
|---|---|---|---|---|---|---|
| Zn | 6 | 213.9 | 0.2 | air-acetylene | 1.2 | 6.5 |
| Fe | 8 | 248.3 | 0.2 | air-acetylene | 0.9 | 6.5 |
| Mn | 4 | 279.5 | 0.2 | air-acetylene | 1.0 | 6.5 |
| Mg | 4 | 285.2 | 0.5 | air-acetylene | 1.1 | 6.5 |
| Ca | 5 | 422.7 | 0.5 | air-acetylene | 1.4 | 6.5 |
| Na | 6 | 589.0 | 0.2 | air-acetylene | 1.1 | 6.5 |
| K | 5 | 766.5 | 0.5 | air-acetylene | 1.2 | 6.5 |

**Table S6:** 24 target compounds in aqueous extracts of radix *Angelicae sinensis* materials and corresponding fragment ions (*M*/*Z*), retention time (*Rt*) in the UPLC-MS/MS analysis in positive ion mode.

| No | Compound | Ion mode | Molecular mass | Fragment ions (*M*/*Z*) | *Rt*/min | Formula |
|---|---|---|---|---|---|---|
| 1 | ferulic acid | $[M+H]^+$ | 194 | 88.9/177.1 | 8.49 | $C_{10}H_{10}O_4$ |
| 2 | isoferulic acid | $[M+H]^+$ | 194 | 89.1/177.2 | 9.08 | $C_{10}H_{10}O_4$ |
| 3 | vanillic acid | $[M+H]^+$ | 168 | 93.2/151.3 | 5.71 | $C_8H_8O_4$ |
| 4 | caffeic acid | $[M+H]^+$ | 180 | 89.2/162.9 | 8.16 | $C_9H_8O_4$ |
| 5 | thymine | $[M+H]^+$ | 126 | 54.1/110.2 | 1.33 | $C_5H_6N_2O_2$ |
| 6 | guanine | $[M+H]^+$ | 151 | 110.3/135.0 | 0.81 | $C_5H_5N_5O$ |
| 7 | adenine | $[M+H]^+$ | 135 | 67.1/119.1 | 0.80 | $C_5H_5N_5$ |
| 8 | cytidine | $[M+H]^+$ | 243 | 95.2/112.2 | 0.79 | $C_9H_{13}N_3O_5$ |
| 9 | γ-aminobutyric acid | $[M+H]^+$ | 103 | 69.0/87.3 | 0.68 | $C_4H_9NO_2$ |
| 10 | *L*-hydroxyproline | $[M+H]^+$ | 131 | 68.1/86.0 | 0.70 | $C_5H_9NO_3$ |
| 11 | *L*-glutamine | $[M+H]^+$ | 146 | 65.1/93.1 | 20.5 | $C_5H_{10}N_2O_3$ |
| 12 | *L*-asparagine | $[M+H]^+$ | 132 | 87.0 | 0.61 | $C_4H_8N_2O_3$ |
| 13 | *Z*-ligustilide | $[M+H]^+$ | 190 | 115.1/173.2 | 18.25 | $C_{12}H_{14}O_2$ |
| 14 | senkyunolide I | $[M+H]^+$ | 224.2 | 207.0 | 10.00 | $C_{12}H_{16}O_4$ |
| 15 | glutamic acid | $[M+H]^+$ | 147 | 102.2/130.4 | 0.69 | $C_5H_9NO_4$ |
| 16 | *L*-arginine | $[M+H]^+$ | 174 | 70.1/130.2 | 0.64 | $C_6H_{14}N_4O_2$ |
| 17 | *L*-phenylalanine | $[M+H]^+$ | 165 | 120.1/103.3 | 2.06 | $C_9H_{11}NO_2$ |
| 18 | *L*-proline | $[M+H]^+$ | 115 | 70.1/130.2 | 0.71 | $C_5H_9NO_2$ |
| 19 | *L*-valine | $[M+H]^+$ | 117 | 55.2/72.1 | 0.81 | $C_5H_{11}NO_2$ |
| 20 | *L*-alanine | $[M+H]^+$ | 89 | 44.1/72.1 | 0.68 | $C_3H_7NO_2$ |
| 21 | *L*-leucine | $[M+H]^+$ | 131 | 86.4 | 1.20 | $C_6H_{13}NO_2$ |
| 22 | *L*-tyrosine | $[M+H]^+$ | 181 | 136.1/165.2 | 1.07 | $C_9H_{11}NO_3$ |
| 23 | *L*-tryptophan | $[M+H]^+$ | 204 | 146.1/188.2 | 3.78 | $C_{11}H_{12}N_2O_2$ |
| 24 | *L*-ornithine | $[M+H]^+$ | 132 | 116.3 | 0.68 | $C_5H_{12}N_2O_2$ |

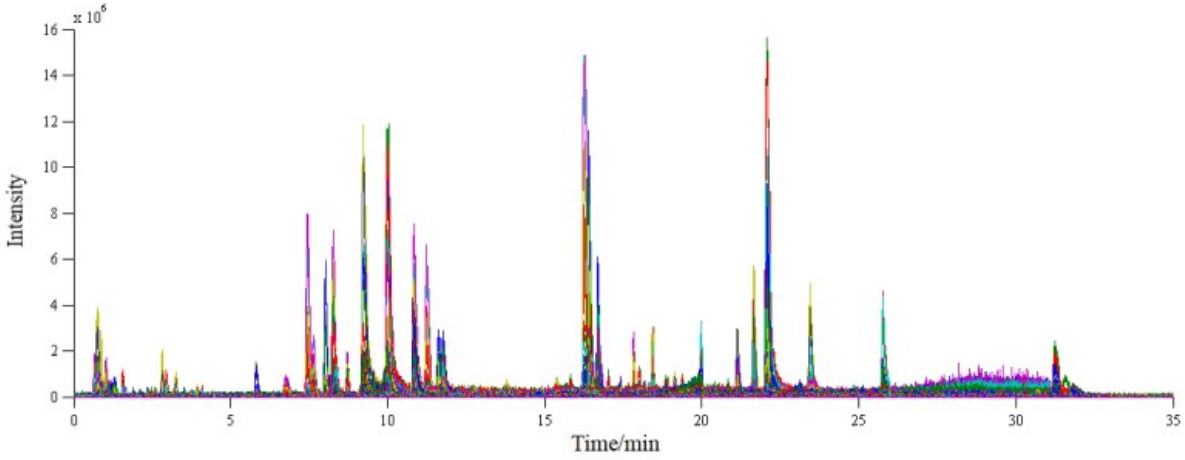


**Figure S1:** Original UPLC-MS/MS chromatograms acquired in the positive ion mode from exemplary aqueous extract solution of one radix *Angelicae sinensis* powder in sample set1.

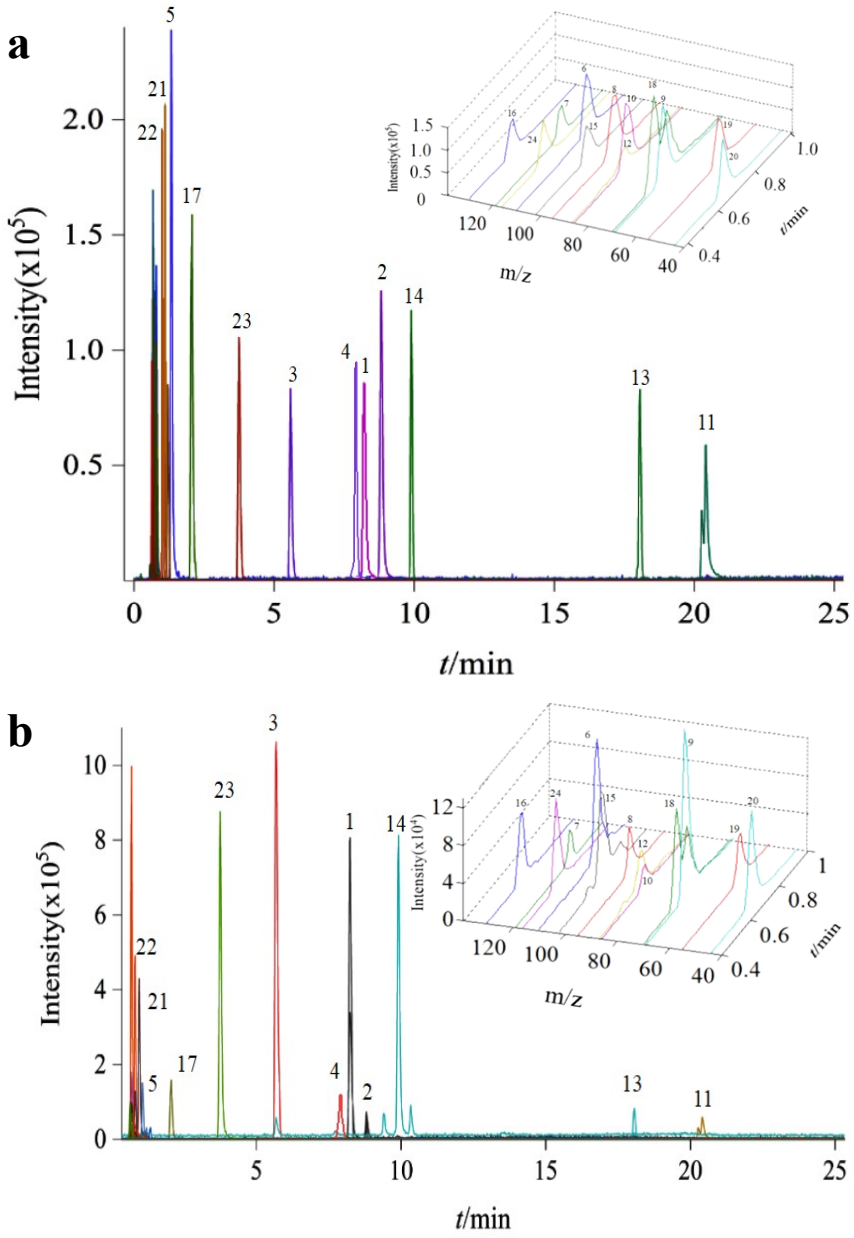


**Figure S2:** Chromatograms acquired at the individual quantitative production ions in the positive ion mode from (**a**) the solutions of 24 standard chemicals and (**b**) the exemplary aqueous extract solution of one radix *Angelicae sinensis* powder in sample set1.

1–ferulic acid, 2–isoferulic acid, 3–vanillic acid, 4–caffeic acid, 5–thymine, 6–guanine, 7–adenine, 8–cytidine, 9–*γ*-aminobutyric acid, 10–*L*-hydroxyproline, 11–*L*-glutamine, 12–*L*-asparagine, 13–*Z*-ligustilide, 14–senkyunolide I, 15–glutamic acid, 16–*L*-arginine, 17–*L*-phenylalanine, 18–*L*-proline, 19–*L*-valine, 20–*L*-alanine, 21–*L*-leucine, 22–*L*-tyrosine, 23–*L*-tryptophan, 24–*L*-ornithine.

**Table S7:** Determination (in mg•g$^{-1}$) of 24 target nutrient compounds in aqueous extracts of 287 radix *Angelicae sinensis* materials in the sample set1 originated from three provincial origins of Gansu (A), Qinghai (B) and Yunnan (C), together with the corresponding values of mean and standard deviation (STD).

| Class | No. | Compound | Content / mg•g$^{-1}$ | mean / mg•g$^{-1}$ | | | STD |
|---|---|---|---|---|---|---|---|
| | | | | A | B | C | mg•g$^{-1}$ |
| Organic acids | 1 | **ferulic acid** | 0.104–7.314 | 0.359 | 0.541 | 1.474 | 1.123 |
| | 2 | isoferulic acid | 0.111–0.791 | 0.156 | 0.183 | 0.275 | 0.136 |
| | 3 | vanillic acid | 0.004–29.080 | 3.798 | 3.818 | 5.408 | 3.370 |
| | 4 | caffeic acid | 0.010–7.476 | 0.569 | 0.335 | 0.667 | 0.769 |
| Amino acids | 5 | *L*-arginine | 0.000–2.543 | 0.678 | 0.218 | 0.683 | 0.643 |
| | 6 | *L*-phenylalanine | 0.000–0.461 | 0.065 | 0.054 | 0.055 | 0.064 |
| | 7 | *L*-proline | 0.001–4.679 | 0.781 | 0.409 | 0.911 | 0.881 |
| | 8 | *L*-valine | 0.000–1.059 | 0.059 | 0.109 | 0.045 | 0.107 |
| | 9 | *L*-alanine | 0.001–2.303 | 0.539 | 0.469 | 0.602 | 0.498 |
| | 10 | *L*-leucine | 0.000–3.897 | 0.095 | 0.119 | 0.200 | 0.327 |
| | 11 | *L*-tyrosine | 0.000–0.282 | 0.055 | 0.046 | 0.048 | 0.051 |
| | 12 | ***L*-tryptophan** | 0.210–1.967 | 0.599 | 0.868 | 1.145 | 0.369 |
| | 13 | *L*-ornithine | 0.003–24.842 | 4.376 | 1.495 | 3.937 | 5.037 |
| | 14 | *L*-glutamine | 0.142–2.250 | 1.000 | 0.821 | 0.786 | 0.561 |
| | 15 | *L*-hydroxyproline | 0.021–349.856 | 29.447 | 15.239 | 16.313 | 32.000 |
| | 16 | *L*-asparagine | 0.001–1.793 | 0.375 | 0.173 | 0.237 | 0.375 |
| | 17 | glutamic acid | 0.000–1.538 | 0.181 | 0.099 | 0.189 | 0.226 |
| | 18 | *γ*-aminobutyric acid | 0.002–6.966 | 0.994 | 0.630 | 1.173 | 1.190 |
| Nucleosides | 19 | thymine | 0.001–0.127 | 0.017 | 0.015 | 0.011 | 0.020 |
| | 20 | guanine | 0.005–6.097 | 0.661 | 0.265 | 0.726 | 0.748 |
| | 21 | adenine | 0.000–1.387 | 0.068 | 0.029 | 0.089 | 0.117 |
| | 22 | cytidine | 0.001–7.536 | 0.281 | 0.204 | 0.204 | 0.542 |
| Phthalides | 23 | ***Z*-ligustilide** | 0.016–3.502 | 1.312 | 1.663 | 1.575 | 0.597 |
| | 24 | **senkyunolide I** | 0.001–2.597 | 0.587 | 0.662 | 0.875 | 0.444 |

**Table S8:** Result of Kruskal-Wallis *H* test and post-hoc multiple comparison of the content of 24 nutrients in aqueous extracts of 241 normal radix *Angelicae sinensis* batches in the sample set1 originated from three provincial origins of Gansu (A), Qinghai (B) and Yunnan (C).

| Compound | *H* value | *P* value | Adjusted *P* value (Bonferroni) | | |
|---|---|---|---|---|---|
| | | | A *vs.* B | A *vs.* C | B *vs.* C |
| ferulic acid | 20.036 | <0.001*** | 0.015* | <0.001*** | 0.589 |
| **isoferulic acid** | 28.995 | <0.001*** | 0.002** | 0.001** | <0.001*** |
| vanillic acid | 22.079 | <0.001*** | 0.238 | <0.001*** | 0.027** |
| guanine | 38.982 | <0.001*** | <0.001*** | 0.427 | <0.001*** |
| adenine | 13.065 | 0.001*** | 0.008** | 0.844 | 0.002** |
| cytidine | 7.978 | 0.019* | 0.015* | 1.000 | 0.180 |
| γ-aminobutyric acid | 11.039 | 0.004** | 0.037* | 0.516 | 0.004** |
| *L*-hydroxyproline | 8.026 | 0.018* | 0.016* | 0.629 | 0.698 |
| *L*-asparagine | 6.778 | 0.034* | 0.030* | 1.000 | 0.239 |
| *Z*-ligustilide | 9.984 | 0.007** | 0.032* | 0.034* | 1.000 |
| senkyunolide I | 18.958 | <0.001*** | 0.071 | <0.001*** | 0.216 |
| glutamic acid | 18.911 | <0.001*** | <0.001*** | 0.261 | 0.123 |
| *L*-arginine | 32.436 | <0.001*** | <0.001*** | 1.000 | <0.001*** |
| *L*-phenylalanine | 10.883 | 0.004** | 0.003** | 0.792 | 0.257 |
| *L*-proline | 35.525 | <0.001*** | <0.001*** | 1.000 | <0.001*** |
| *L*-alanine | 27.840 | <0.001*** | <0.001*** | 1.000 | <0.001*** |
| *L*-tyrosine | 7.041 | 0.030* | 0.034* | 0.407 | 1.000 |
| ***L*-tryptophan** | 83.197 | <0.001*** | <0.001*** | <0.001*** | 0.028 |
| *L*-ornithine | 25.361 | <0.001*** | <0.001*** | 1.000 | 0.001** |
| caffeic acid | 4.949 | 0.084 | – | – | – |
| thymine | 0.863 | 0.649 | – | – | – |
| *L*-glutamine | 4.261 | 0.119 | – | – | – |
| *L*-valine | 2.362 | 0.307 | – | – | – |
| *L*-leucine | 2.398 | 0.301 | – | – | – |

Note: *$P < 0.05$ for statistically significant differences in the nutrient content among the batches across three origins, **$P < 0.01$ for highly significant differences, and ***$P < 0.001$ for extremely significant differences.

The distribution of the IBR values of the content responses of 24 nutrients of 241 radix *Angelicae sinensis* materials in the sample set1 was visualized in histogram for each class of 132 A-batches, 59 B-batches and 50 C-batches, respectively (Figure S3). It was pronounced that the IBR values were not normally distributed. Therefore, excluding 46 abnormal samples, Kruskal-Wallis *H* test and post-hoc multiple comparison were carried out on the IBR values. The comparison of the IBR distributions unraveled that: (i) there presented significant differences in content response between the A-batches, B-batches and C-batches; (ii) the C-batches had larger IBRs in terms of its median value of 9.86, than those of both A-batches (with IBR median = 5.52) and B-batches (with IBR median =2.59). The $25^{th}$–$75^{th}$ percentile ranges of IBR values were 2.41–9.99 for A-batches, 0.91–7.26 for B-batches, 5.48–16.76 for C-batches, respectively.

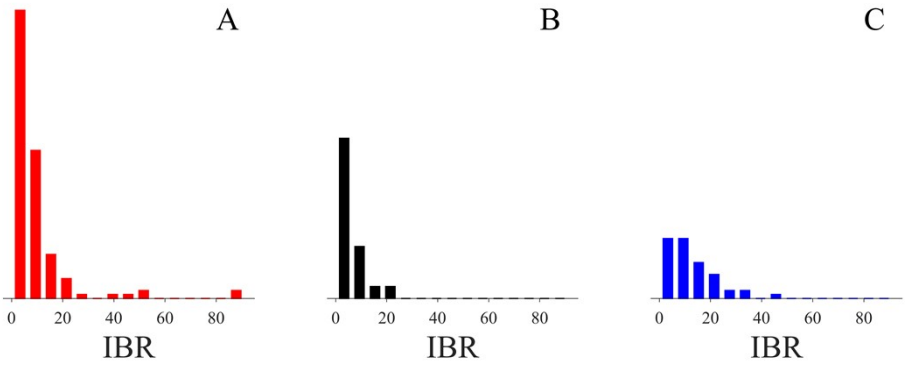


**Figure S3:** Distributions of the IBR values calculated from the content responses of 24 nutrients of 241 radix *Angelicae sinensis* materials in sample set1 originated from three geographic origins of Gansu (A), Qinghai (B) and Yunnan (C).

**Table S9:** Calibrations of 15 metal elements resulted from ICP-MS and AAS measurements ($n$=3)

| Element | Regression equation | Determination coefficient ($R^2$) | Linear range/μg•L$^{-1}$ | Limit of detection (LOD) /μg•L$^{-1}$, ($n$=15) |
|---|---|---|---|---|
| **ICP-MS Method** | | | | |
| Pb | y=9641.8x | 1.0000 | 0–200 | 0.0213 |
| Cd | y=994.1x | 0.9998 | 0–200 | 0.0196 |
| As | y=770.2x | 0.9996 | 0–200 | 0.0168 |
| Hg | y=1123.6x | 0.9998 | 0–200 | 0.0215 |
| Sb | y=3144.2x | 1.0000 | 0–200 | 0.0189 |
| Ni | y=1734.1x | 1.0000 | 0–200 | 0.0176 |
| Cu | y=3887.3x | 1.0000 | 0–200 | 0.0241 |
| Cr | y=6494.8x | 0.9988 | 0–200 | 0.0192 |
| **AAS Method** | | | | |
| Zn | y=0.0857x+0.2060 | 0.9978 | 500–2500 | 10 |
| Fe | y=0.0426x+0.0109 | 0.9986 | 1000–5000 | 18 |
| Mn | y=0.0955x+0.0130 | 0.9982 | 200–2500 | 11 |
| Mg | y=0.2659x+0.1035 | 0.9992 | 500–2500 | 3 |
| Ca | y=0.0283x+0.0020 | 0.9996 | 1000–5000 | 11 |
| Na | y=0.1970x+0.1962 | 0.9994 | 500–2500 | 12 |
| K | y=0.1156x+0.0769 | 0.9984 | 500–2500 | 15 |

The ICP-MS and AAS data were collected in triplicate experimental runs ($n$=3), and the mean values were subsequently calculated for each of both standard and digested solutions, and used for the quantitative calibration and prediction. Meanwhile, the limits of detection (LODs) were estimated as triple standard deviation of the signal acquired from 15 independently prepared reagent blanks ($n$=15). The linear ranges were also individually computed, and all seemed satisfactory. In order to validate this testing method, a reference material of CRM GSB-26-celery (GBW 09607) was used, as received from the Institute of Geophysical and Geochemical Exploration (IGGE), Chinese Academy of Geological Sciences, China. As a result, the ultimate determinations of the celery by such an ICP-MS and AAS method were in good agreement with the certified reference values (data not shown), which indicated that the precision of the present element quantitative analysis was acceptable.

**Table S10:** Kruskal-Wallis *H* test result for the contents of 14 metals in the RAS materials of the sample set2 originated from ten planting origins of Gansu.

| Element | *P* value | Element | *P* value |
|---|---|---|---|
| Mg | 0.057 | Cu | 0.891 |
| Ca | 0.299 | Cr | 0.121 |
| K | ***0.026*** | Pb | ***0.027*** |
| Na | ***0.021*** | Cd | 0.835 |
| Fe | 0.308 | As | ***0.039*** |
| Zn | 0.561 | Sb | 0.799 |
| Mn | 0.519 | Ni | ***0.043*** |