

Table S1. Source merchant and lot number information of Xiaochaihu capsules.

| Lot number | Number | Source Merchant |
|------------|--------|---|
| 20200502 | S1 | Yunnan Yunlong Pharmaceutical CO., LTD. |
| 20190502 | S2 | |
| 20190701 | S3 | |
| 20200402 | S4 | |
| 20210201 | S5 | |
| 20210102 | S11 | |
| 20200202 | S12 | |
| 32008061 | S6 | Zhejiang Pralife Pharmaceutical CO., LTD |
| 32008291 | S7 | |
| 32009071 | S8 | |
| 32008281 | S9 | |
| 32008271 | S10 | |

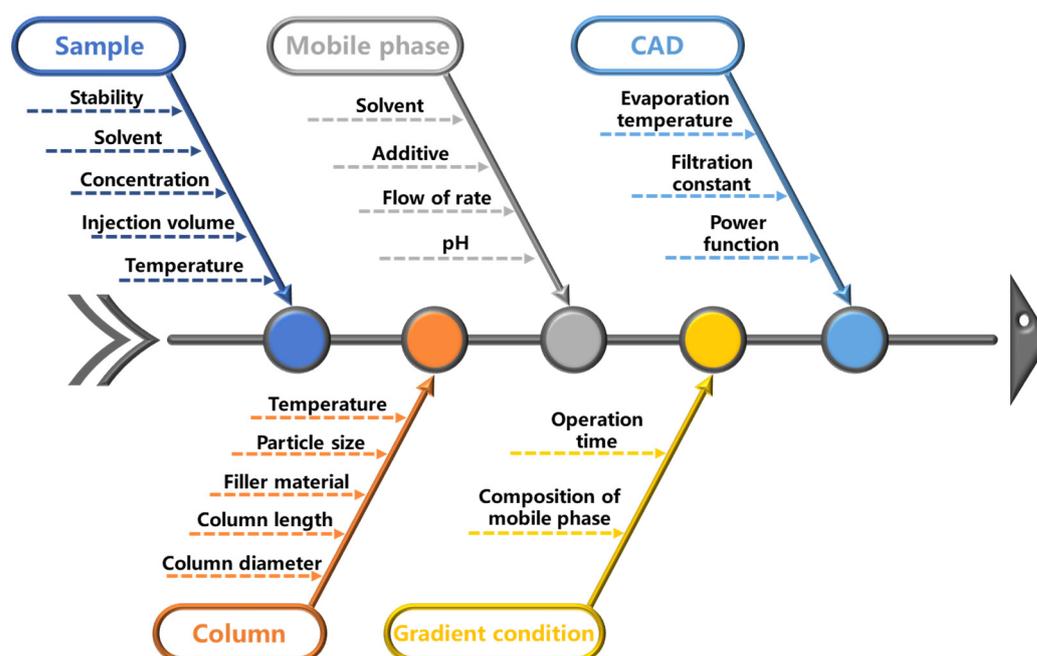


Figure S1. Fishbone diagram of potential critical method parameters.

Table S2. LC-Q-TOF-MS analysis of some sugar components of Xiaochaihu capsules.

| Peak number | t _R (min) | Measured value (m/z) | Ion type | Chemical formula | ppm | Name | CAS | Remarks |
|-------------|----------------------|----------------------|------------------------|--|-------|-----------|---------------|----------------|
| 2 | 12.889 | 151.0606 | [M- H] ⁻ | C ₅ H ₁₂ O ₅ | -3.66 | Ribitol | 488- 81-3 | Common peak |
| 3 | 14.194 | 179.0555 | [M- H] ⁻ | C ₆ H ₁₂ O ₆ | -3.18 | Fructose | 7660- 25-5 | Common peak |
| 5 | 17.020 | 179.0554 | [M- H] ⁻ | C ₆ H ₁₂ O ₆ | -4.13 | Glucose | 50-99- 7 | Common peak |
| 6 | 19.963 | 341.1085 | [M- H] ⁻ | C ₁₂ H ₂₂ O ₁₁ | -1.65 | Sucrose | 57-50- 1 | Common peak |
| 7 | 21.887 | 341.1079 | [M- H] ⁻ | C ₁₂ H ₂₂ O ₁₁ | -3.18 | Maltose | 133- 99-3 | |
| 8 | 24.011 | 503.1604 | [M- H] ⁻ | C ₁₈ H ₃₂ O ₁₆ | -2.89 | Raffinose | 512- 69-6 | |
| 9 | 26.870 | 665.2135 | [M- H] ⁻ | C ₂₄ H ₄₂ O ₂₁ | -2.00 | Stachyose | 470- 55-3 | Common peak |

Table S3. Fingerprint similarity evaluation results of 10 batches of Xiaochaihu capsule sample solution.

| Sample number | Similarity | Sample number | Similarity |
|---------------|------------|---------------|------------|
| S1 | 0.942 | S6 | 0.989 |
| S2 | 0.996 | S7 | 0.997 |
| S3 | 0.997 | S8 | 0.998 |
| S4 | 0.993 | S9 | 0.998 |
| S5 | 0.930 | S10 | 0.998 |

1. Method validation

1.1. Method validation of fingerprint

Injection precision was tested by consecutively analysing the same sample 6 times. Method repeatability was tested by preparing 6 parallel samples using the same procedure. For the

sample stability test, the samples were injected at 0, 4, 8, 12, 16, and 24 h. A reference peak was chosen. The results were expressed by the relative standard deviation (RSD) of the relative retention time and relative peak areas of each common peak with respect to the reference peaks.

1.2. Method validation of content determination

1.2.1. Linear investigation

A series of mixed standard solution with different concentration were injected for analysis. The peak area of each component was used as the vertical coordinate and the concentration was used as the horizontal coordinate to make the standard curve. The linear regression equation, analytical range, the limit of detection (LOD) and limit of quantification (LOQ) were calculated. Among them, the LOD was calculated as shown in Equation (S1), the LOQ was calculated as shown in Equation (S2).

$$LOD = \frac{3.3\sigma}{s} \text{ (S1)}$$

$$LOQ = \frac{10\sigma}{s} \text{ (S2)}$$

Where σ is the deviation of the response value, and s is the slope of the standard curve.

1.2.2. Injection precision

The experimental procedure referred to 1.1. The results were expressed by the RSD of the peak area and the retention time of each content determination component.

1.2.3. Method repeatability

The experimental procedure referred to 1.1. The results were expressed by the RSD of the content of each component.

1.2.4. Sample stability

The experimental procedure referred to 1.1. The results were expressed by the RSD of the content of each component.

1.2.5. Recovery

Recovery can represent the accuracy of the method. 9 sample solutions with known contents were divided into three groups. The concentration levels were set low, medium and high. Compared to the amount of the components in the sample solutions, the amount of the chemical reference substances added was about 0.8:1.0, 1.0:1.0 and 1.2:1.0, respectively. The

results were expressed by the average and RSD of each component recovery.

Table S4. The relative retention time of injection precision, method repeatability and sample stability.

| Peak number | Method repeatability | | Injection precision | | Sample stability | |
|-------------|----------------------|---------|---------------------|---------|------------------|---------|
| | Average | RSD (%) | Average | RSD (%) | Average | RSD (%) |
| 1 | 0.84 | 0.08 | 0.84 | 0.05 | 0.84 | 0.13 |
| 2 | 0.92 | 0.04 | 0.92 | 0.07 | 0.92 | 0.07 |
| 3 | 1.00 | 0.00 | 1.00 | 0.00 | 1.00 | 0.00 |
| 4 | 1.15 | 0.05 | 1.15 | 0.08 | 1.15 | 0.07 |
| 5 | 1.26 | 0.08 | 1.26 | 0.05 | 1.26 | 0.13 |
| 6 | 1.52 | 0.06 | 1.52 | 0.09 | 1.52 | 0.17 |
| 9 | 2.06 | 0.04 | 2.06 | 0.09 | 2.06 | 0.19 |

Table S5. The relative peak areas of each common peak of injection precision, method repeatability and sample stability.

| Peak number | Method repeatability | | Injection precision | | Sample stability | |
|-------------|----------------------|---------|---------------------|---------|------------------|---------|
| | Average | RSD (%) | Average | RSD (%) | Average | RSD (%) |
| 1 | 0.03 | 3.75 | 0.03 | 2.41 | 0.03 | 1.32 |
| 2 | 0.33 | 0.74 | 0.33 | 0.91 | 0.33 | 1.18 |
| 3 | 1.00 | 0.00 | 1.00 | 0.00 | 1.00 | 0.00 |
| 4 | 0.01 | 2.41 | 0.01 | 3.42 | 0.01 | 3.05 |
| 5 | 0.09 | 3.14 | 0.09 | 2.76 | 0.09 | 2.71 |
| 6 | 0.53 | 0.67 | 0.53 | 0.86 | 0.54 | 1.06 |
| 9 | 0.16 | 1.80 | 0.17 | 1.99 | 0.17 | 2.28 |

Table S6. The linear equation, coefficient of determination and analytical range of each component.

| Name | Linear equation | R ² | analytical range (mg/mL) | LOD (mg/mL) | LOQ (mg/mL) |
|-----------|-----------------|----------------|--------------------------|-------------|-------------|
| Ribitol | y = 179.59x | 0.9999 | 0.06512~0.1172 | 0.002042 | 0.006805 |
| Fructose | y = 150.22x | 1 | 0.2189~0.3941 | 0.004787 | 0.015957 |
| Sucrose | y = 120.84x | 1 | 0.1636~0.2944 | 0.009466 | 0.031553 |
| Stachyose | y = 87.067x | 0.9999 | 0.06767~0.1218 | 0.004105 | 0.013684 |

Table S7. Injection precision of the peak area.

| Name | 1 | 2 | 3 | 4 | 5 | 6 | Average | RSD (%) |
|-----------|--------|--------|--------|--------|--------|--------|---------|---------|
| Ribitol | 16.550 | 16.613 | 16.339 | 16.424 | 16.408 | 16.384 | 16.453 | 0.642 |
| Fructose | 50.974 | 49.866 | 49.149 | 49.491 | 50.112 | 49.681 | 49.879 | 1.260 |
| Sucrose | 27.144 | 26.346 | 26.047 | 26.779 | 26.412 | 26.428 | 26.526 | 1.440 |
| Stachyose | 8.259 | 8.451 | 8.491 | 8.297 | 8.288 | 8.366 | 8.359 | 1.135 |

Table S8. Injection precision of retention time.

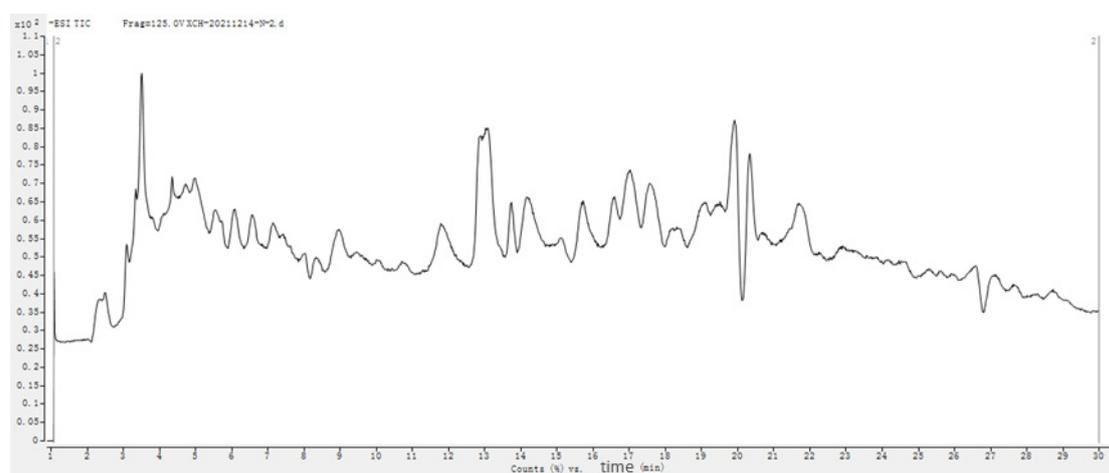
| Name | 1 (min) | 2 (min) | 3 (min) | 4 (min) | 5 (min) | 6 (min) | Average (min) | RSD (%) |
|-----------|---------|---------|---------|---------|---------|---------|---------------|---------|
| Ribitol | 12.009 | 12.012 | 12.019 | 12.023 | 12.041 | 12.041 | 12.024 | 0.116 |
| Fructose | 12.987 | 13.001 | 13.018 | 13.021 | 13.020 | 13.020 | 13.011 | 0.108 |
| Sucrose | 19.721 | 19.723 | 19.729 | 19.725 | 19.731 | 19.726 | 19.726 | 0.019 |
| Stachyose | 26.766 | 26.771 | 26.772 | 26.773 | 26.776 | 26.779 | 26.773 | 0.017 |

Table S9. Method repeatability of content determination.

| Name | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 5 (%) | 6 (%) | Average (%) | RSD (%) |
|-----------|-------|-------|-------|-------|-------|-------|-------------|---------|
| Ribitol | 2.380 | 2.310 | 2.284 | 2.296 | 2.265 | 2.202 | 2.289 | 2.552 |
| Fructose | 8.572 | 8.326 | 8.294 | 8.230 | 8.143 | 8.072 | 8.273 | 2.108 |
| Sucrose | 5.616 | 5.541 | 5.489 | 5.459 | 5.474 | 5.329 | 5.485 | 1.737 |
| Stachyose | 2.380 | 2.412 | 2.320 | 2.319 | 2.385 | 2.304 | 2.353 | 1.886 |

Table S10. Sample stability of content determination.

| Name | 0h (%) | 4h (%) | 8h (%) | 12h (%) | 16h (%) | 24h (%) | Average (%) | RSD (%) |
|-----------|--------|--------|--------|---------|---------|---------|-------------|---------|
| Ribitol | 2.403 | 2.380 | 2.440 | 2.395 | 2.443 | 2.402 | 2.411 | 0.025 |
| Fructose | 8.539 | 8.572 | 8.890 | 8.506 | 8.703 | 8.532 | 8.624 | 0.148 |
| Sucrose | 5.774 | 5.616 | 5.907 | 5.748 | 5.798 | 5.765 | 5.768 | 0.093 |
| Stachyose | 2.417 | 2.380 | 2.447 | 2.464 | 2.485 | 2.435 | 2.438 | 0.037 |

**Figure S2.** The total ion chromatogram of LC-Q-TOF-MS.