

Supplementary information

Raman mapping as quantitative tool for visual analysis of mineral

Chinese medicine

Qian Xu, Jie Chen, Yingmeng Li, Yi Zhou, Yang Jin, Liying Zhang,* Shuhu Du

School of Pharmacy, Nanjing Medical University, Nanjing, Jiangsu 211166, China

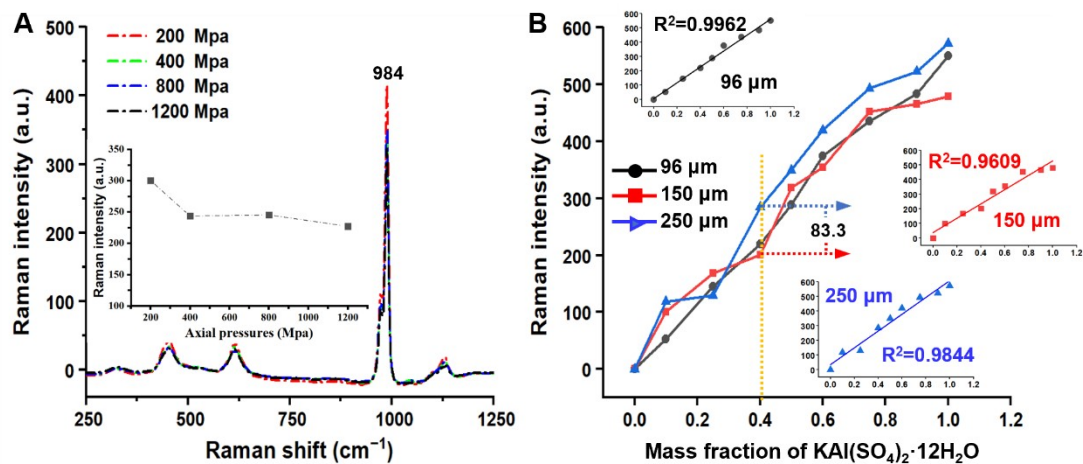


Fig. S1 (A) Raman spectra of the test tablets prepared by different pressures (200, 400, 800 and 1200 Mpa). Inset: the change of Raman intensity (at 984 cm⁻¹) with the axial pressures. Mass ratios of KAl(SO₄)₂·12H₂O to NaCl is 1:1 and particle sizes are ~96 μm. (B) Evolution of Raman intensities (at 984 cm⁻¹) with the mass fractions of KAl(SO₄)₂·12H₂O under different particle sizes (black circle, 96 μm; red square, 150 μm; blue triangle, 250 μm). The insets: the corresponding linear correlation of Raman intensity (at 984 cm⁻¹) with the mass fraction of KAl(SO₄)₂·12H₂O from 0% to 100%.

Operation mechanism of imaging algorithm of three substances

In the experiment, all the Raman spectra data obtained by Raman mapping were used to represent the distribution of their components in the tablets by running the Matrix Laboratory (Matlab) code. The code running detail by Matlab (R2021a) is as follows: take the maximum values of characteristic peaks at the displacement of 984 cm⁻¹ and 1048 cm⁻¹ in the whole data set in the whole data set, and then divide the characteristic peaks 984 cm⁻¹ and 1048 cm⁻¹ on each spectrum by two different ratios, and compare this ratio with the fixed threshold. The characteristic peak whose proportion is greater than the threshold is calculated as the compound, which represents in this region. According to the corresponding proportion, it is calculated as the representative composition if the proportion of the two characteristic peaks is greater than the threshold in this region, and when the proportion of the two characteristic peaks is lower than the threshold, it is the auxiliary material.

The Matlab imaging algorithms was also validated by commercially available drug, *Anfen Ka Pilin Pian*, which contains a combination of acetaminophen, aspirin,

and caffeine. For Raman mapping, 40,000 spectra were collected from the tablet. The visual analysis data is shown in Fig. S2.

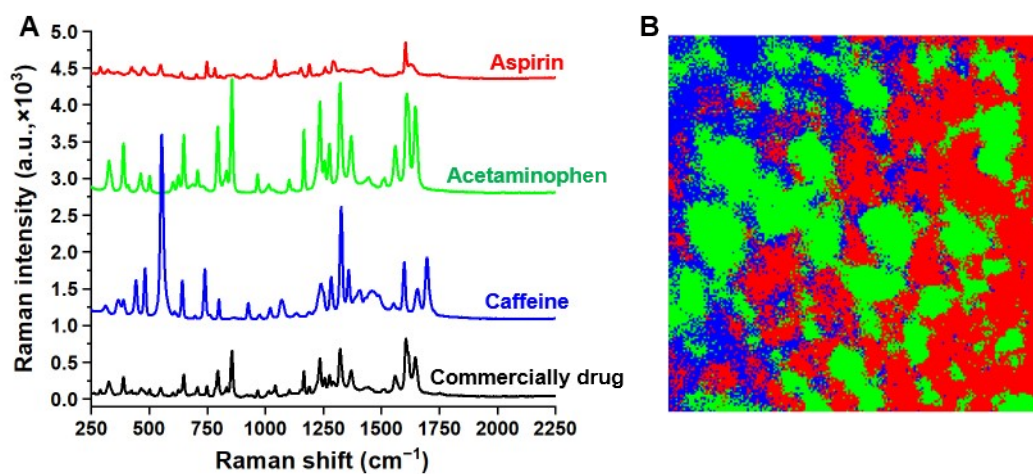


Fig. S2 (A) Raman spectra of aspirin, acetaminophen, caffeine and the commercially drug (*Anfen Ka Pilin Pian*). (B) Pseudo-colored image for the visual distribution of acetaminophen (green), aspirin (red) and other substances including caffeine (blue).

Table S1. Precision of the proposed method.

Number ^a	984/cm ⁻¹ intensity	1048/cm ⁻¹ intensity	I ₉₈₄ / I ₁₀₄₈ values	RSD (%) (intra-day, n = 6)
1	139.34	478.20	0.2914	
2	135.81	475.61	0.2855	
3	135.72	476.23	0.2850	1.11
4	138.79	477.69	0.2905	
5	138.66	477.36	0.2905	
6	139.46	476.45	0.2927	

^aThe spectra were obtained from six points within the same tablet.

Table S2. Reproducibility of the proposed method.

Samples ^a	984/cm ⁻¹ intensity	1048/cm ⁻¹ intensity	I ₉₈₄ / I ₁₀₄₈ Values	RSD (%) (n = 6)
1	134.03	471.31	0.2844	
2	143.32	481.56	0.2976	
3	151.50	541.71	0.2797	4.47
4	152.48	530.92	0.2872	
5	132.80	472.45	0.2811	
6	152.54	588.01	0.2594	

^aSix batches of tablets were independently prepared and the corresponding Raman intensity ratios (I/I₀) obtained from the average spectra of the test tablets.

Table S3. Stability of the proposed method.

Time (min)	984/cm ⁻¹ intensity	1048/cm ⁻¹ intensity	I ₉₈₄ / I ₁₀₄₈ Values	RSD (%) (n = 6)
0	103.43	489.86	0.2111	
30	104.94	489.39	0.2144	
60	103.72	488.82	0.2121	2.17
90	109.93	495.61	0.2218	
120	108.80	494.91	0.2198	
180	110.25	498.95	0.2209	

Table S4. Recoveries of aluminum potassium sulfate dodecahydrate-spiked samples (n=3).

Sample	Content (mg)	Added (mg)	Found (mg)	Recovery (%)	RSD (%)
1	20.4	16.2	36.4	99.0	0.54
	20.3	16.1	36.3	99.5	
	20.6	16.4	37.0	100.1	
2	20.1	20.4	40.8	101.6	2.2
	20.3	20.7	40.4	97.3	
	20.6	20.8	41.3	99.8	
3	20.3	23.8	44.3	100.8	1.3
	20.0	23.6	43.2	98.2	
	20.2	24.1	44.1	99.1	