# Preparation of Theophylline-Benzoic Acid Cocrystal and <br> On-Line Monitoring of Cocrystallization Process in 

## Solution by Raman Spectroscopy

Yaohui Huang ${ }^{1}$, Ling Zhou ${ }^{1, *}$, Wenchao Yang ${ }^{1}$, Yang Li ${ }^{1}$, Yongfan Yang ${ }^{1}$, Zaixiang Zhang ${ }^{1}$, Chang Wang ${ }^{1}$, Xia Zhang ${ }^{1}$ and Qiuxiang Yin ${ }^{1,2,3, *}$<br>1 State Key Laboratory of Chemical Engineering, School of Chemical Engineering and Technology, Tianjin University, Tianjin 300072, China;<br>2 Collaborative Innovation Center of Chemical Science and Engineering (Tianjin), Tianjin 300072, China;<br>${ }^{3}$ Key Laboratory Modern Drug Delivery and High Efficiency in Tianjin University, Tianjin 300072, China;

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## Appendix A:

Figure S1. (a) The variation of Raman spectra at $1270-1360 \mathrm{~cm}^{-1}$; (b) The change of relative peak intensity of 1323/1331 cm ${ }^{-1}$ in TP-BA cocrystal formation in slurry crystallization at 298.15 K .

Figure S2. (a) The variation of Raman spectra at 1120-1200 $\mathrm{cm}^{-1}$; (b) The change of relative peak intensity of $1161 / 1171 \mathrm{~cm}^{-1}$ in TP-BA cocrystal formation in slurry crystallization at 298.15 K

Figure S3. (a) The variation of Raman spectra at $890-940 \mathrm{~cm}^{-1}$; (b) The change of relative peak intensity of 918/925 $\mathrm{cm}^{-1}$ in TP-BA cocrystal formation in slurry crystallization at 298.15 K

Figure S4. HPLC chromatograms of slurry crystallization products in Table 3: $\exp 1$ (a); $\exp 2$ (b); $\exp 3$
(c); $\exp 4$ (d) and cooling crystallization product (e)

## Appendix B:

Table S1 Information about Raman spectra in the range of $1640-1720 \mathrm{~cm}^{-1}$ in Figure 5 a

Table S2 Information about Raman spectra in the range of $1270-1360 \mathrm{~cm}^{-1}$ in Figure S1a

Table S3 Information about Raman spectra in the range of 1120-1200 $\mathrm{cm}^{-1}$ in Figure S2a

Table S4 Information about Raman spectra in the range of $890-940 \mathrm{~cm}^{-1}$ in Figure S3a

## Appendix A:



Figure S1. (a) The variation of Raman spectra at $1270-1360 \mathrm{~cm}^{-1}$; (b) The change of relative peak intensity of $1323 / 1331 \mathrm{~cm}^{-1}$ in TP-BA cocrystal formation in slurry crystallization at 298.15 K . The information about time interval of Raman spectra are listed in Table S2.


Figure S2. (a) The variation of Raman spectra at $1120-1200 \mathrm{~cm}^{-1}$; (b) The change of relative peak intensity of $1161 / 1171 \mathrm{~cm}^{-1}$ in TP-BA cocrystal formation in slurry crystallization at 298.15 K . The information about time interval of Raman spectra are listed in Table S3.


Figure S3. (a) The variation of Raman spectra at $890-940 \mathrm{~cm}^{-1}$; (b) The change of relative peak intensity of $918 / 925 \mathrm{~cm}^{-1}$ in TP-BA cocrystal formation in slurry crystallization at 298.15 K . The information about time interval of Raman spectra are listed in Table S4.


Figure S4. HPLC chromatograms of slurry crystallization products in Table 3: $\exp 1$ (a); $\exp 2$ (b); $\exp 3$ (c); $\exp 4$ (d) and cooling crystallization product (e)

## Appendix B:

Table S1 Information about Raman spectra in the range of $1640-1720 \mathrm{~cm}^{-1}$ in Figure 5 a

| Total spectra <br> number | Total recording time <br> $/ \min$ | Time point of first <br> spectra $/ \mathrm{min}$ | Time interval <br> $/ \mathrm{min}$ |
| :---: | :---: | :---: | :---: |
| 90 | 90 | 1 | 1 |

Table S2 Information about Raman spectra in the range of $1270-1360 \mathrm{~cm}^{-1}$ in Figure S1a

| Total spectra <br> number | Total recording time <br> $/ \min$ | Time point of first <br> spectra $/ \mathrm{min}$ | Time interval <br> $/ \mathrm{min}$ |
| :---: | :---: | :---: | :---: |
| 90 | 90 | 1 | 1 |

Table S3 Information about Raman spectra in the range of $1120-1200 \mathrm{~cm}^{-1}$ in Figure S2a

| Total spectra <br> number | Total recording time <br> $/ \min$ | Time point of first <br> spectra $/ \mathrm{min}$ | Time interval <br> $/ \mathrm{min}$ |
| :---: | :---: | :---: | :---: |
| 90 | 90 | 1 | 1 |

Table S4 Information about Raman spectra in the range of $890-940 \mathrm{~cm}^{-1}$ in Figure S3a

| Total spectra <br> number | Total recording time <br> $/ \min$ | Time point of first <br> spectra $/ \mathrm{min}$ | Time interval <br> $/ \mathrm{min}$ |
| :---: | :---: | :---: | :---: |
| 90 | 90 | 1 | 1 |


[^0]:    * Correspondence: zhouling@tju.edu.cn (L.Z.); qxyin@tju.edu.cn.(Q.X.Y.)

