Electronic Supplementary Information for

Polymorph Control of 5-Fluorouracil during Ball Milling Process

Fenghua Chen,[*,a, b] *Jie Fan,*[a] *Xiuzhi Chen,*[a] *Yanping Li,* [a] *Chengfeng Liang,* [a] *Shizhao Ren* [a] *and Rongrong Xue*[*,a, b]

[a] School of Resources and Chemical Engineering, Sanming University, Sanming 365004, Fujian, China.

[b] Fujian Engineering Research Center for Advanced Fluorine-containing Materials, Sanming 365004, Fujian, China.

Corresponding Authors
**(F. C.) E-mail: fenghuachen@fjsmu.edu.cn.*
**(R. X.) E-mail: rongrongxue@fjsmu.edu.cn.*

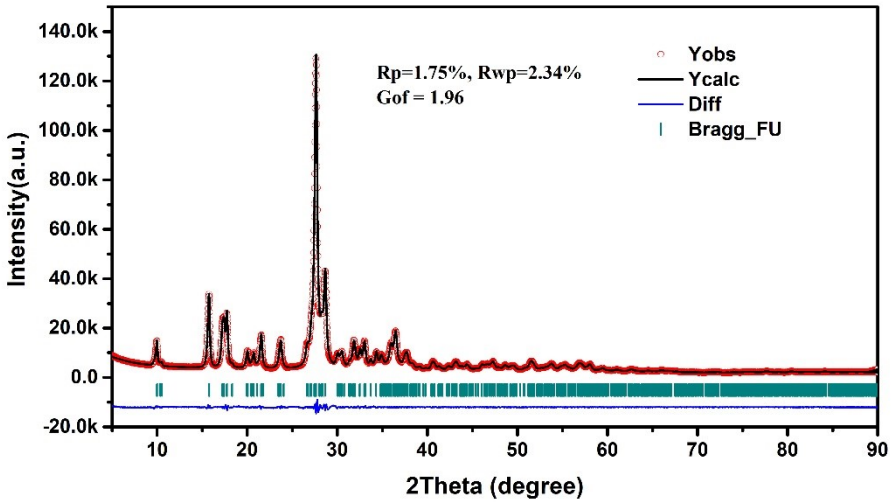

Figure S1. PXRD pattern of Form III and the simulated PXRD pattern obtained with the TOPAS academic and Le Bail method.

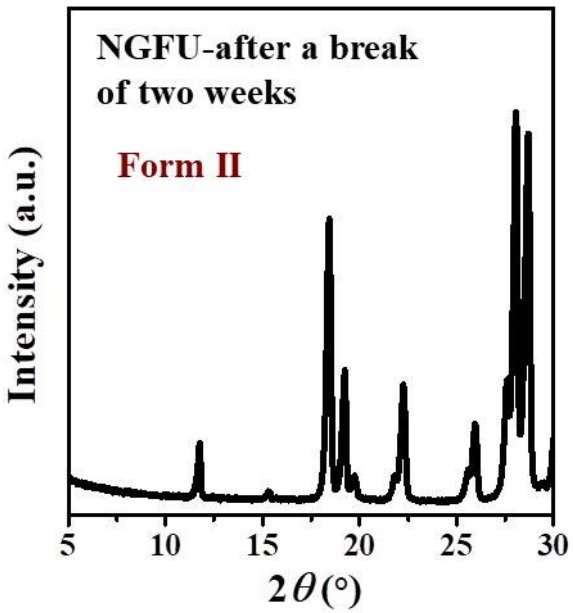

Figure S2. PXRD pattern of product obtained by neat grinding RFU once after a 2 week break in our laboratory.

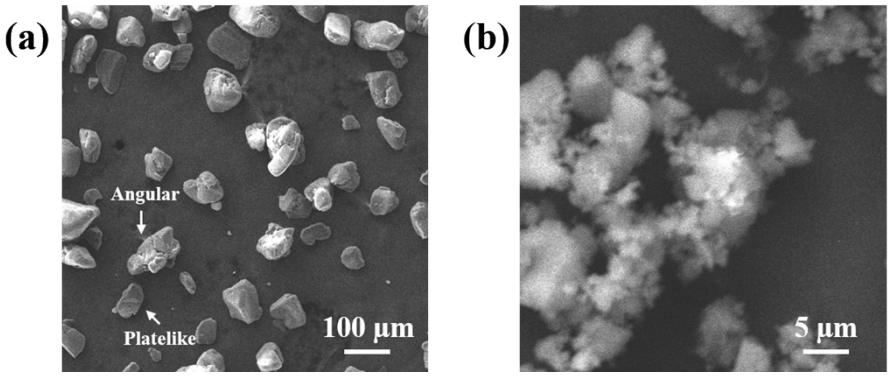

Figure S3. SEM images of (a) RFU and (b) Form II prepared through neat grinding RFU once. The particle size is significantly reduced after ball milling. RFU is angular and plate-like crystal with a size of tens of microns. Form II is composed of micron particles (a few microns) and particles with sizes lower than 1 µm.

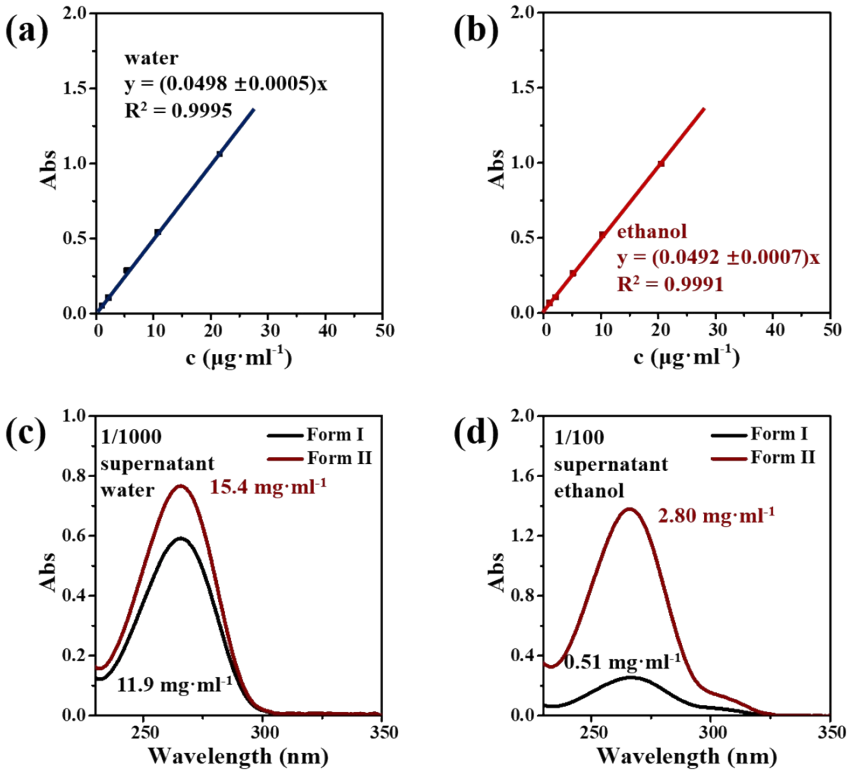

Figure S4. Working curves between absorption at 265 nm and the concentration of (a) aqueous solution or (b) ethanol solution of 5-FU; UV-Vis spectra of (c) 1000 times diluted supernatant of Form I or Form II water dispersion, (d) 100 times diluted supernatant of Form I or Form II ethanol dispersion. The similar working curves of 5-FU in aqueous and ethanol solutions indicate that the absorption coefficients of 5-FU in water and ethanol are extremely close.

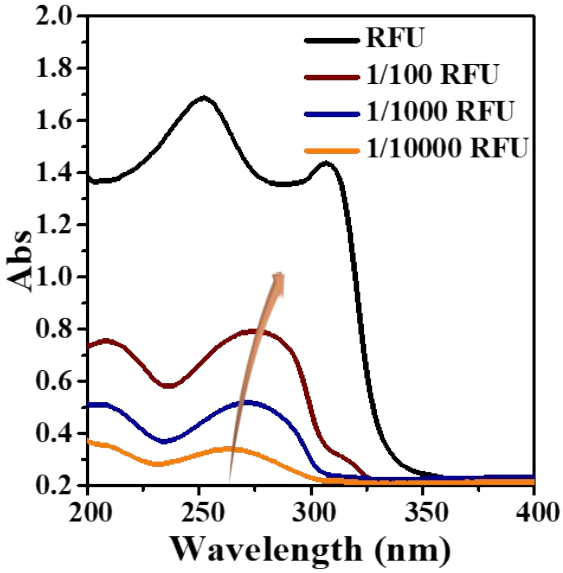

Figure S5. DRS spectra of RFU with different proportions of NaCl. Grinding and other sample preparation methods were not used here for prevention of damage to the solid structure of RFU. The positions and intensities of the DRS peaks are closely related to the content of 5-FU in the samples diluted with NaCl.