*Supporting information*

# Gefitinib salt/cocrystal with phenolic acids as promising solid−state approach to improve solubility

Yao Zou, [a] Xin Meng, [a] Baoxi Zhang,[a] Hongmei Yu, [a] Guorong He, [b] Ningbo Gong, *[a] Yang Lu, *[a] and Guanhua Du [b]

[a] *Beijing Key Laboratory of Polymorphic Drugs, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, China*

[b] *Beijing City Key Laboratory of Drug Target Identification and Drug Screening, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College. Beijing 100050, China.*

**Table and Figure of Contents**

**Table S1.** Hydrogen bond geometrical parameters of crystal structures.

| Connection | D···H/ Å | H···A/ Å | D···A/ Å | ∠(DHA)/ ° | Symmetry |
|---|---|---|---|---|---|
| | | | **GEF−3−HBA** | | |
| $N_1$–$H_1$···$O_4$ | 0.86 | 2.32 | 3.143 | 159 | [x, y, z] |
| $N_4$–$H_4$···$O_5$ | 1.04 | 1.54 | 2.575 | 172 | [x−1, y, z] |
| $O_6$–$H_6$···$N_3$ | 0.82 | 1.92 | 2.715 | 164 | [x, −y+3/2, z+1/2] |
| | | | **GEF−FA** | | |
| $N_1$–$H_1$···$O_6$ | 0.86 | 2.20 | 3.011 | 157 | [x, −y+1/2, z+1/2] |
| $N_4$–$H_4$···$O_7$ | 1.03 | 1.55 | 2.565 | 169 | [x, y, z] |
| $O_4$–$H_{4B}$···$N_3$ | 0.82 | 2.07 | 2.874 | 165 | [−x+1, −y+1, −z] |
| | | | **GEF−4−HBA** | | |
| $N_1$–$H_{1a}$···$O_4$ | 0.88 | 2.19 | 3.008 | 155 | [1+x, y−1, z] |
| $N_1$–$H_{1b}$···$O_6$ | 0.88 | 2.15 | 2.888 | 141 | [1−x, y−1, −z+1] |
| $O_5$–$H_{5b}$···$N_3$ | 0.84 | 1.68 | 2.492 | 161 | [−x, −y+2, −z+1] |
| $O_6$–$H_6$···$N_3$ | 0.84 | 1.91 | 2.667 | 149 | [x, y, z] |
| | | | **GEF−35DNB** | | |
| $N_1$–$H_1$···$O_6$ | 0.86 | 2.00 | 2.850 | 170 | [x, y, z] |
| $N_4$–$H_4$···$O_7$ | 0.98 | 1.72 | 2.678 | 166 | [x, y, z] |
| $O_{11}$–$H_{11A}$···$N_3$ | 0.82 | 1.72 | 2.505 | 158 | [x, y, z] |
| | | | **GEF−SA** | | |
| $N_{1A}$–$H_{1A}$···$O_{4C}$ | 0.86 | 1.99 | 2.818 | 160 | [x, y, z] |
| $N_{1B}$–$H_{1B}$···$O_{5C}$ | 0.86 | 2.00 | 2.832 | 162 | [x, y, z] |
| $N_{3B}$–$H_{3B}$···$O_{4A}$ | 0.86 | 1.84 | 2.700 | 174 | [1/2−x,1−y, −1/2+z] |
| $N_{4A}$–$H_{4A}$···$O_{5A}$ | 0.98 | 1.81 | 2.778 | 170 | [1−x, 1/2+y, 1/2−z] |
| $N_{4B}$–$H_{4B}$···$O_{4B}$ | 0.98 | 1.74 | 2.695 | 165 | [x, y, z] |
| $O_{5D}$–$H_{5D}$···$N_{3A}$ | 0.82 | 1.95 | 2.732 | 159 | [1/2+x, 3/2−y, −z] |
| $O_{6A}$–$H_{6A}$···$O_{5A}$ | 0.82 | 1.92 | 2.622 | 143 | [x, y, z] |
| $O_{6B}$–$H_{6B}$···$O_{5B}$ | 0.82 | 1.79 | 2.502 | 145 | [x, y, z] |
| $O_{6C}$–$H_{6C}$···$O_{5C}$ | 0.82 | 1.82 | 2.542 | 146 | [x, y, z] |
| $O_{6D}$–$H_{6D}$···$O_{4D}$ | 0.82 | 1.78 | 2.505 | 146 | [x, y, z] |

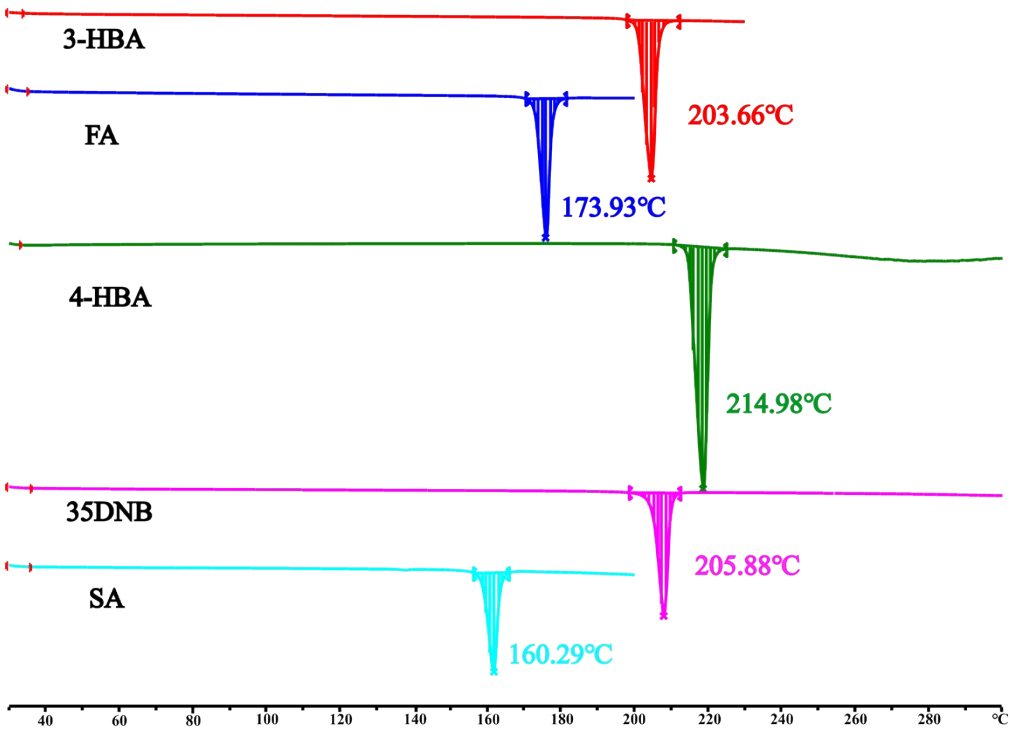


**Fig. S1** The DSC thermograms of CCFs used in this study.

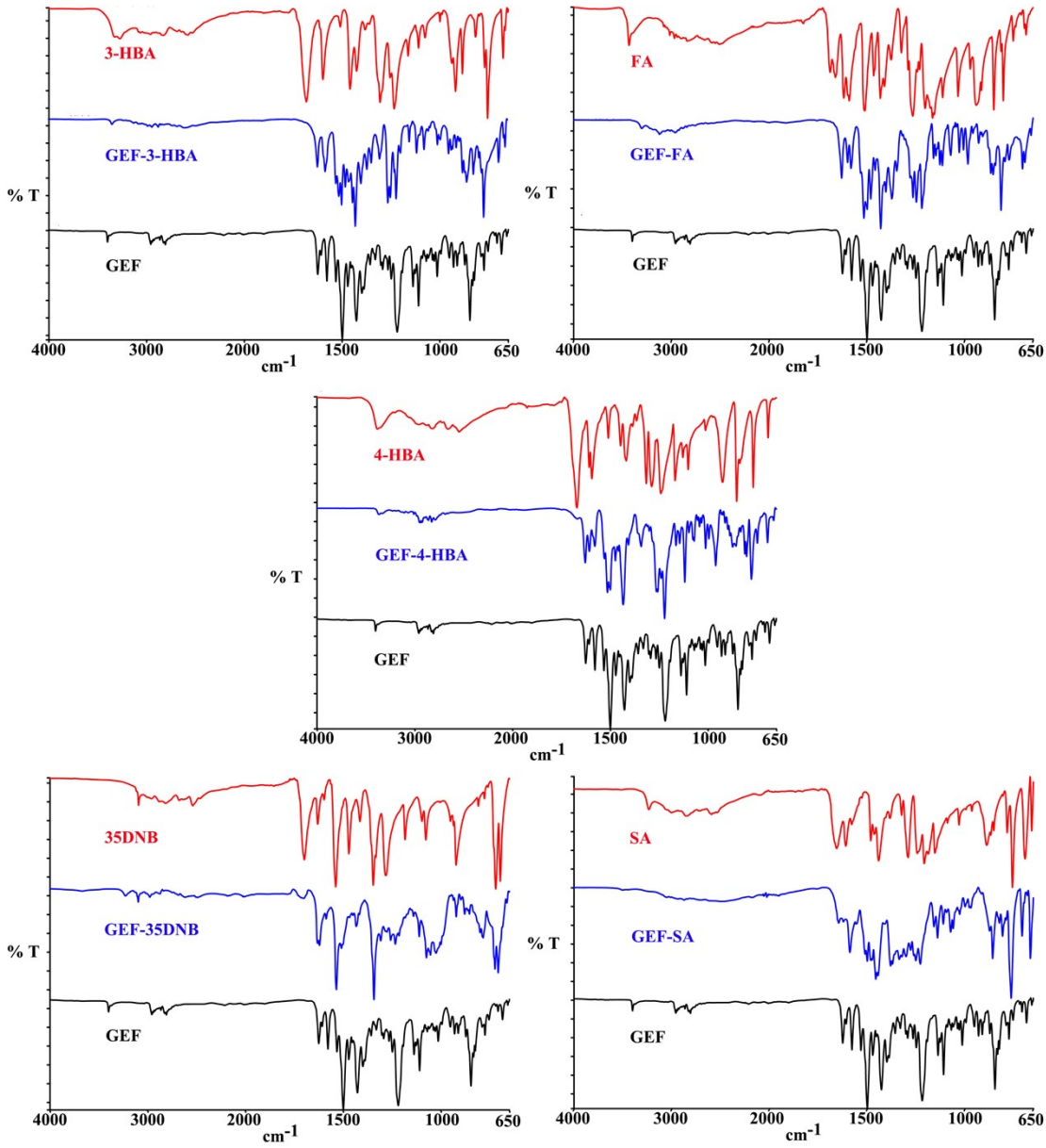


**Fig. S2** FT−IR spectra of GEF, CCFs, and the corresponding salts/cocrystals.

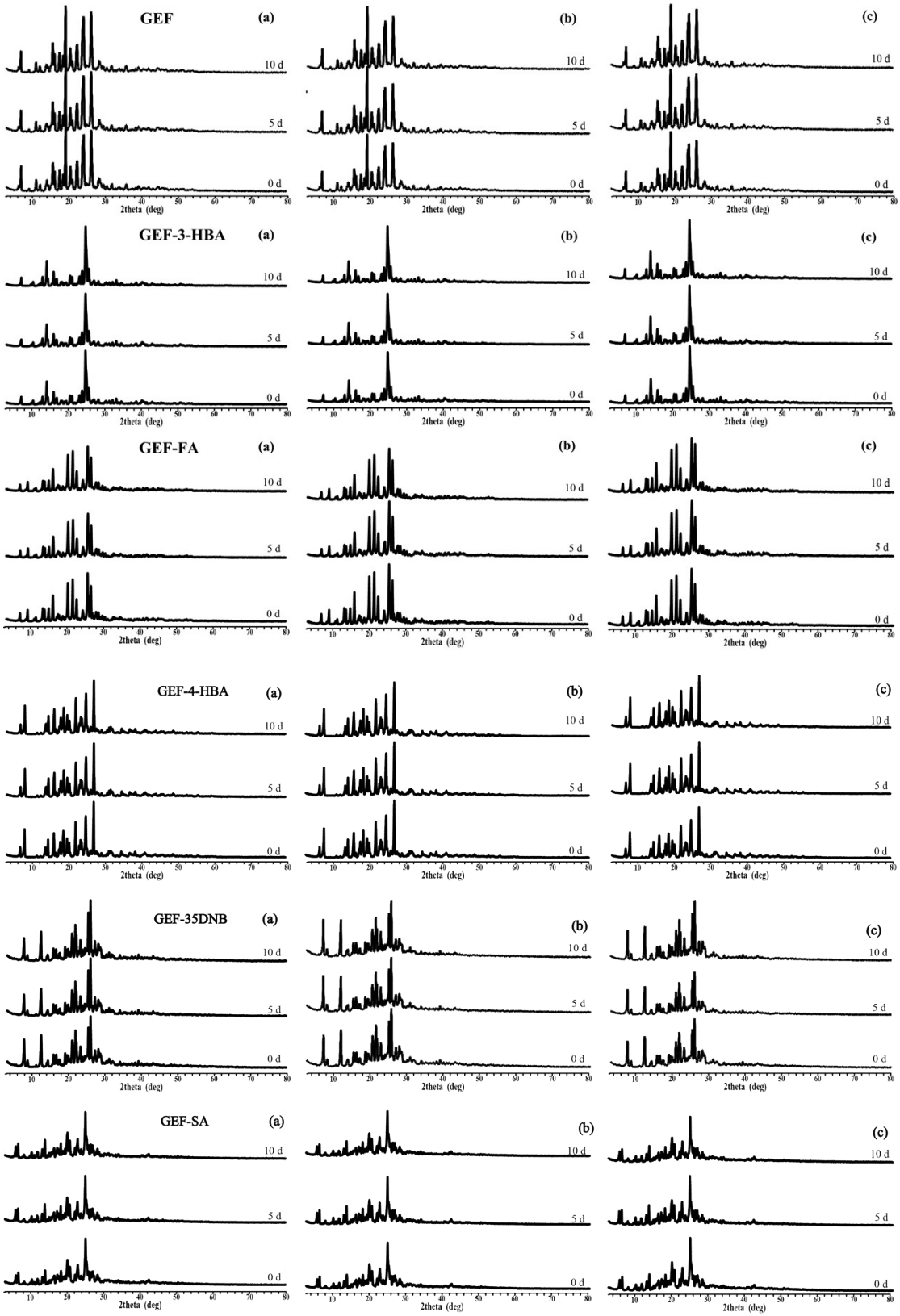


**Fig. S3** Accelerated stability results of GEF, GEF−3−HBA, GEF−FA, GEF−4−HBA, GEF−35DNB and GEF−SA. (a) high temperature (60 ± 1 °C); (b) high humidity (90 ± 5%, 25 °C); (c) illumination (4500 ± 500 lx, 25 °C)

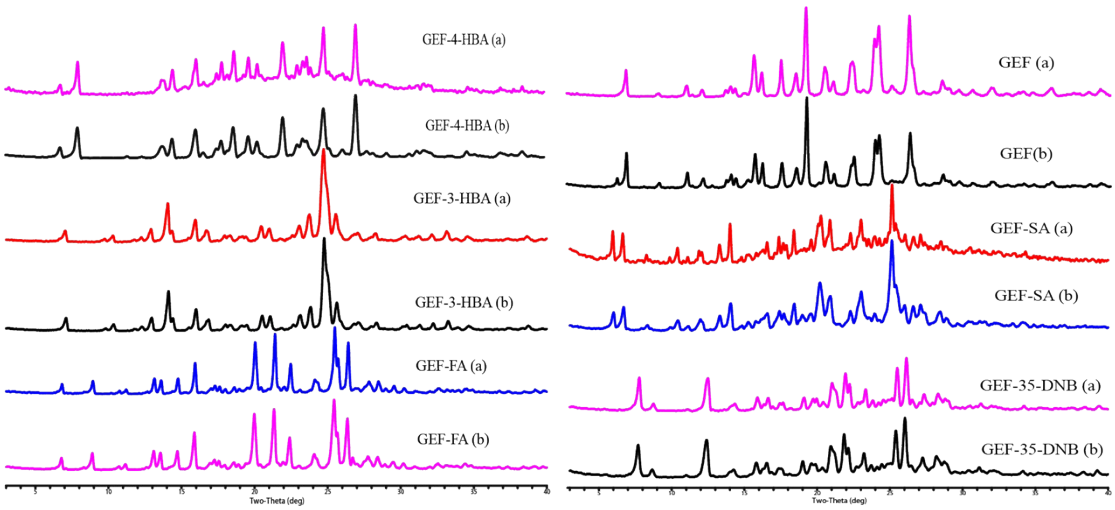


**Fig. S4** The PRXD patterns of GEF, GEF−3−HBA, GEF−FA, GEF−4−HBA, GEF−35DNB and GEF−SA before and after dissolution experiment (a)the initial phases; (b) the bottom phases.