

Electronic Supplementary Information (ESI)

Famciclovir-fumaric acid: an all-in-one multicomponent system with salt, cocrystal and salt-cocrystal continuum.

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Table S1. Details of crystallization experiments and results

| S.No | Molar ratio | Sample quantity | Solvent | Crystallization method | Obtained solid form |
|------|------------------|-----------------|--------------------------------|--------------------------------|--|
| 1 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol | Slow Evaporation | FAM-FUM (1:0.5) + FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II |
| 2 | FAM-FUM (1:2) | 20mg:14.4mg | 1mL Methanol | Slow Evaporation | FAM-FUM (1:0.5) + FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II |
| 3 | FAM-FUM (1:0.5) | 20mg:3.6mg | 1mL Methanol | Slow Evaporation | FAM-FUM (1:0.5) |
| 4 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 5 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 6 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Ethanol | Slow Evaporation | FAM-FUM (2:2) Form-I + Form-II |
| 7 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL i-Propanol | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 8 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL n-propanol | Slow Evaporation | FAM-FUM (1:0.5) + FAM-FUM- Form-I |
| 9 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL DMF | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 10 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL DMSO | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 11 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL n-Butanol | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 12 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL Methanol | Liquid Assisted Grinding (LAG) | FAM-FUM (2:2) Form-I |
| 13 | FAM-FUM (2:1) | 20mg:3.6mg | 0.5mL Methanol | LAG | FAM-FUM (2:2) Form-I |
| 14 | FAM-FUM (1:1) | 20mg:7.2mg | Few drops Ethanol | LAG | FAM-FUM (2:2) Form-I |
| 15 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL n-Propanol | Slurry | FAM-FUM (2:2) Form-I |
| 16 | FAM-FUM (2:1) | 20mg:3.6mg | Few drops Ethanol | LAG | FAM-FUM (2:2) Form-I + FAM-FUM (1:0.5) |
| 17 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL i-Propanol | Slurry | FAM-FUM (2:2) Form-I |
| 18 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL n-Butanol | Slurry | FAM-FUM (2:2) Form-I + FAM-FUM (1:0.5) |
| 19 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL Acetone | Slurry | FAM-FUM (2:2) Form-I + FAM-FUM (1:0.5) |
| 20 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL Acetonitrile | Slurry | FAM-FUM (2:2) Form-I |
| 21 | FAM-FUM (1:0.5) | 20mg:3.6mg | 0.5mL n-Propanol | Slurry | FAM-FUM (1:0.5) |
| 22 | FAM-FUM (1:0.5) | 20mg:3.6mg | 0.5mL n-Butanol | Slurry | FAM-FUM (1:0.5) |
| 23 | FAM-FUM (1:0.5) | 20mg:3.6mg | 0.5mL i-Propanol | Slurry | FAM-FUM (1:0.5) |
| 24 | FAM-FUM (1:0.5) | 20mg:3.6mg | 0.5mL Acetone | Slurry | FAM-FUM (1:0.5) |
| 25 | FAM-FUM (1:0.5) | 20mg:3.6mg | 0.5mL Acetonitrile | Slurry | FAM-FUM (2:2) Form-I + FAM-FUM (1:0.5) |
| 26 | FAM-FUM (1:1) | 20mg:7.2mg | 1.5mL Methanol | Slow Evaporation | FAM-FUM (1:0.5) + FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II |
| 27 | FAM-FUM (1:1) | 50mg:18mg | 0.5mL n-Propanol | Slurry | FAM-FUM (1:0.5) |
| 28 | FAM-FUM (1:0.5) | 50mg:9mg | 0.5mL i-Propanol | Slurry | FAM-FUM (1:0.5) |
| 29 | FAM-FUM (1:2) | 20mg:14.4mg | 0.5mL n-Propanol | Slurry | FAM-FUM (2:2) Form-I + FAM-FUM (1:0.5) |
| 30 | FAM-FUM (1:2) | 20mg:14.4mg | 0.5mL i-Propanol | Slurry | FAM-FUM (2:2) Form-I |
| 31 | FAM-FUM (1:2) | 20mg:14.4mg | 0.5mL i-Propanol + 0.5mL Water | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 32 | FAM-FUM (1:2) | 20mg:14.4mg | 0.5mL Acetone | Slurry | FAM-FUM (2:2) Form-I |
| 33 | FAM-FUM (1:2) | 20mg:14.4mg | 0.5mL n-Butanol | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 34 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL Dichloromethane | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 35 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL Toluene | Slurry | FAM-FUM (2:2) Form-I |
| 36 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL Ethyl acetate | Slurry | FAM-FUM (2:2) Form-I |
| 37 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL Nitromethane | Slurry | FAM-FUM (2:2) Form-I |
| 38 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL Chloroform | Slurry | FAM-FUM (2:2) Form-I + FAM-FUM (1:0.5) |
| 39 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol + 10ML Hexane | Anti-solvent addition | No precipitate |
| 40 | FAM-FUM-1:1.5 | 20mg:10.8mg | 0.5mL i-Propanol | Slurry | FAM-FUM (1:0.5) |
| 41 | FAM-FUM-1:1.25 | 20mg:8.9mg | 0.5mL i-Propanol | Slurry | FAM-FUM (1:0.5) |
| 42 | FAM-FUM-1:1 (B1) | 20mg:7.2mg | 1mL Methanol | Slurry | FAM-FUM (2:2) Form-I |
| 43 | FAM-FUM-1:1 (B2) | 20mg:7.2mg | 1mL Methanol | Slurry | FAM-FUM (2:2) Form-I |
| 44 | FAM-FUM-1:1 (B3) | 20mg:7.2mg | 1mL Methanol | Slurry | FAM-FUM (2:2) Form-I |
| 45 | FAM-FUM-1:1 (B4) | 20mg:7.2mg | 1mL Methanol | Slurry | FAM-FUM (2:2) Form-I |
| 46 | FAM-FUM-1:1 (B5) | 20mg:7.2mg | 1mL Methanol | Slurry | FAM-FUM (2:2) Form-I |
| 47 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL Ethyl acetate | Slurry | FAM-FUM (2:2) Form-I |
| 48 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL n-Propanol | Slurry | FAM-FUM (2:2) Form-I + FAM-FUM (1:0.5) |
| 49 | FAM-FUM (1:1) | 50mg:18mg | 1mL Methanol | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 50 | FAM-FUM (1:1) | 50mg:18mg | 1mL Methanol+1mL Water | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 51 | FAM-FUM (1:1) | 20mg:7.2mg | 1.5mL Methanol | Slow Evaporation | FAM-FUM (2:2) Form-I |

| | | | | | |
|----|-----------------|-------------|---|------------------|--|
| 52 | FAM-FUM (1:1) | 20mg:7.2mg | 2mL Methanol | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 53 | FAM-FUM (1:1) | 20mg:7.2mg | 2.5mL Methanol | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 54 | FAM-FUM (1:1) | 20mg:7.2mg | 3mL Methanol | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 55 | FAM-FUM (1:1.5) | 20mg:10.8mg | 1.5mL Methanol | Slow Evaporation | FAM-FUM (1:0.5) + FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II |
| 56 | FAM-FUM (1:2) | 20mg:14.4mg | 1.5mL Methanol | Slow Evaporation | FAM-FUM (2:2) Form-I + FUM crystal |
| 57 | FAM-FUM (1:2.5) | 20mg:18mg | 1.5mL Methanol | Slow Evaporation | FAM-FUM (2:2) Form-I + FUM crystal |
| 58 | FAM-FUM (1:3) | 20mg:21.6mg | 1.5mL Methanol | Slow Evaporation | FAM-FUM (2:2) Form-I + FUM crystal |
| 59 | FAM-FUM (1:1) | 20mg:7.2mg | 1.5mL Methanol | Slow Evaporation | FAM-FUM (1:0.5) + FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II |
| 60 | FAM-FUM (1:1) | 20mg:7.2mg | Few drops Methanol | Slurry | FAM-FUM (1:0.5) |
| 61 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL Methanol | Slurry | FAM-FUM (1:0.5) |
| 62 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL Methanol + 0.5mL Acetonitrile | Slurry | FAM-FUM (1:0.5) + FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II |
| 63 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL Ethanol + 0.5mL Acetonitrile | Slurry | FAM-FUM (2:2) Form-I + FAM-FUM (1:0.5) |
| 64 | FAM-FUM (1:1.5) | 20mg:10.8mg | 0.5mL Methanol | Slurry | FAM-FUM (1:0.5) |
| 65 | FAM-FUM (1:1.5) | 20mg:10.8mg | 0.5mL Ethanol | Slurry | FAM-FUM (2:2) Form-I + FAM-FUM (1:0.5) |
| 66 | FAM-FUM (1:2) | 20mg:14.4mg | 0.5mL Methanol | Slurry | FAM-FUM (2:2) Form-I + FAM-FUM (1:0.5)+FUM |
| 67 | FAM-FUM (1:2) | 20mg:14.4mg | 0.5mL Ethanol | Slurry | FAM-FUM (2:2) Form-I + FAM-FUM (1:0.5)+FUM |
| 68 | FAM-FUM (1:2.5) | 20mg:18mg | 0.5mL Methanol | Slurry | FAM-FUM (2:2) Form-I + FAM-FUM (1:0.5)+FUM |
| 69 | FAM-FUM (1:2.5) | 20mg:18mg | 0.5mL Ethanol | Slurry | FAM-FUM (2:2) Form-I + FAM-FUM (1:0.5)+FUM |
| 70 | FAM-FUM (1:3) | 20mg:21.6mg | 0.5mL Methanol | Slurry | FAM-FUM (2:2) Form-I + FAM-FUM (1:0.5)+FUM |
| 71 | FAM-FUM (1:3) | 20mg:21.6mg | 0.5mL Ethanol | Slurry | FAM-FUM (2:2) Form-I +FUM |
| 72 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol | Slow Evaporation | FAM-FUM (1:0.5) + FAM-FUM (2:2) Form-II |
| 73 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Ethanol | Slow Evaporation | FAM-FUM (2:2) Form-I + FAM-FUM (1:0.5) |
| 74 | FAM-FUM (1:2) | 20mg:14.4mg | 1mL Methanol | Slow Evaporation | FAM-FUM (1:0.5) + FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II |
| 75 | FAM-FUM (1:2) | 20mg:14.4mg | 1mL Ethanol | Slow Evaporation | FAM-FUM (2:2) Form-I + FAM-FUM (1:0.5) |
| 76 | FAM-FUM (1.5:1) | 30mg:7.2mg | 0.5mL Methanol | Slurry | FAM-FUM (2:2) Form-I + FAM-FUM (1:0.5) |
| 77 | FAM-FUM (1.5:1) | 30mg:7.2mg | 0.5mL Ethanol | Slurry | FAM-FUM (2:2) Form-I + FAM-FUM (1:0.5) |
| 78 | FAM-FUM (1.5:1) | 30mg:7.2mg | 0.5mL Acetonitrile | Slurry | FAM-FUM (1:0.5) + FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II |
| 79 | FAM-FUM (1.5:1) | 30mg:7.2mg | 0.5mL Acetone | Slurry | FAM-FUM (1:0.5) |
| 80 | FAM-FUM (1.5:1) | 30mg:7.2mg | 0.5mL i-Propanol | Slurry | FAM-FUM (1:0.5) |
| 81 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL i-Propyl acetate | Slurry | FAM-FUM (2:2) Form-I |
| 82 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL t-Butyl methyl ether | Slurry | FAM-FUM (2:2) Form-I + FAM-FUM (1:0.5) |
| 83 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL Methyl ethyl ketone | Slurry | FAM-FUM (2:2) Form-I + FAM-FUM (1:0.5) |
| 84 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL Hexane | Slurry | FAM-FUM (1:0.5) + EXTRA PEAK |
| 85 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL 1,2Dichloroethane | Slurry | FAM-FUM (2:2) Form-I |
| 86 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL Methanol + 1mL Acetonitrile | Slow Evaporation | FAM-FUM (1:0.5) + FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II |
| 87 | FAM-FUM (1:2) | 20mg:14.4mg | 0.5mL Methanol + 1mL Acetonitrile | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 88 | FAM-FUM (1:1) | 50mg:18mg | 0.5mL Methanol + 0.5mL Acetonitrile | Slurry | FAM-FUM (1:0.5) |
| 89 | FAM-FUM (1:1) | 20mg:7.2mg | Few drops Methanol + Few drops Acetonitrile | Slurry | FAM-FUM (2:2) Form-I + FAM-FUM (1:0.5) |
| 90 | FAM-FUM (1:2) | 20mg:14.4mg | Few drops Methanol + Few drops Acetonitrile | Slurry | FAM-FUM (2:2) Form-I |
| 91 | FAM-FUM (1:1) | 50mg:18mg | 1.5mL Methanol + 1.5mL Acetonitrile | Slow Evaporation | FAM-FUM (1:0.5) + FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II |
| 92 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol + 1mL Acetonitrile | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 93 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol + 2mL Acetonitrile | Slow Evaporation | FAM-FUM (1:0.5) + FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II |
| 94 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol + 3mL | Slow Evaporation | FAM-FUM (1:0.5) + FAM-FUM (2:2) |

| | | | Acetonitrile | | Form-I + FAM-FUM (2:2) Form-II |
|-----|-----------------|------------|---|-------------------------|--|
| 95 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol + 4mL Acetonitrile | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 96 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol + 5mL Acetonitrile | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 97 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol | Cooling Crystallization | FAM-FUM (1:0.5) |
| 98 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Ethanol | Cooling Crystallization | FAM-FUM (1:0.5) |
| 99 | FAM-FUM (1:1) | 20mg:7.2mg | 2mL Acetonitrile + 1mL Ethanol | Cooling Crystallization | FAM-FUM (1:0.5) + FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II |
| 100 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol + 1mL Acetonitrile | Cooling Crystallization | FAM-FUM (1:0.5) |
| 101 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol + 3mL Acetonitrile | Cooling Crystallization | FAM-FUM (2:2) Form-I |
| 102 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol + 3mL Acetonitrile | Slow Evaporation | FAM-FUM (1:0.5) + FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II |
| 103 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL Methanol + 3mL Acetonitrile | Slow Evaporation | FAM-FUM (1:0.5) + FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II |
| 104 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL Methanol + 0.5mL Acetonitrile | Slow Evaporation | FAM-FUM (1:0.5) + FAM-FUM (2:2) Form-II |
| 105 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Acetonitrile + Few drops Water | Slow Evaporation | FAM-FUM (1:0.5) + FAM-FUM (2:2) Form-II |
| 106 | FAM-FUM (1:1) | 20mg:7.2mg | 3mL Acetonitrile + Fewdrops Water | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 107 | FAM-FUM (1:1) | 20mg:7.2mg | 3mL Acetonitrile +0.5mL Methanol | Slow Evaporation | FAM-FUM (1:0.5) + FAM-FUM (2:2) Form-I |
| 108 | FAM-FUM (1:1) | 50mg:18mg | 3mL Acetonitrile +Few drops Water | Slow Evaporation | FAM-FUM (1:0.5) + FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II |
| 109 | FAM-FUM (1:1) | 50mg:18mg | 3mL Acetonitrile + 1mL Methanol | Slow Evaporation | FAM-FUM (1:0.5) + FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II |
| 110 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Nitromethane + 1mL Methanol | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 111 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol + 3mLToluene | Slow Evaporation | FAM-FUM (1:0.5) + FAM-FUM (2:2) Form-I |
| 112 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL H2O + 3mL Nitromethane | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 113 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol | Lyophilization | FAM-FUM (2:2) Form-I |
| 114 | E-113 | | 1mL Ethyl acetate | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 115 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol | Rotary Evaporation | FAM-FUM (2:2) Form-I |
| 116 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol + 1mL Acetonitrile | Rotary Evaporation | FAM-FUM (2:2) Form-I |
| 117 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL n-Propanol | Slurry | FAM-FUM (1:0.5) |
| 118 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Acetonitrile | Slurry | FAM-FUM (2:2) Form-I |
| 119 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL i-Propyl acetate | Slurry | FAM-FUM (1:0.5) + FAM-FUM (2:2) Form-I |
| 120 | FAM-FUM (1:1) | 100mg:36mg | 2mL Acetonitrile | Slurry | FAM-FUM (2:2) Form-I |
| 121 | FAM-FUM (1:1) | 50mg:15mg | 1mL Acetonitrile | Slurry | FAM-FUM (2:2) Form-I |
| 122 | FAM-FUM (1:1) | 50mg:18mg | 0.5mL n-Propanol | Slurry | FAM-FUM (1:0.5) |
| 123 | FAM-FUM (1:1) | 50mg:18mg | 1mL n-Propanol | Slurry | FAM-FUM (1:0.5) |
| 124 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol + 3mL Hexane | Vapour Diffusion | FAM-FUM (2:2) Form-I |
| 125 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Ethanol + 3mL Hexane | Vapour Diffusion | FAM-FUM (2:2) Form-I |
| 126 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol + 3mL EtOAc | Vapour Diffusion | FAM-FUM (2:2) Form-I |
| 127 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL Methanol + 1mL EtOAc + 3mL Hexane | Vapour Diffusion | FAM-FUM (2:2) Form-I |
| 128 | FAM-FUM (1:0.5) | 100mg:18mg | 1mL Acetonitrile | Slurry | FAM-FUM (1:0.5) |
| 129 | FAM-FUM (1:0.5) | 100mg:18mg | 1mL IPA | Slurry | FAM-FUM (1:0.5) |
| 130 | FAM-FUM (1:1) | 100mg:36mg | 1mL Acetonitrile | Slurry | FAM-FUM (2:2) Form-I |
| 131 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL n-propanol | LAG | FAM-FUM (2:2) Form-I |
| 132 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL IPA | LAG | FAM-FUM (2:2) Form-I |
| 133 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Acetonitrile | LAG | FAM-FUM (2:2) Form-I |
| 134 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Dioxane | LAG | FAM-FUM (1:0.5) + FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II + unknown phase |
| 135 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Ethyl acetate | LAG | FAM-FUM (2:2) Form-I |
| 136 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Toluene | LAG | FAM-FUM (2:2) Form-I |
| 137 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methyl ethyl ketone | LAG | FAM-FUM (2:2) Form-I |

| | | | | | |
|-----|-----------------|--------------|---|------------------------------------|--|
| 138 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL n-Butanol | LAG | FAM-FUM (2:2) Form-I |
| 139 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Acetic Acid | LAG | FAM-FUM (2:2) Form-I |
| 140 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL Dioxane | LAG | FAM-FUM (2:2) Form-I + unknown phase |
| 141 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Dioxane | LAG | FAM-FUM (2:2) Form-I + unknown phase |
| 142 | FAM-FUM (1:0.5) | 20mg:3.6mg | 1mL drops Dioxane | LAG | FAM-FUM (1:0.5) + FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II + unknown phase |
| 143 | FAM-FUM (1:2) | 20mg:14.4mg | 1mL drops Dioxane | LAG | FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II + unknown phase |
| 144 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL Dioxane + 0.5mL Methanol | LAG | FAM-FUM (1:0.5) |
| 145 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL Dioxane + Few drops Methanol + | Slurry | FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II + unknown phase |
| 146 | FAM-FUM (1:1) | 20mg:7.2mg | Few drops Dioxane + few drops Methanol + | Slurry | FAM-FUM (1:0.5) + FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II + unknown phase |
| 147 | FAM-FUM (1:1) | 20mg:7.2mg | 0.5mL Dioxane + 0.5mL Toluene | Slurry | FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II + unknown phase |
| 148 | FAM-FUM (1:2) | 20mg:14.4mg | 0.5mL Dioxane | Slurry | FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II + unknown phase |
| 149 | FAM-FUM (1:2) | 20mg:14.4mg | 0.5mL Dioxane + Few drops Methanol | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 150 | FAM-FUM (1:2) | 20mg:14.4mg | 0.5mL Dioxane + 0.5mL Methanol | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 151 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Acetic Acid + Few drops Methanol + Few drops Acetonitrile | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 152 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Formic Acid + Few drops Methanol + Few drops Acetonitrile | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 153 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Acetic acid | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 154 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 155 | FAM-FUM (1:1.1) | 20mg:7.9mg | 1mL Methanol | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 156 | FAM-FUM (1:1.2) | 20mg:8.75mg | 1mL Methanol | Slow Evaporation | FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II |
| 157 | FAM-FUM (1:1.3) | 20mg:9.47mg | 1mL Methanol | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 158 | FAM-FUM (1:1.4) | 20mg:10.19mg | 1mL Methanol | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 159 | FAM-FUM (1:1.5) | 20mg:10.91mg | 1mL Methanol | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 160 | FAM-FUM (1:2) | 20mg:14.4mg | 1mL Methanol | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 161 | FAM-FUM (1:2) | 20mg:14.4mg | 1mL Dioxane | Slow Evaporation | FAM-FUM (2:2) Form-I |
| 162 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Dioxane | Rotary Evaporation | FAM-FUM (1:0.5) |
| 163 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Dioxane + 1mL Acetonitrile | Rotary Evaporation | FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II + unknown phase |
| 164 | FAM-FUM (1:2) | 20mg:14.4mg | 1mL Dioxane | Rotary Evaporation | FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II + unknown phase |
| 165 | FAM-FUM (1:2) | 20mg:14.4mg | 1mL Dioxane + 1mL Acetonitrile | Rotary Evaporation | FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II + unknown phase |
| 166 | FAM-FUM (1:2) | 20mg:14.4mg | 1mL Dioxane | Rotary Evaporation | FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II + unknown phase |
| 167 | FAM-FUM (1:1) | 20mg:7.2mg | 2mL Dioxane | LAG | FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II + unknown phase |
| 168 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol+ 3mL Acetonitrile | Without heating & Slow Evaporation | FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II + FAM-FUM (1:0.5) |
| 169 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol+ 3mL Acetonitrile | Without heating & Slow Evaporation | FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II + FAM-FUM (1:0.5) |
| 170 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol+ 3mL Acetonitrile | Without heating & Slow Evaporation | FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II + FAM-FUM (1:0.5) |
| 171 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol+ 3mL Acetonitrile | Without heating & Slow Evaporation | FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II + FAM-FUM (1:0.5) |
| 172 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol+ 3mL Acetonitrile | Without heating & Slow Evaporation | FAM-FUM (2:2) Form-I + FAM-FUM (2:2) Form-II + FAM-FUM (1:0.5) |
| 173 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol+ 3mL Acetonitrile | Fast Evaporation (in Petri dishes) | FAM-FUM (2:2) Form-I |
| 174 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol+ 3mL Acetonitrile | Fast Evaporation (in Petri dishes) | FAM-FUM (2:2) Form-I |
| 175 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol+ 3mL Acetonitrile | Fast Evaporation (in Petri dishes) | FAM-FUM (2:2) Form-I |
| 176 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol+ 3mL Acetonitrile | Fast Evaporation (in Petri dishes) | FAM-FUM (2:2) Form-I |
| 177 | FAM-FUM (1:1) | 20mg:7.2mg | 1mL Methanol+ 3mL Acetonitrile | Fast Evaporation (in Petri dishes) | FAM-FUM (2:2) Form-I |

Table S2. Crystal data of famciclovir-fumaric acid complexes (at 293K)

| Compound name | Famciclovir-fumaric acid (2:2) Cocrystal | Famciclovir-fumaric acid (2:2) Salt | Famciclovir-fumaric acid (1:0.5) Salt-cocrystal intermediate |
|--|--|---|--|
| Compound code | FAM-FUM (2:2) polymorph I | FAM-FUM (2:2) polymorph II | FAM-FUM (1:0.5) |
| Chemical formula | 2(C ₁₄ H ₁₉ N ₅ O ₄). 2(C ₄ H ₄ O ₄) | 1(C ₁₄ H ₂₀ N ₅ O ₄) ⁺ . 1(C ₄ H ₃ O ₄) ⁻ . 1(C ₁₄ H ₁₉ N ₅ O ₄). 1(C ₄ H ₄ O ₄) | 1(C ₁₄ H ₁₉ N ₅ O ₄). 0.5(C ₄ H ₄ O ₄) |
| Formula Mass | 874.82 | 874.83 | 379.36 |
| Crystal system | Triclinic | Monoclinic | Monoclinic |
| <i>a</i> /Å | 11.439(3) | 14.012(10) | 14.056(4) |
| <i>b</i> /Å | 13.954(3) | 7.541(6) | 7.578(3) |
| <i>c</i> /Å | 15.137(3) | 39.34(3) | 17.799(7) |
| <i>α</i> /° | 67.808(5) | 90 | 90 |
| <i>β</i> /° | 86.239(4) | 91.659(10) | 106.960(10) |
| <i>γ</i> /° | 68.249(5) | 90 | 90 |
| Unit cell volume/Å ³ | 2070.2(8) | 4154(5) | 1813.4(11) |
| Temperature /K | 293(2) | 293(2) | 293(2) |
| Space group | <i>P</i> $\bar{1}$ | <i>P</i> 2 ₁ / <i>n</i> | <i>P</i> 2 ₁ / <i>n</i> |
| Formula units per unit cell, <i>Z</i> | 2 | 4 | 4 |
| Radiation type | MoK α | MoK α | MoK α |
| Crystal size /mm ³ | 0.44 x 0.40 x 0.27 | 0.33 x 0.30 x 0.18 | 0.30 x 0.12 x 0.10 |
| Absorption coefficient, μ /mm ⁻¹ | 0.116 | 0.112 | 0.108 |
| No. of reflections measured | 51311 | 41831 | 28018 |
| No. of independent reflections | 8118 | 9549 | 4163 |
| No. of independent reflections (<i>I</i> >2 σ (<i>I</i>)) | 5206 | 4242 | 2697 |
| <i>R</i> _{int} | 0.0396 | 0.0844 | 0.0999 |
| Final <i>RI</i> values (<i>I</i> > 2 σ (<i>I</i>)) | 0.0526 | 0.0614 | 0.0524 |
| Final <i>wR</i> (<i>F</i> ²) values (<i>I</i> > 2 σ (<i>I</i>)) | 0.1359 | 0.1484 | 0.1201 |
| Final <i>RI</i> values (all data) | 0.0876 | 0.1589 | 0.0910 |
| Final <i>wR</i> (<i>F</i> ²) values (all data) | 0.1669 | 0.2009 | 0.1466 |
| Goodness of fit on <i>F</i> ² | 1.019 | 0.999 | 1.050 |
| Difference density max and min, e/Å ³ | 0.363 and -0.215 | 0.377 and -0.356 | 0.317 and -0.311 |
| CCDC number | 2244824 | 2244826 | 2244825 |

Table S3. Crystal data of famciclovir anhydrous and monohydrate form (redetermined at 100K)

| | | |
|--|---|---|
| Compound name | Famciclovir anhydrous form | Famciclovir monohydrate form |
| Compound code | Anhydrous form | Monohydrate |
| Chemical formula | C ₁₄ H ₁₉ N ₅ O ₄ | C ₁₄ H ₁₉ N ₅ O ₄ .H ₂ O |
| Formula Mass | 321.34 | 339.36 |
| Crystal system | Monoclinic | Triclinic |
| <i>a</i> /Å | 11.005(4) | 9.4819(9) |
| <i>b</i> /Å | 12.739(4) | 10.0041(8) |
| <i>c</i> /Å | 11.783(4) | 17.2683(16) |
| α /° | 90 | 83.820(4) |
| β /° | 107.323(12) | 75.769(5) |
| γ /° | 90 | 84.708(4) |
| Unit cell volume/Å ³ | 1577.0(9) | 1574.9(2) |
| Temperature /K | 100(2) | 100(2) |
| Space group | <i>P</i> 2 ₁ / <i>c</i> | <i>P</i> $\bar{1}$ |
| Formula units per unit cell, <i>Z</i> | 4 | 4 |
| Radiation type | MoK α | MoK α |
| Crystal size /mm ³ | 0.26 x 0.23 x 0.14 | 0.33 x 0.27 x 0.20 |
| Absorption coefficient, μ /mm ⁻¹ | 0.102 | 0.110 |
| No. of reflections measured | 18841 | 36511 |
| No. of independent reflections | 4596 | 9170 |
| No. of independent reflections (<i>I</i> > 2 σ (<i>I</i>)) | 3834 | 6390 |
| <i>R</i> _{int} | 0.0334 | 0.0631 |
| Final <i>RI</i> values (<i>I</i> > 2 σ (<i>I</i>)) | 0.0454 | 0.0542 |
| Final <i>wR</i> (<i>F</i> ²) values (<i>I</i> > 2 σ (<i>I</i>)) | 0.1071 | 0.1063 |
| Final <i>RI</i> values (all data) | 0.0576 | 0.0936 |
| Final <i>wR</i> (<i>F</i> ²) values (all data) | 0.1141 | 0.1211 |
| Goodness of fit on <i>F</i> ² | 1.024 | 1.039 |
| Difference density max and min, e/Å ³ | 0.333 and -0.314 | 0.362 and -0.426 |
| CCDC number | 2244828 | 2244827 |

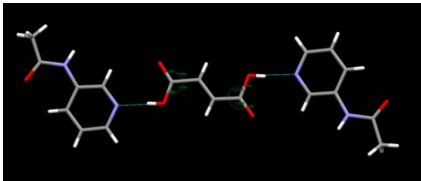
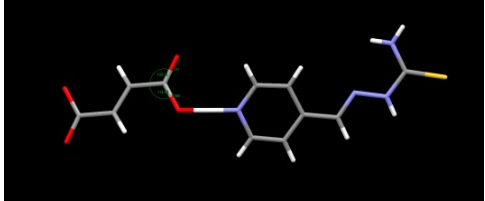
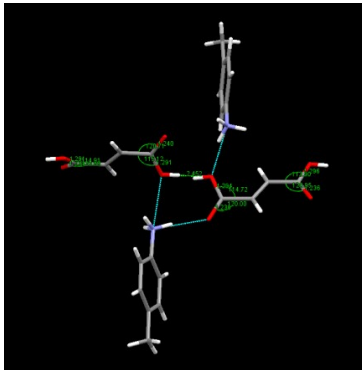
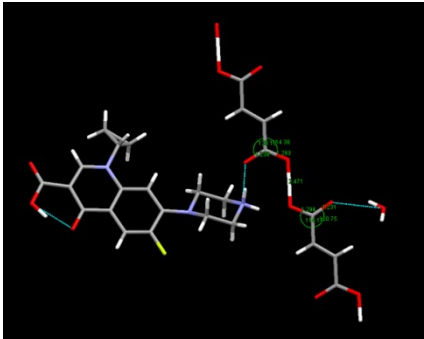
Table S4. Bond distances and bond angles of carboxylic acid of fumaric acid and aminopyrimidine ring of famciclovir (crystal data at 100K).

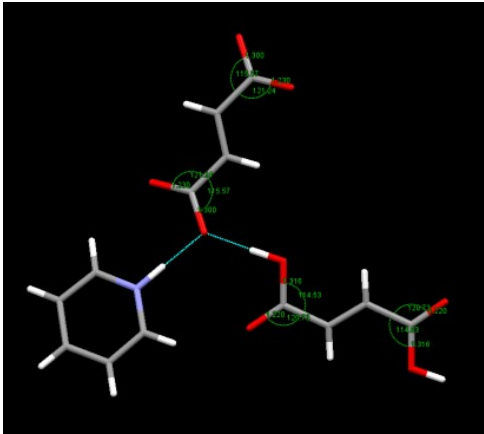
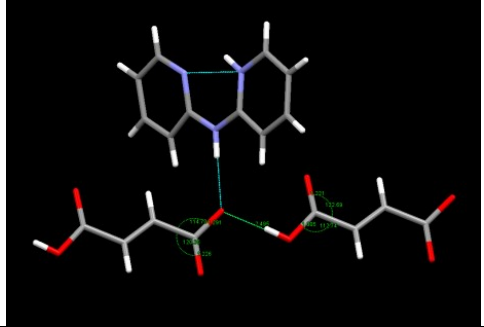
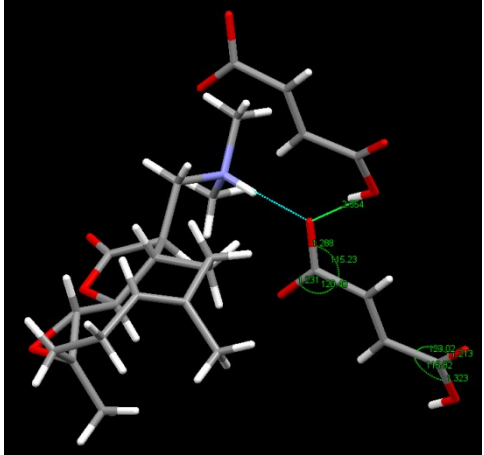
| Parameter | Famciclovir anhydrous | Famciclovir monohydrate | FAM-FUM 2:2 Form I Cocrystal | FAM-FUM 2:2 Form II Salt | FAM-FUM 1:0.5 Salt-cocrystal Intermediate |
|------------------------------|-----------------------|-------------------------|------------------------------|--------------------------|---|
| Fumaric acid coformer | | | | | |
| C=O /Å | - | - | 1.216 | 1.257 | 1.235 |
| C-O /Å | - | - | 1.315 | 1.259 | 1.290 |
| | | | 1.215 | 1.213 | |
| | | | 1.323 | 1.310 | |
| | | | 1.210 | 1.206 | |
| | | | 1.330 | 1.309 | |
| | | | 1.212 | 1.216 | |
| | | | 1.316 | 1.319 | |
| ∠O-C-C /° | - | - | 111.69 | 116.47 | 114.88 |
| ∠O=C-C /° | - | - | 124.28 | 119.23 | 119.89 |
| | | | 112.29 | 112.75 | |
| | | | 123.85 | 123.09 | |
| | | | 114.79 | 113.55 | |
| | | | 121.21 | 121.80 | |
| | | | 111.77 | 112.38 | |
| | | | 123.79 | 123.15 | |
| Famciclovir drug | | | | | |
| C2-N1 /Å | 1.334 | 1.335 1.329 | 1.340 1.339 | 1.356 1.338 | 1.356 |
| C1-N1 /Å | 1.368 | 1.359 1.358 | 1.366 1.366 | 1.372 1.336 | 1.372 |
| C1-N2 /Å | 1.347 | 1.352 1.349 | 1.344 1.351 | 1.329 1.346 | 1.339 |
| ∠C2-N1-C1 /° | 118.05 | 117.63 117.89 | 119.59 119.04 | 122.97 119.05 | 120.78 |
| ∠C3-C2-N1 /° | 120.67 | 120.93 120.74 | 119.54 119.70 | 117.07 119.39 | 118.48 |
| ∠N3-C1-N1 /° | 126.27 | 127.16 127.12 | 125.58 125.97 | 122.68 126.27 | 124.33 |
| ∠N1-C1-N2 /° | 116.77 | 115.90 115.84 | 116.04 116.34 | 117.09 116.36 | 116.71 |

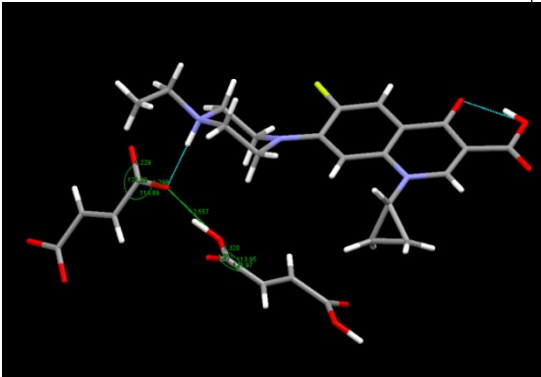
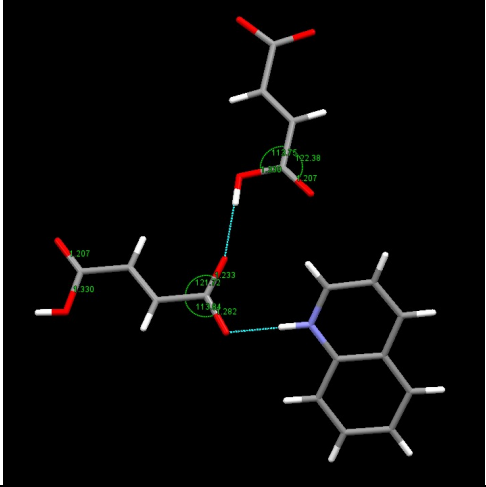
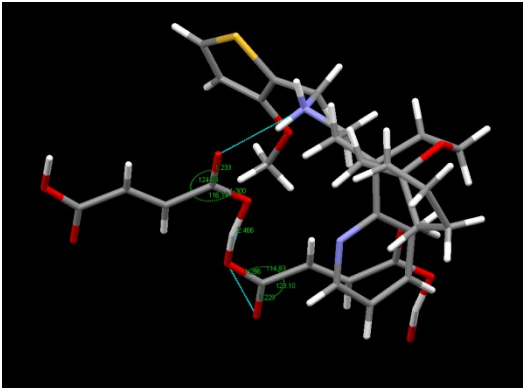
Table S5. Bond distances and bond angles of carboxylic acid of fumaric acid and aminopyrimidine ring of famciclovir (crystal data at 293K)

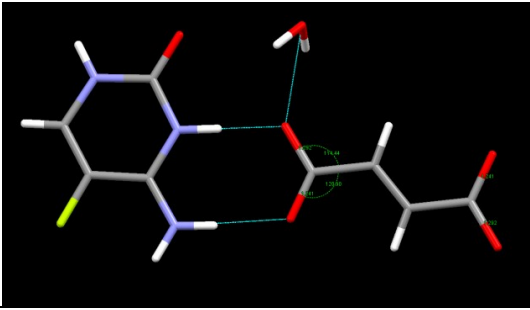
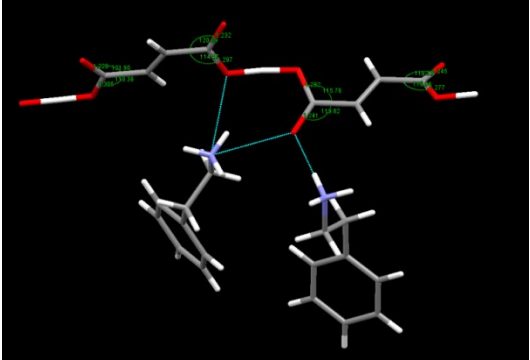
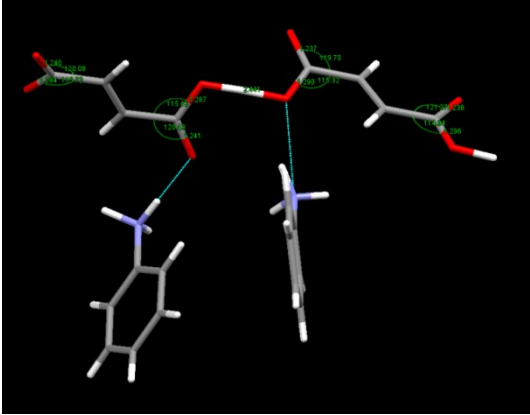
| | FAM-FUM 2:2 Form I Cocrystal | FAM-FUM 2:2 Form II Salt | FAM-FUM 1:0.5 Salt-cocrystal Intermediate |
|------------------------------|------------------------------------|--------------------------------|---|
| Fumaric acid coformer | | | |
| C=O /Å | 1.201 | 1.230 | 1.223 |
| C-O /Å | 1.282 | 1.249 | 1.279 |
| | 1.207 | 1.190 | |
| | 1.285 | 1.296 | |
| | 1.210 | 1.164 | |
| | 1.301 | 1.275 | |
| | 1.202 | 1.201 | |
| | 1.303 | 1.302 | |
| ∠O-C-C /° | 113.28 | 116.05 | 114.88 |
| ∠O=C-C /° | 122.82 | 119.50 | 119.89 |
| | 111.69 | 113.05 | |
| | 124.39 | 123.19 | |
| | 116.87 | 114.12 | |
| | 120.89 | 120.67 | |
| | 112.83 | 112.25 | |
| | 123.18 | 123.44 | |
| Famciclovir drug | | | |
| C2-N1 /Å | 1.325 | 1.340 | |
| | 1.332 | 1.329 | |
| C1-N1 /Å | 1.364 | 1.357 | |
| | 1.360 | 1.355 | |
| C1-N2 /Å | 1.340 | 1.319 | |
| | 1.334 | 1.342 | |
| ∠C2-N1-C1 /° | 118.71 | 122.88 | |
| | 119.27 | 118.75 | |
| ∠C3-C2-N1 /° | 120.09 | 117.27 | |
| | 119.91 | 119.42 | |
| ∠N3-C1-N1 /° | 126.06 | 123.15 | |
| | 125.79 | 126.54 | |
| ∠N1-C1-N2 /° | 116.21 | 117.07 | |
| | 115.82 | 116.14 | |

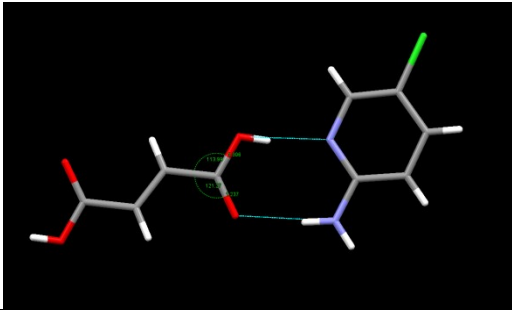
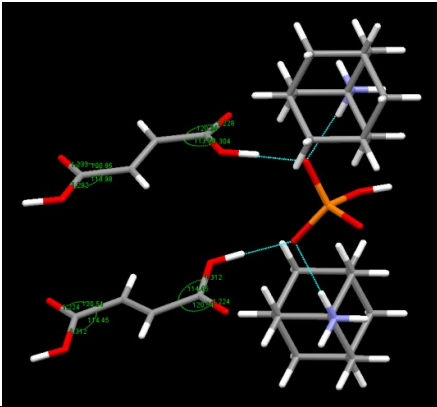
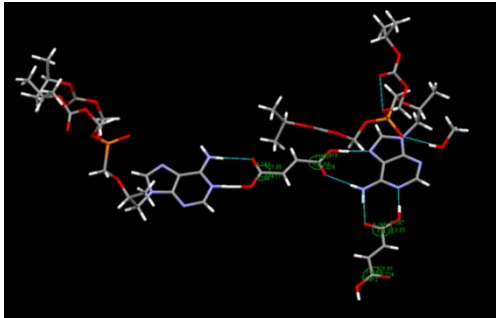
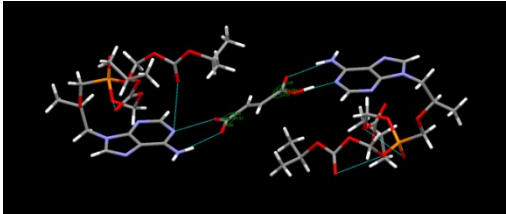
Table S6. Identification of neutral/ionic/intermediate state of fumaric acid based on the observed distance and angles in fumaric acid complexes reported in CSD.

| S.No | CSD REFCODE | Parameters $\Delta\text{C-O} / \text{\AA}$ $\Delta\text{C-C-O} / ^\circ$ | Assigned as | Suggested as |
|------|---|--|--|--|
| | Neutral zone ($\Delta\text{C-O}$, 0.07-0.15 \AA ; $\Delta\text{C-C-O}$, 5-15 $^\circ$) | | | |
| 1 | NEWRIR  | 0.062 3.834 0.129 10.075 | Neutral Neutral | Ionic Neutral |
| | Ionic zone ($\Delta\text{C-O}$, 0.0-0.07 \AA ; $\Delta\text{C-C-O}$, 0-5 $^\circ$) | | | |
| 2 | TOQNEV  | 0.074 5.635 | Salt | Neutral |
| | Transition zone ($\Delta\text{C-O}$, 0.04-0.07 \AA ; $\Delta\text{C-C-O}$, 5-9 $^\circ$) | | | |
| 3 | XOJFEJ  | 0.06 7.058 0.052 5.962 0.056 5.289 0.051 5.593 | Neutral Neutral Ionic Ionic | Intermediate Intermediate Intermediate Intermediate |
| 4 | VELREM  | 0.063 6.58 0.045 5.806 | Neutral Ionic | Intermediate Intermediate |

| S.No | CSD REFCODE | Parameters $\Delta C-O / \text{\AA}$ $\Delta C-C-O / ^\circ$ | Assigned as | Suggested as |
|------|---|--|----------------------|-----------------------------|
| 5 | XAFYUC  | 0.096 6.204 0.07 5.67 | Neutral Ionic | Neutral Intermediate |
| 6 | HUSSUJ  | 0.084 9.953 0.065 5.632 | Neutral Ionic | Neutral Intermediate |
| 7 | POWMOE  | 0.11 7.2 0.057 5.17 | Neutral Ionic | Neutral Intermediate |

| S.No | CSD REFCODE | Parameters $\Delta C-O / \text{\AA}$ $\Delta C-C-O / ^\circ$ | Assigned as | Suggested as |
|------|---|--|----------------------|----------------------------------|
| 8 | PILSUA  | 0.109 8.022 0.069 6.422 | Neutral Ionic | Intermediate Ionic |
| 9 | RABYID  | 0.123 8.63 0.049 7.875 | Neutral Ionic | Neutral Intermediate |
| 10 | MILZAK  | 0.057 8.272 0.067 7.896 | Neutral Ionic | Intermediate Intermediate |

| S.No | CSD REFCODE | Parameters $\Delta C-O / \text{\AA}$ $\Delta C-C-O / ^\circ$ | Assigned as | Suggested as |
|------|---|--|--------------------------------------|--|
| 11 | DINJUH  | 0.051 6.46 | Ionic | Intermediate |
| 12 | COCPEQ  | 0.065 6.125 0.077 8.52 0.032 3293 0.041 4.052 | Neutral Neutral Ionic Ionic | Intermediate Neutral Ionic Ionic |
| 13 | COCPOA  | 0.058 7.228 0.046 5.001 0.044 4.358 0.053 4.376 | Neutral Neutral Ionic Ionic | Intermediate Intermediate Ionic Ionic |

| S.No | CSD REFCODE | Parameters $\Delta C-O / \text{\AA}$ $\Delta C-C-O / ^\circ$ | Assigned as | Suggested as |
|------|---|---|--|--|
| 14 | KURGOU01  | 0.069 7.28 | Neutral | Neutral |
| 15 | LEGJAK  | 0.088 6.095 0.071 6.401 0.059 6.882 | Neutral Neutral Neutral | Neutral Neutral Intermediate |
| 16 | DUXSEV  | 0.088 7.156 0.085 6.529 0.05 6.946 0.052 7.897 | Neutral Neutral Ionic Neutral | Neutral Neutral Intermediate Intermediate |
| 17 | DUXSAR  | 0.076 9.354 0.059 7.532 | Neutral Ionic | Neutral Intermediate |

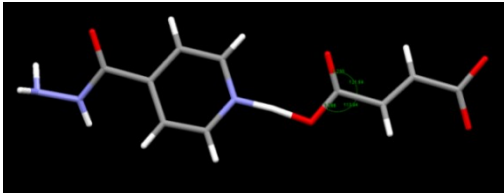
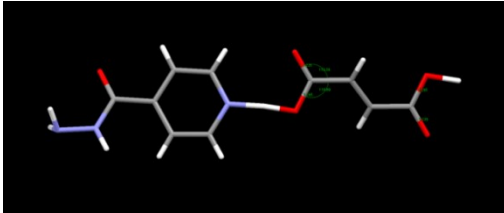
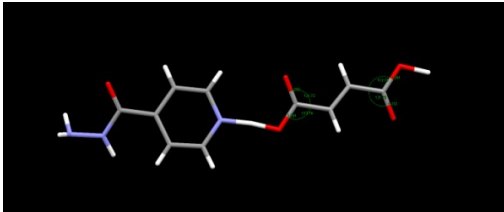
| S.No | CSD REFCODE | Parameters $\Delta C-O / \text{\AA}$ $\Delta C-C-O / ^\circ$ | Assigned as | Suggested as |
|------|---|--|-------------|--------------|
| 18 | LATSUW  | 0.058 7.703 | Ionic | Intermediate |
| 19 | LATTAD01  | 0.06 2.672 | Ionic | Intermediate |
| 20 | LATTAD02  | 0.059 7.982 | Neutral | Intermediate |

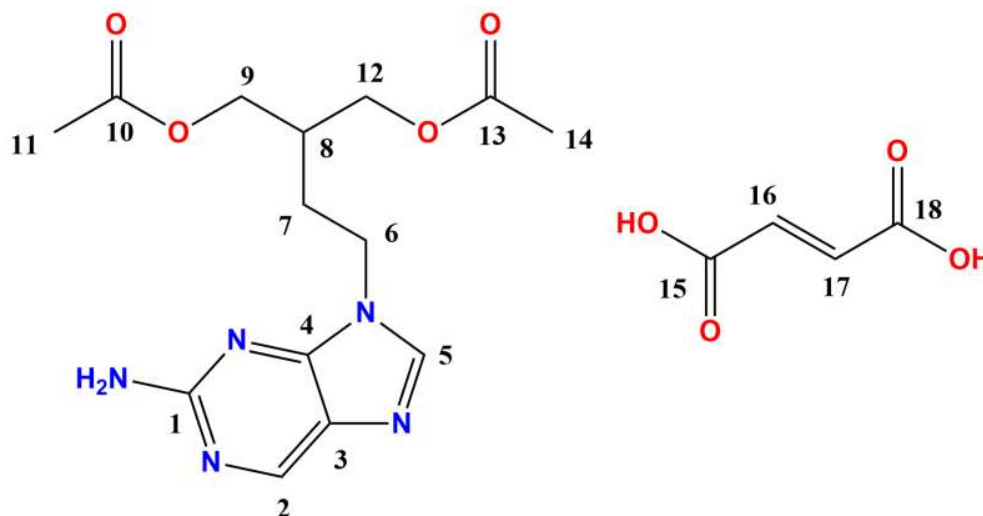
Table S7. Rietveld analysis of phase mixtures.

| Sample | Final Rwp | FAM-FUM (2:2) form I | FAM-FUM (2:2) form II | FAM-FUM (1:0.5) crystal |
|--------|-----------|-------------------------|--------------------------|----------------------------|
| 1 | 12.86 | 17.2% | 54.4% | 28.4% |
| 2 | 13.83 | 16.8% | 47.1% | 36.1% |
| 3 | 13.72 | 21.1% | 59.1% | 19.8% |
| 4 | 13.08 | 4.9% | 48.1% | 47% |
| 5 | 12.07 | 29.8% | 46.3% | 23.9% |
| 6 | 12.62 | 18.1% | 56.1% | 24.4% |
| 7 | 10.34 | 47.5% | 22.6% | 29.9% |
| 8 | 11.99 | 30.8% | 29.0% | 40.1% |

Table S8. FT-IR spectral analysis of famciclovir, fumaric acid and famciclovir-fumaric acid complexes.

| S.No | Solid form | O-H stretching / cm ⁻¹ | N-H stretching / cm ⁻¹ | C=O stretching / cm ⁻¹ | O-H bending / cm ⁻¹ |
|------|--|--------------------------------------|--------------------------------------|---|-----------------------------------|
| 1 | Famciclovir (FAM) | - | 3329.9 3162.6 | 1744.6 (ester) 1727.2 (ester) | - |
| 2 | Fumaric acid (FUM) | 2820.3 2655.0 2509.2 | - | 1664.9 (acid) | 1421.4 |
| 3 | FAM-FUM (2:2) form I (cocrystal) | 3395.0 2442.2 1881.0 | 3326.6 3213.1 | 1745.0 (ester) 1730.1 (ester) 1700.6 (acid) | 1426.6 |
| 4 | FAM-FUM (1:0.5) Salt-cocrystal intermediate | 3434.4 | 3313.2 3179.9 | 1730.4 (ester) 1644.4 (acid) 1466.6 (acid) | 1432.4 |

Table S9. SS-NMR (^{13}C CP-MAS) spectral analysis of famciclovir, fumaric acid and famciclovir-fumaric acid complexes.



| S.No | Carbon atoms | FAM (ppm) | FUM (ppm) | FAM-FUM 1:0.5 (ppm) | FAM-FUM 2:2 form I (ppm) |
|------|--------------------------------|----------------|-----------|---------------------|----------------------------------|
| 1 | FAM ester (C13, C10) | 171.6 169.6 | - | 172.1 171.3 | 168.3 166.8 |
| 2 | FUM carboxylic acid (C15, C18) | - | 172.3 | 174.6 | 172.8 173.6 |
| 3 | FAM purine ring (C1) | 161.6 | - | 140.3 | 159.8 |
| 4 | FAM purine ring (C2, C4) | 153.4 151.6 | - | 156.7 155.7 | 153.3 147.7 |
| 5 | FAM purine ring (C5) | 143.4 | - | 146.3 | 145.7 141.8 |
| 6 | FUM alkene (C16, C17) | - | 136.1 | 137.1 | 136.5 134.5 132.8 131.5 |
| 7 | FAM purine ring (C3) | 126.9 | - | 126.5 | 125.4 123.4 |
| 8 | FAM NEPD chain (C9, C12) | 61.1 58.1 | - | 64.9 59.0 | 65.7 55.4 |
| 9 | FAM NEPD chain (C6) | 40.6 | - | 42.3 | 42.1 |
| 10 | FAM NEPD chain (C8) | 35.9 | - | 36.2 | 37.6 |
| 11 | FAM NEPD chain (C7) | 28.9 | - | 23.6 | 33.3 27.7 |
| 12 | FAM NEPD chain (C11, C14) | 20.0 | - | 20.5 | 21.6 |

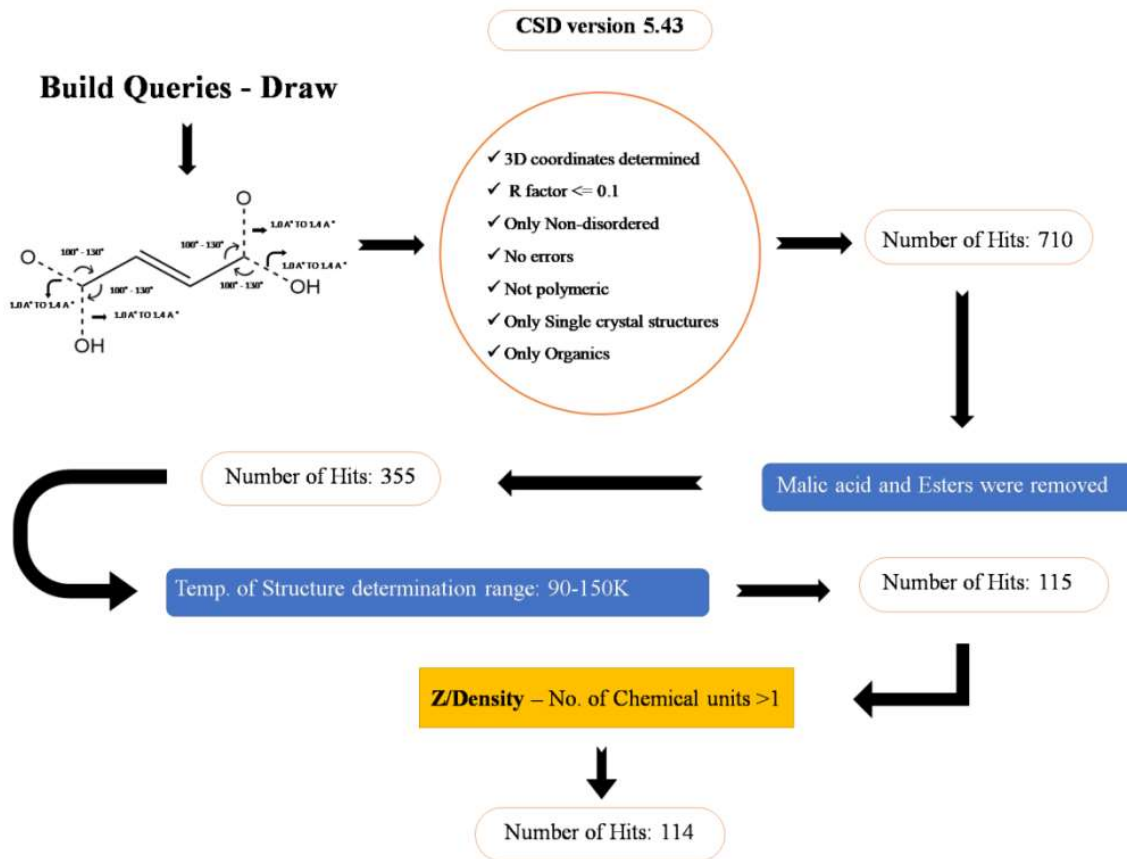
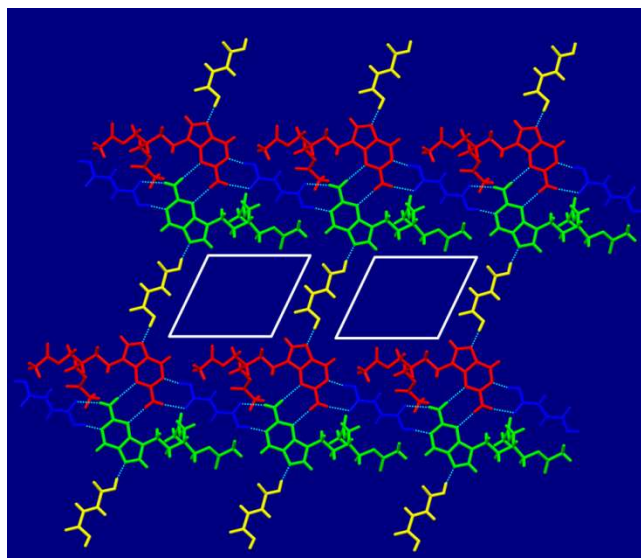
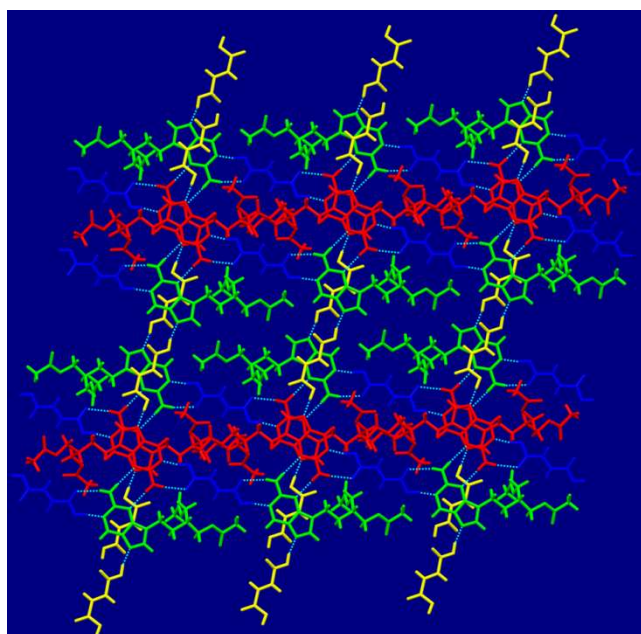


Figure S1. Schematic representation of “search criteria” employed to extract good quality fumaric acid complexes (114 hits) from the Cambridge Structural Database.

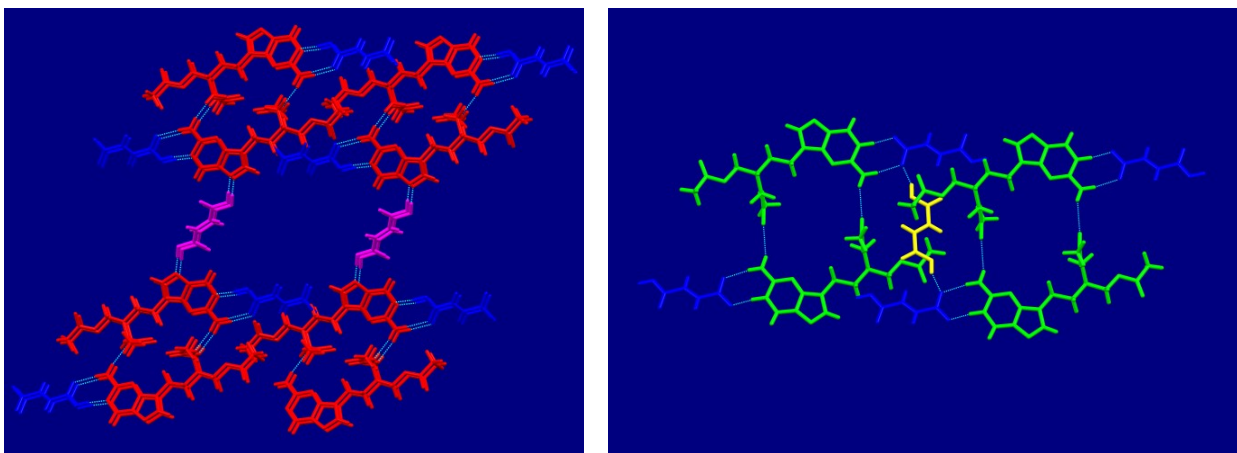


(a)



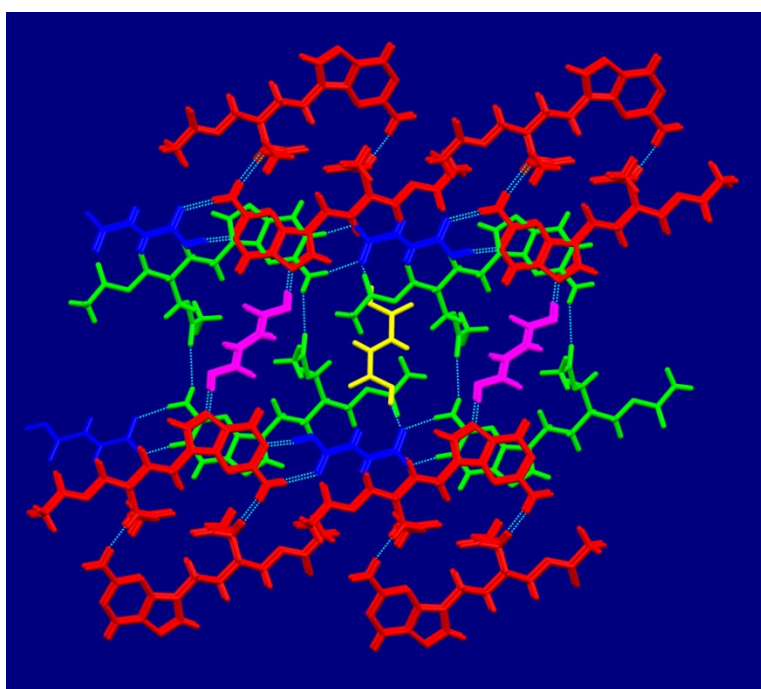
(b)

Figure S2. Crystal packing diagrams of FAM-FUM 2:2 form I. The symmetry independent molecules are shown in different colors. (a) Formation of robust two-dimensional (2D) hydrogen bonded grid networks with cavities by aminopyrimidine-aminopyrimidine, acid-pyrimidine, and acid-imidazole synthons. (b) Parallel 2D networks facilitate close packing of fanciclovir side chains and utilize the space in the cavities.



(a)

(b)



(c)

Figure S3. Crystal packing diagrams of FAM-FUM (2:1+0.5+0.5 or 2:2) form II. The symmetry independent molecules are shown in different colors. (a) Formation of helical network of famciclovir molecules by N-H \cdots O interaction (red color FAM) and interlinking of helical networks with fumaric acid molecules by acid-pyrimidine synthon (blue color FUM) and acid-imidazole (magenta FUM). (b) Formation of $R_2^2(26)$ with second symmetry independent famciclovir molecule (green color FAM) and interlinking with fumaric molecules via acid-pyrimidine (blue color FUM) and acid-acid synthon (blue and yellow FUM). (c) Intertwining of 2D networks shown in figures S3a and S3b and utilization of cavities for close packing of side chains of famciclovir (green FAM) and fumaric acid (yellow FUM).

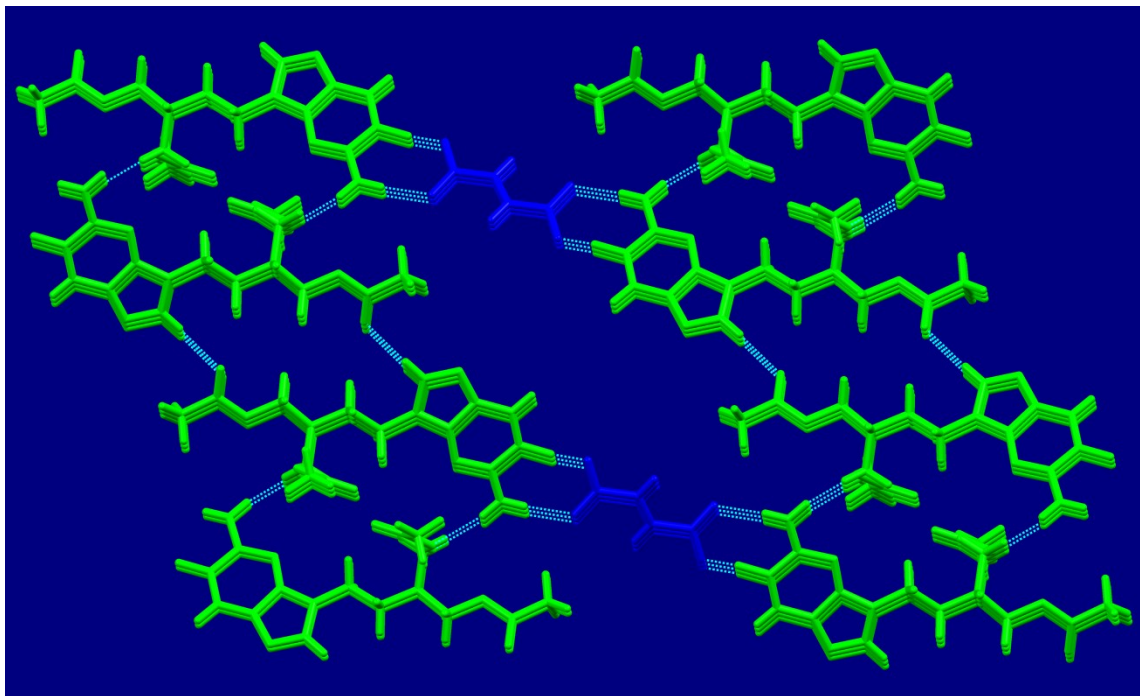


Figure S4. Crystal packing diagrams of FAM-FUM 1:0.5 crystal. The drug and coformer molecules are shown in different colors. The acetate group of famciclovir participates in a helix via N-H \cdots O hydrogen bond with the 2-aminopyrimidine ring (green color FAM) and extends the crystal packing a centrosymmetric C-H \cdots O motif between imidazole C-H and acetate O atom of famciclovir (green color FAM molecules). The helical networks are connected by acid-pyrimidine heterosynthon with fumaric acid (blue color FUM).

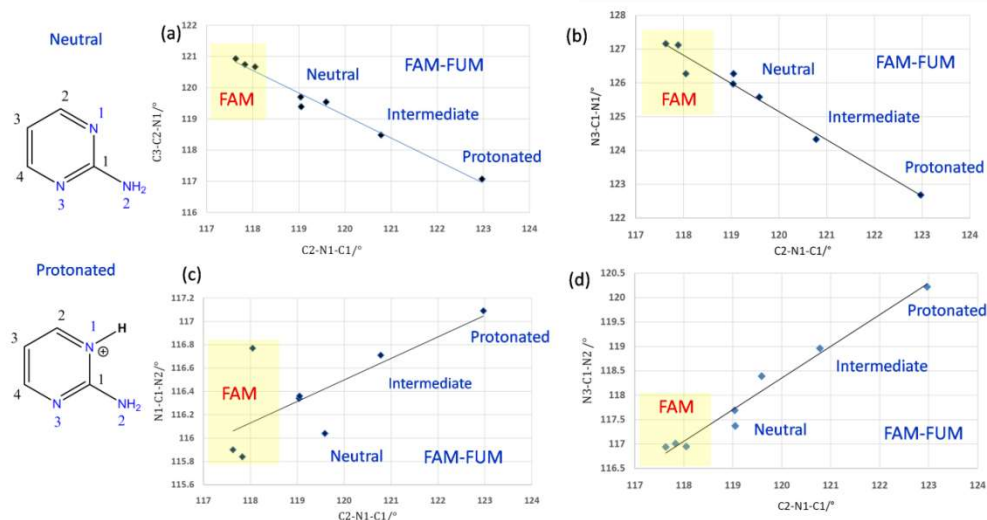


Figure S5. Scatter plots of bond angles of 2-aminopyrimidine ring of famciclovir (anhydrous and monohydrate) and famciclovir-fumaric acid crystalline forms (FAM-FUM 2:2 form I, FAM-FUM 2:2 form II and FAM-FUM 1:0.5). The atom labels of 2-aminopyrimidine ring are shown for neutral and protonated rings on the left hand side. (a) Scatter plot of $\angle C1-N1-C2$ vs $\angle C3-C2-N1$ (b) Scatter plot of $\angle C1-N1-C2$ vs $\angle N3-C1-N1$ (c) Scatter plot of $\angle C1-N1-C2$ vs $\angle N1-C1-N2$ (d) Scatter plot of $\angle C1-N1-C2$ vs $\angle N3-C1-N2$. The neutral, ionic and intermediate states are well distinguished on all plots.

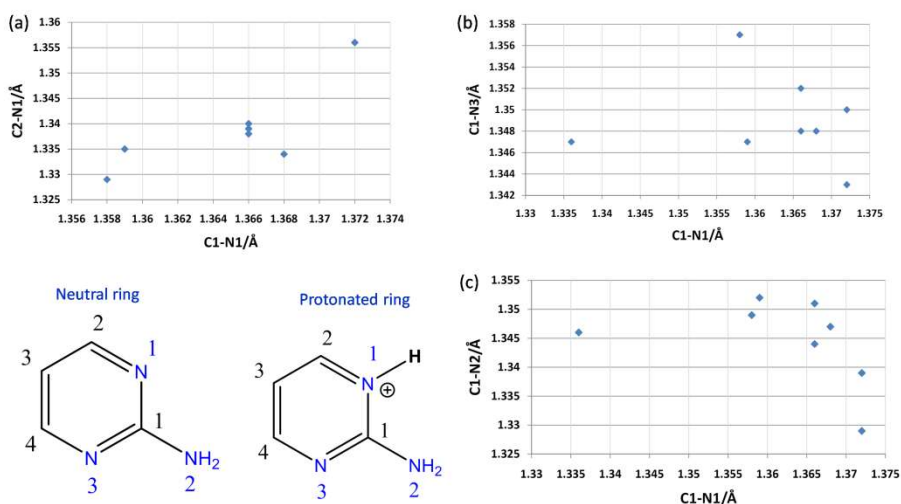


Figure S6. Scatter plots of bond distances of 2-aminopyrimidine ring of famciclovir (anhydrous and monohydrate) and famciclovir-fumaric acid crystalline forms (FAM-FUM 2:2 form I, FAM-FUM 2:2 form II and FAM-FUM 1:0.5). The atom labels of 2-aminopyrimidine ring are shown for neutral and protonated rings on the left bottom. (a) Scatter plot of bond distances $C1-N1$ vs $C2-N1$ (b) Scatter plot of bond distances $C1-N1$ vs $C1-N3$ (c) Scatter plot of bond distances $C1-N1$ vs $C1-N2$. The neutral and ionic states are well distinguished, but the intermediate state is very close to the ionic state.

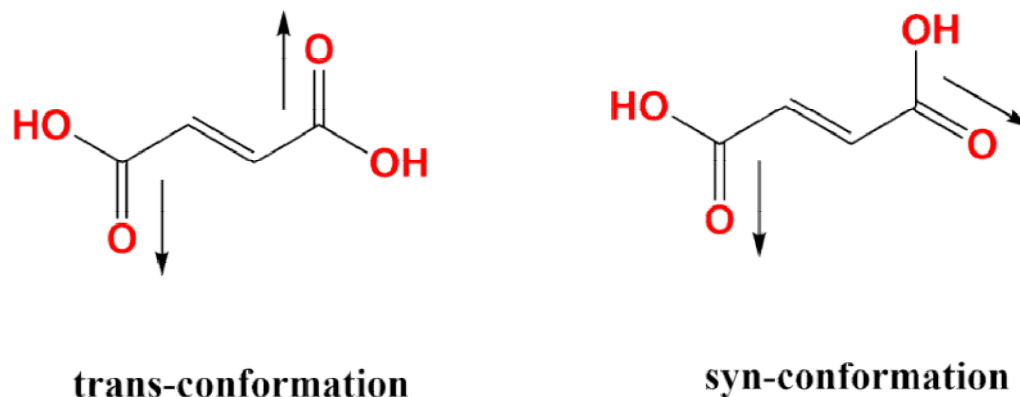


Figure S7. Two conformations of fumaric acid. The trans-conformation has two carbonyls pointing in opposite directions, while syn-conformation has two carbonyls on the same side.

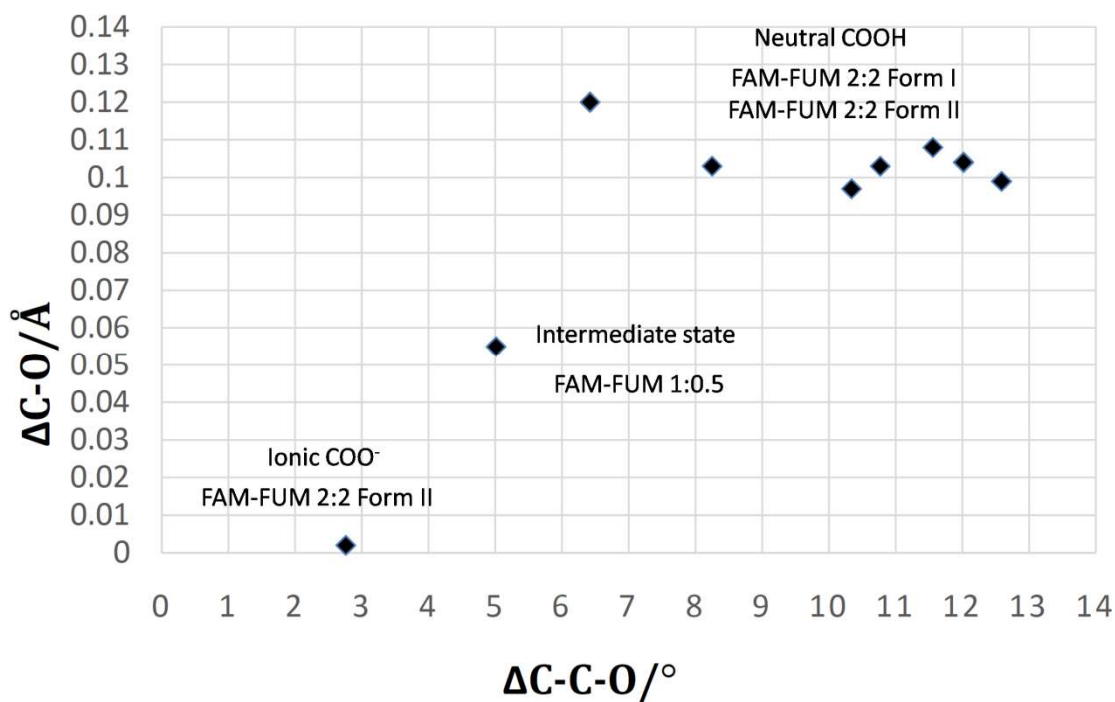
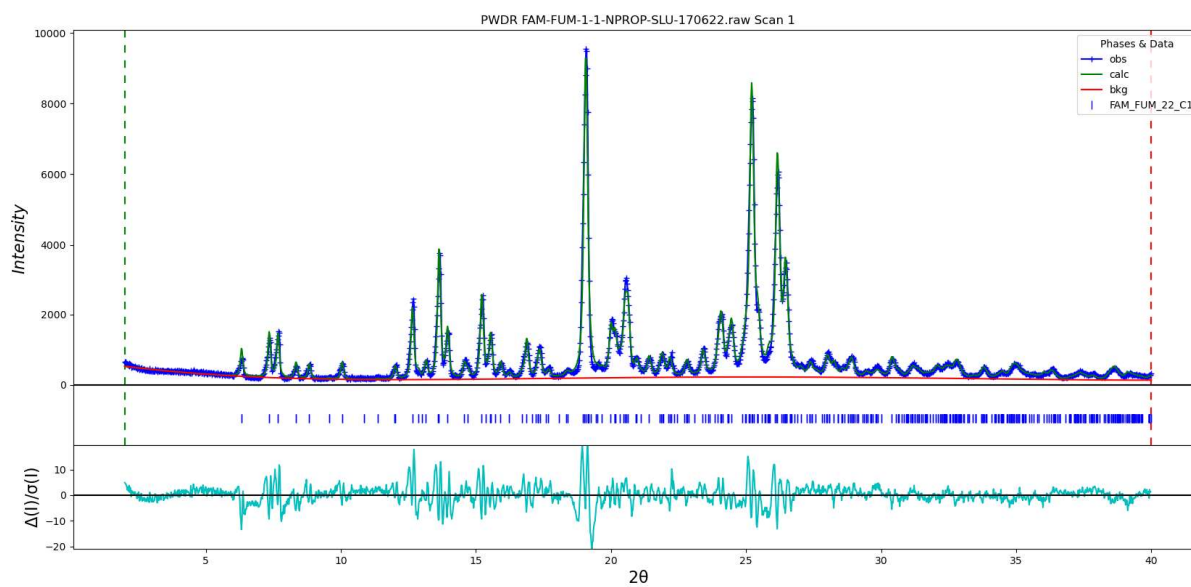
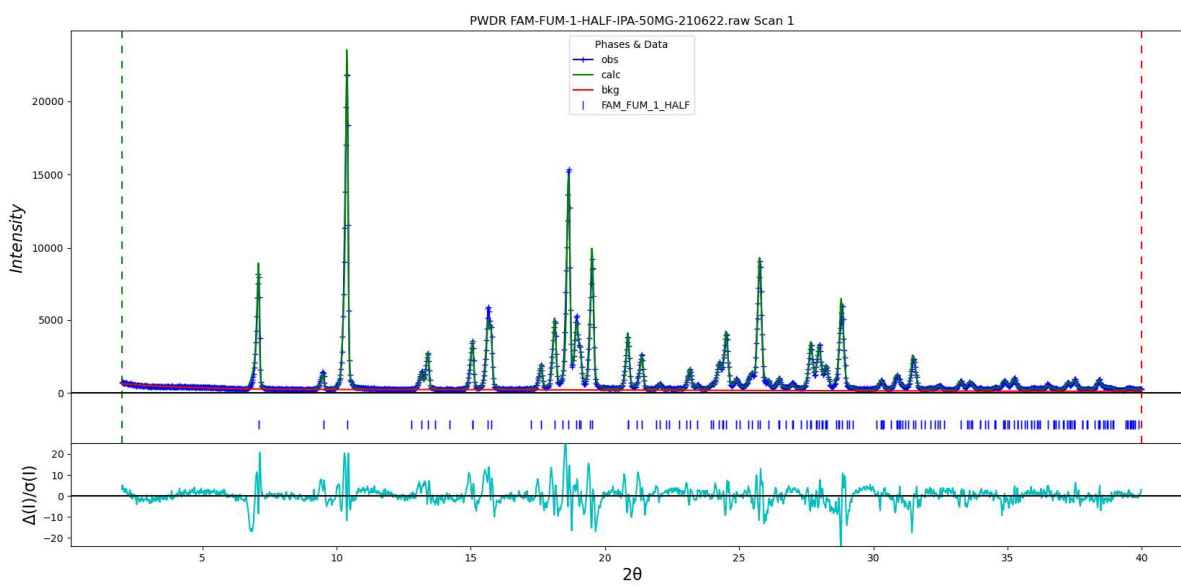


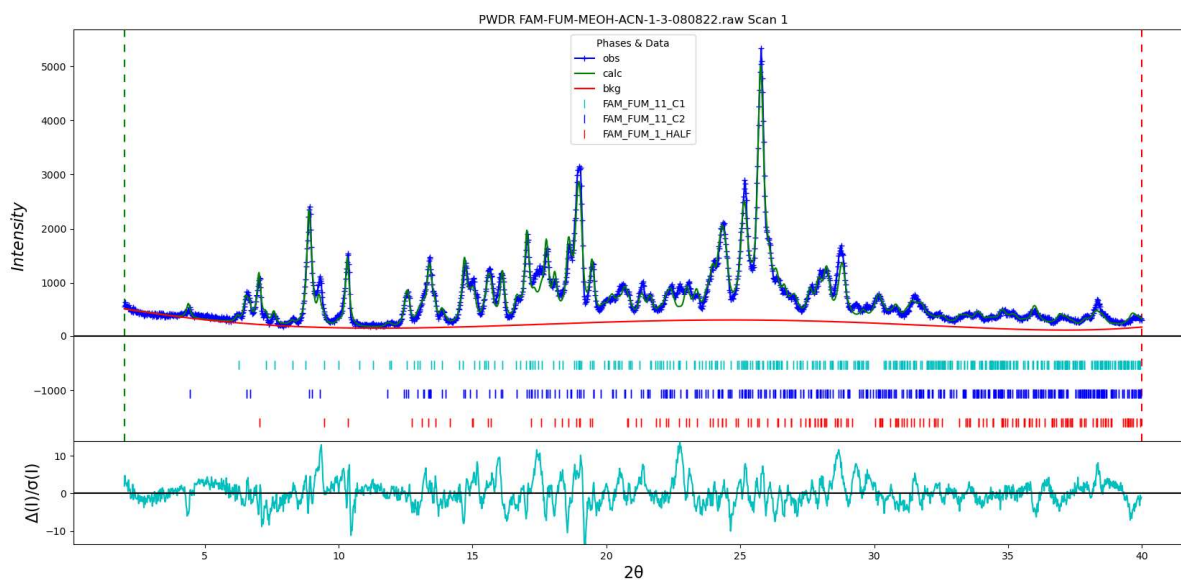
Figure S8. Scatter plot of bond angles ($\Delta C-C-O / ^\circ$, difference of $\angle C-C=O$ and $C-C-O / ^\circ$) vs bond distances ($\Delta C-O / \text{Å}$, difference of $C=O$ and $C-O / \text{Å}$) of famciclovir-fumaric acid complexes. Three different states of the complexes have distinct values. The neutral state as fumaric acid is seen in FAM-FUM 2:2 form I and form II (right top), the ionic state as fumarate in FAM-FUM 2:2 form II (left bottom) and the intermediate state in between fully ionic and fully neutral in FAM-FUM 1:0.5 (in the transition zone of neutral and ionic states).



(a)

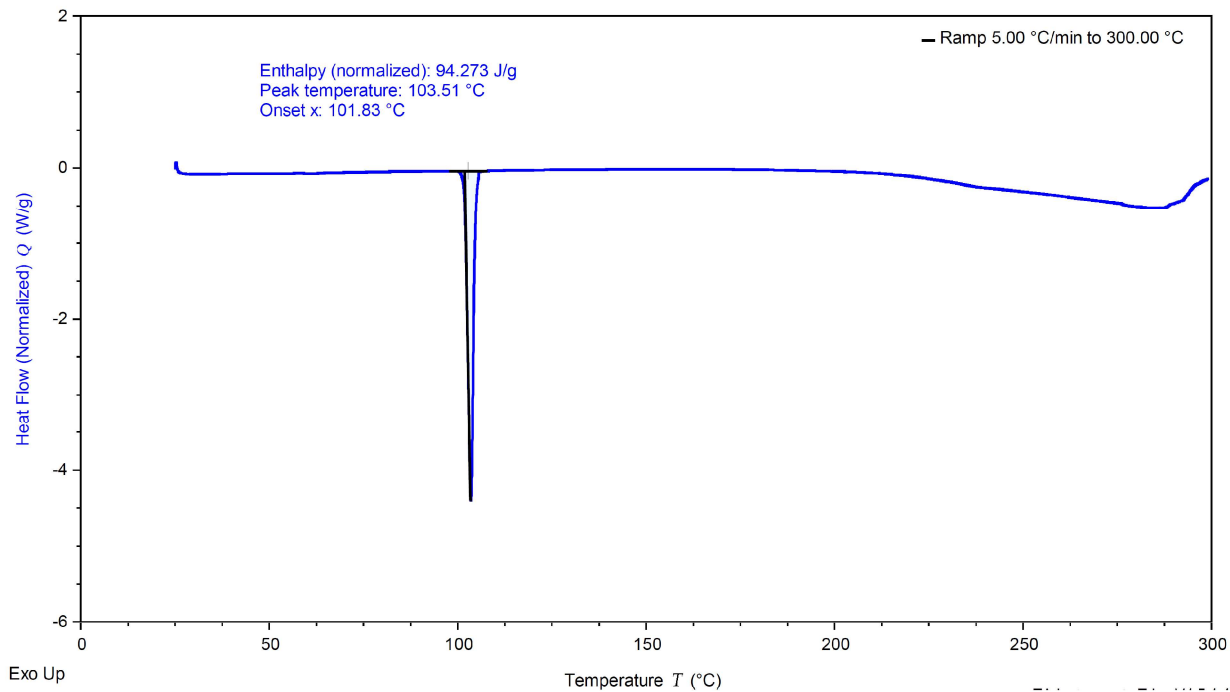


(b)

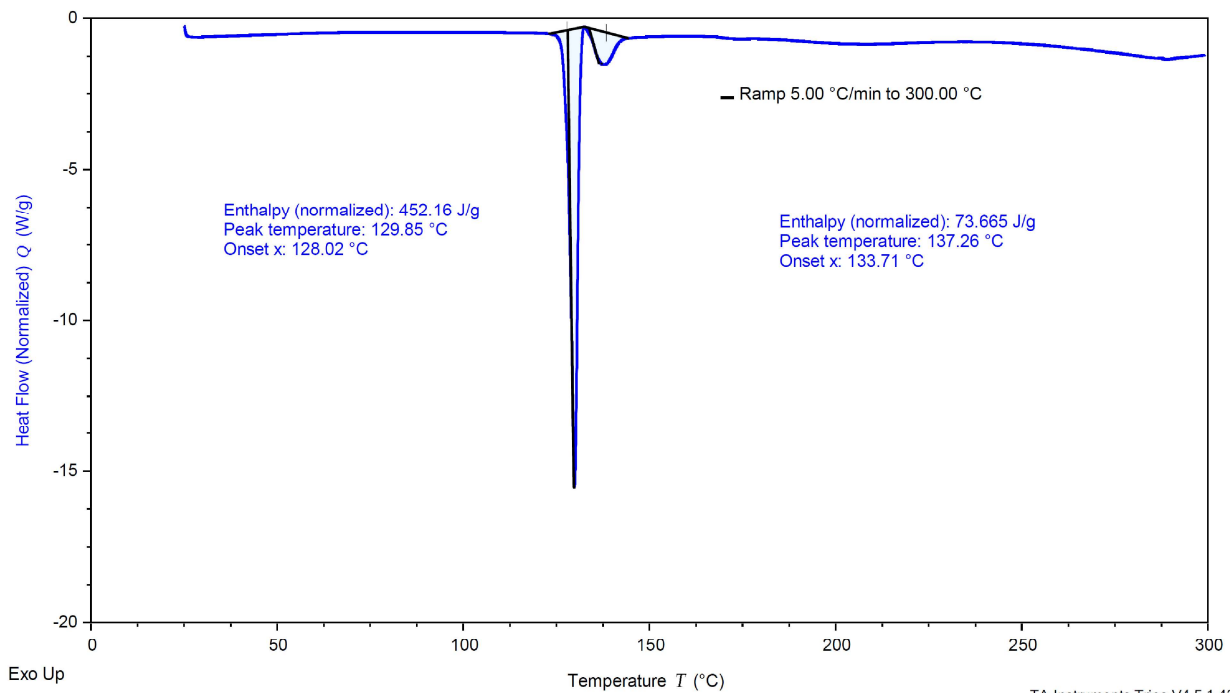


(c)

Figure S9. Rietveld refinement plots of (a) FAM-FUM 2:2 form I (b) FAM-FUM 1:0.5 and (c) mixture with high content of FAM-FUM 2:2 form II. The samples were found to be phase pure in the case of FAM-FUM 2:2 form I and FAM-FUM 1:0.5, while the mixture sample is represented by 54.4% FAM-FUM 2:2 form II, 28.4% of FAM-FUM 1:0.5 and 17.2% of FAM-FUM 2:2 form I. The blue trace in the plots represents experimental pattern, green trace for calculated profile, red trace for background, cyan trace represents residual between calculated and observed pattern and tick marks are indicative of hkl values of crystal structures.



(a)



(b)

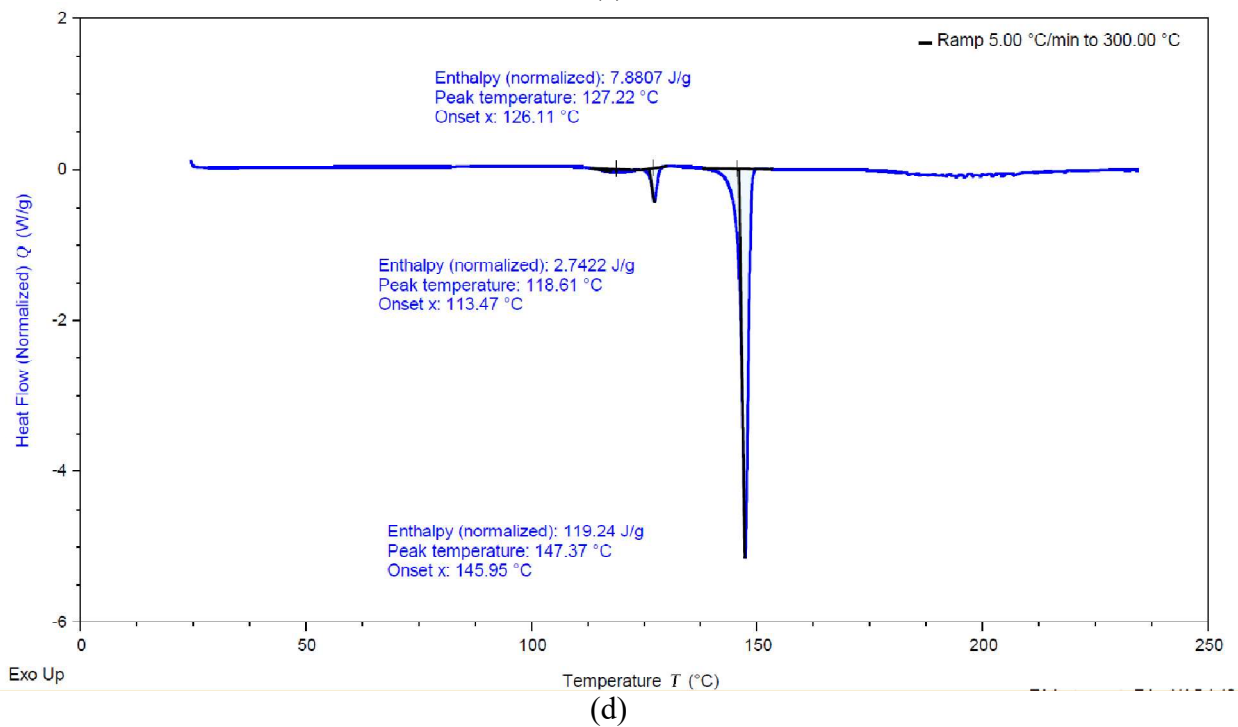
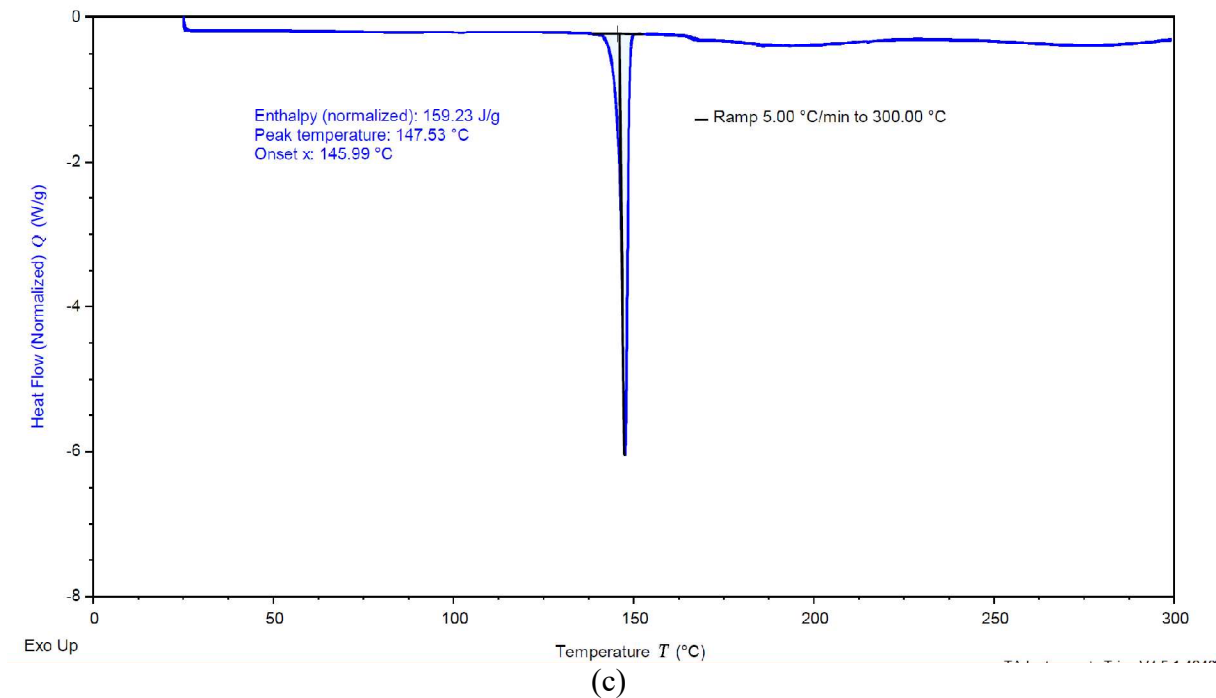
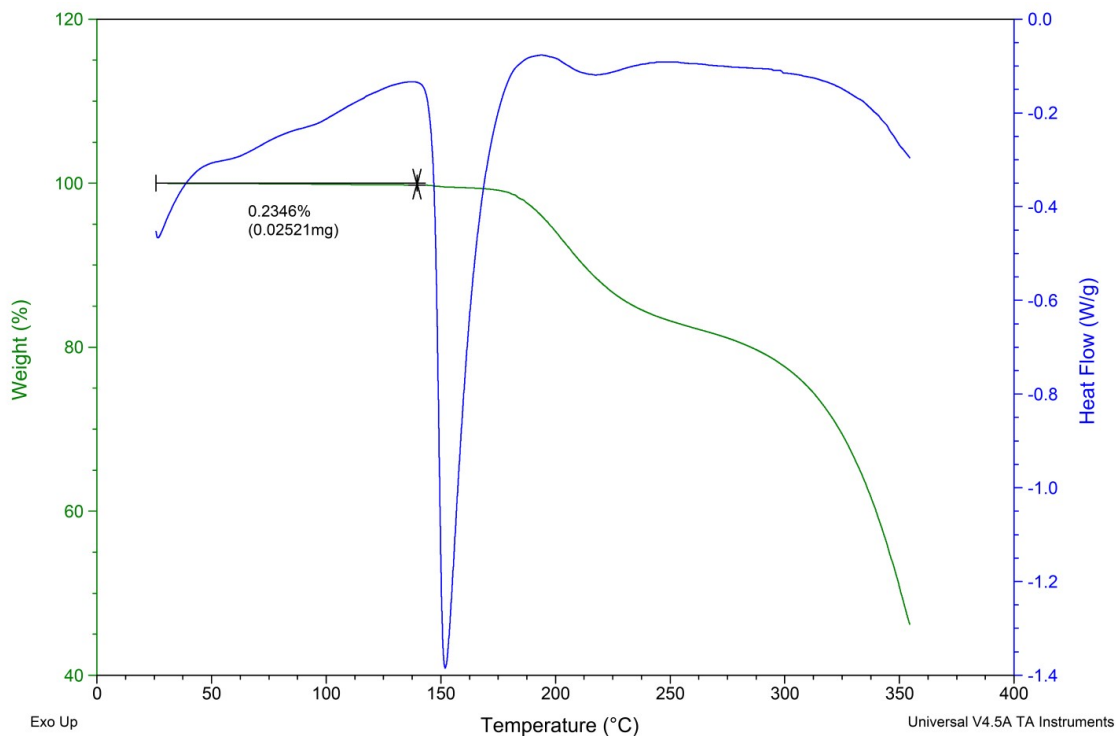
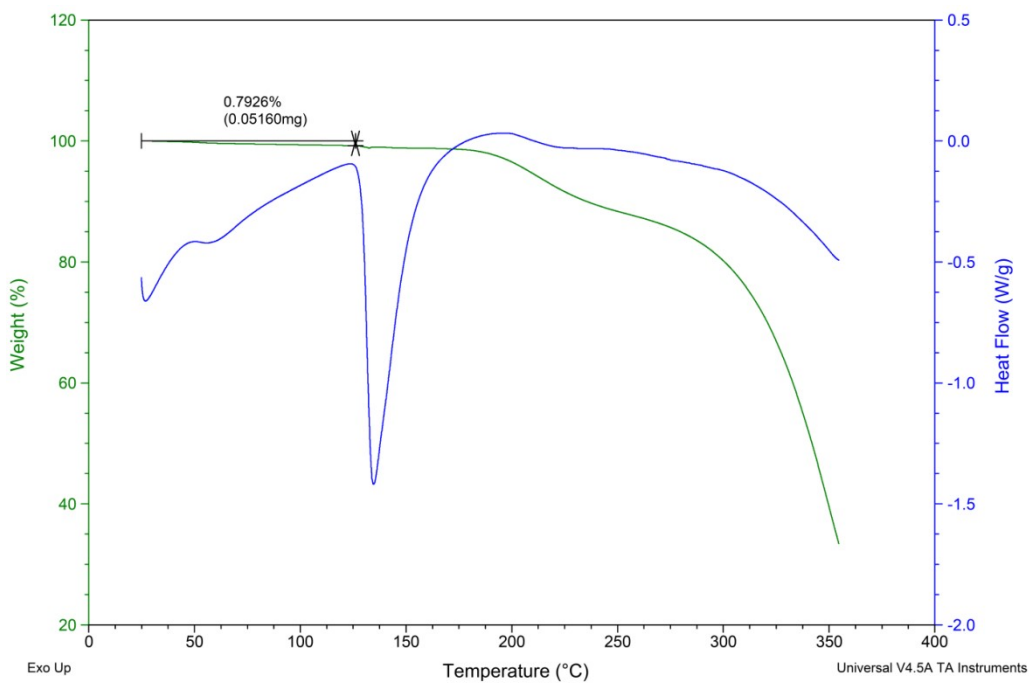


Figure S10. Differential Scanning Calorimetry thermogram plots. (a) Famciclovir (b) FAM-FUM 1:0.5 (c) FAM-FUM 2:2 form I (d) three-phase mixture with high content of FAM-FUM 2:2 form II.



(a)



(b)

Figure S11. TGA plots of (a) FAM-FUM 2:2 form I (b) FAM-FUM 1:0.5. The 2:2 form I showed almost negligible weight loss (0.2%) in the temperature range from RT to onset of melting temperature, while FAM-FUM 1:0.5 showed small amount of weight loss of 0.8% arising from surface bound moisture.