Novel Co-crystals of the Nutraceutical Sinapic Acid

Abhijeet S. Sinha, U. B. Rao Khandavilli, Emma O’Connor,
Benjamin J. Deadman, Anita R. Maguire and Simon E. Lawrence

simon.lawrence@ucc.ie

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List of co-formers used for the co-crystallization of Sinapic Acid

- Oxalic acid
- Succinic acid
- Adipic acid
- Pimelic acid
- Suberic acid
- Azelaic acid
- Benzoic acid
- 4-Aminobenzoic acid
- 4-Hydroxybenzoic acid
- Isonicotinic acid

**Figure 1.** Carboxylic acids used as co-formers (blue – failed; green – success).

- Urea
- Benzamide
- Anthranilamide
- 4-Aminobenzamide
- Salicylamide
- 4-Hydroxybenzamide
- Isonicotinamide
- Nicotinamide

**Figure 2.** Amides used as co-formers (blue – failed; green – success).
Figure 3. Pyridines used as co-formers (blue – failed; green – success).

Figure 4. Model active pharmaceutical ingredients (APIs) used as co-formers (blue – failed; green – success).
Single crystal XRD data for Sinapic Acid (SA)

**Figure 5.** ORTEP diagram of the structure of SA.

**Figure 6.** Crystal packing diagram of the structure of SA.
Figure 7. Photograph of SA crystal.
Sinapic Acid + Isonicotinic Acid (SA.INC)

Figure 8. IR spectrum of SA.INC.

Figure 9. Expanded view of the IR spectrum of SA.INC (green) compared with SA (black) and INC (red).
Figure 7. PXRD pattern of SA.INC.

Figure 10. DSC spectrum of SA.INC.
Sinapic Acid + Nicotinamide (SA.NIA)

Figure 8. IR spectrum of SA.NIA.

Figure 13. Expanded view of the IR spectrum of SA.NIA (green) compared with SA (black) and NIA (red).
Figure 14. DSC spectrum of SA.NIA.

Figure 15. PXRD pattern of SA.NIA.
Figure 16. ORTEP diagram of the structure of SA.NIA.

Figure 17. Crystal packing diagram of the structure of SA.NIA.
Figure 18. Photograph of SA.NIA crystal.
Sinapic Acid + 4-Pyridinecarbonitrile (SA.PYC)

Figure 19. IR spectrum of SA.PYC.

Figure 20. Expanded view of the IR spectrum of SA.PYC (green) compared with SA (black) and PYC (red).
Figure 21. DSC spectrum of SA.PYC.

Figure 22. PXRD pattern of SA.PYC.
Figure 23. ORTEP diagram of the structure of SA.PYC.

Figure 24. Crystal packing diagram of the structure of SA.PYC.
Figure 25. Photograph of SA.PYC crystal.
Sinapic Acid + 6-Propyl-2-Thiouracil + Acetonitrile (SA.PTU.2MeCN)

Figure 26. IR spectrum of SA.PTU.2MeCN.

Figure 27. Expanded view of the IR spectrum of SA.PTU.2MeCN (green) compared with SA (black) and PTU (red).
Figure 28. DSC spectrum of SA.PTU.2MeCN.

Figure 29. TGA spectrum of SA.PTU.2MeCN.
Figure 30. PXRD pattern of SA.PTU.2MeCN.

Figure 31. PXRD pattern overlay of SA.PTU.2MeCN single crystal data collected at 100 K (blue) and 298 K (black).
Figure 32. ORTEP diagram of the structure of SA.PTU.2MeCN.

Figure 33. Crystal packing diagram of the structure of SA.PTU.2MeCN.
Figure 34. Photograph of \textit{SA.PTU.2MeCN} crystal.
**Desolvation experiments with SA.PTU.2MeCN**

**Figure 35.** PXRD pattern of SA.PTU.2MeCN (blue) compared with desolvated sample (black), sinapic acid (green), and 6-propyl-2-thiouracil (red).

**Figure 36.** DSC spectrum of SA.PTU.2MeCN heated at 150 °C for 3 h.
Figure 37. IR spectrum of a 1:1 dry grind mixture of SA with PTU.

Figure 38. Expanded view of the IR spectrum of a 1:1 dry grind mixture of SA with PTU (green) compared with SA (black) and PTU (red).
Figure 39. PXRD pattern of a 1:1 dry grind mixture of SA with PTU (black) compared with sinapic acid (green), and 6-propyl-2-thiouracil (red).

Figure 40. DSC spectrum of a 1:1 dry grind mixture of SA with PTU.
Table 1. Key hydrogen-bond parameters for the crystal structures.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Interaction</th>
<th>d(D-H)/Å</th>
<th>d(DH•••A)/Å</th>
<th>d(D•••A)/Å</th>
<th>Angle(D-H•••A)°</th>
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<tr>
<td>SA</td>
<td>O10-H10–O11</td>
<td>0.97(2)</td>
<td>1.68(2)</td>
<td>2.6410(15)</td>
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<td>O14-H14–O11</td>
<td>0.88(3)</td>
<td>2.07(3)</td>
<td>2.8594(17)</td>
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<td>O14-H14–O15</td>
<td>0.88(3)</td>
<td>2.16(2)</td>
<td>2.6561(17)</td>
<td>115.1(19)</td>
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<td>SA.NIA</td>
<td>O10-H10–O11</td>
<td>0.82</td>
<td>1.81</td>
<td>2.626(3)</td>
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<td>O14-H14–N17</td>
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<td>1.95</td>
<td>2.681(3)</td>
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<td>O14-H14–O12</td>
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<td>2.28</td>
<td>2.714(3)</td>
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<td>N25-H25A–O15</td>
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<td>2.317(19)</td>
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<td>N25-H25A–O14</td>
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<td>2.473(18)</td>
<td>3.228(3)</td>
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<td>N25-H25B–O24</td>
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<td>2.036(11)</td>
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<td>SA.PYC</td>
<td>O10-H10–O27</td>
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<td>1.75</td>
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<td>O14-H14–N41</td>
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<td>O26-H26–O11</td>
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<td>O30-H30–N33</td>
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<td>1.99</td>
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<td>SA.PTU.2MeCN</td>
<td>N18-H18–O11</td>
<td>0.881(5)</td>
<td>1.935(7)</td>
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<td>N22-H22–S23</td>
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<td>2.452(6)</td>
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<td>O10-H10–O24</td>
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<td>O14-H14–N33</td>
<td>0.839(5)</td>
<td>2.012(10)</td>
<td>2.820(2)</td>
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Stability of Sinapic Acid (SA)

**Figure 41.** Stability of sinapic acid (SA) based on PXRD data.

**Figure 42.** HPLC analysis of sinapic acid measured at 250 nm (top), 280 nm (middle) and 320 nm (bottom) (SA).
Figure 43. HPLC analysis of sinapic acid (SA) after 6 weeks at 40 °C and 75% RH, measured at 250 nm (top), 280 nm (middle) and 320 nm (bottom).
Stability of Sinapic Acid + Isonicotinic Acid (SA.INC)

**Figure 44.** Stability of SA.INC based on PXRD data.

**Figure 45.** HPLC analysis of isonicotinic acid measured at 250 nm (top), 280 nm (middle) and 320 nm (bottom) (INC).
Figure 46. HPLC analysis of SA.INC after 6 weeks at 40 °C and 75% RH, measured at 250 nm (top), 280 nm (middle) and 320 nm (bottom).
Stability of Sinapic Acid + Nicotinamide (SA.NIA)

Figure 47. Stability of SA.NIA based on PXRD data.

Figure 48. HPLC analysis of nicotinamide measured at 250 nm (top), 280 nm (middle) and 320 nm (bottom) (NIA).
Figure 49. HPLC analysis of SA.NIA after 6 weeks at 40 °C and 75% RH, measured at 250 nm (top), 280 nm (middle) and 320 nm (bottom).
Stability of Sinapic Acid + 4-Pyridinecarbonitrile (SA.PYC)

Figure 50. Stability of SA.PYC based on PXRD data.

Figure 51. HPLC analysis of 4-pyridinecarbonitrile measured at 250 nm (top), 280 nm (middle) and 320 nm (bottom) (PYC).
Figure 52. HPLC analysis of SA.PYC after 6 weeks at 40 °C and 75% RH, measured at 250 nm (top), 280 nm (middle) and 320 nm (bottom).
Stability of Sinapic Acid + 6-Propyl-2-Thiouracil + Acetonitile (SA.PTU.2MeCN)

**Figure 53.** Stability of SA.PTU.2MeCN based on PXRD data.

**Figure 54.** Comparison of SA.PTU.2MeCN PXRD theoretical pattern (blue) with actual (black), 2 week stability (green), sinapic acid (red), and 6-propyl-2-thiouracil (brown) spectra.
Figure 55. HPLC analysis of 6-propyl-2-thiouracil measured at 250 nm (top), 280 nm (middle) and 320 nm (bottom) (PTU).

Figure 56. HPLC analysis of SA.PTU.2MeCN after 6 weeks at 40 °C and 75% RH, measured at 250 nm (top), 280 nm (middle) and 320 nm (bottom).