Microwave assisted slurry conversion crystallization for manufacturing of new co-crystals of sulfamethazine and sulfamerazine

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PXRD patterns for various samples:

![PXRD patterns](image)

**Figure S1.** PXRD patterns of sulfamethazine (SMT), salicylic acid (SA), co-crystal obtained from CSD (simulated) and co-crystal from microwave assisted slurry crystallization (experimental).
Figure S2. PXRD patterns of sulfamethazine (SMT), anthranilic acid (AA), co-crystal obtained from CSD (simulated) and co-crystal from microwave assisted slurry crystallization (experimental).

Figure S3. PXRD patterns of sulfamethazine (SMT), benzamide (BEN), co-crystal obtained from CSD (simulated) and co-crystal from microwave assisted slurry crystallization (experimental).
Figure S4. PXRD patterns of sulfamethazine (SMT), aspirin (ASP), co-crystal obtained from CSD (simulated) and co-crystal from microwave assisted slurry crystallization (experimental).

Figure S5. PXRD patterns of sulfamethazine (SMT), salicylamide (SAL) and solid from microwave assisted slurry crystallization.
**Figure S6.** PXRD patterns of sulfamerazine (SMR), salicylic acid (SA) and solid from microwave assisted slurry crystallization.

**Figure S7.** PXRD patterns of sulfamerazine (SMR), nicotinamide (NIC) and solid from microwave assisted slurry crystallization.
**Figure S8.** PXRD patterns of sulfamerazine (SMR), benzamide (BEN) and solid from microwave assisted slurry crystallization.

**Figure S9.** PXRD patterns of sulfamerazine (SMR), aspirin (ASP) and solid from microwave assisted slurry crystallization.
**Figure S10.** PXRD patterns of SMR-AA co-crystal after 6 months (bench), after 1 day, and after 1 and 9 weeks under accelerated conditions of 40 °C and RH 75 % (stability study).

**Figure S11.** PXRD patterns of SMR-SAL co-crystal after 6 months (bench), after 1 day, and after 1 and 9 weeks under accelerated conditions of 40 °C and RH 75 % (stability study).
Figure S12. PXRD patterns of SMT-NIC co-crystal after 6 months (bench), after 1 day, and after 1 and 9 weeks under accelerated conditions of 40 °C and RH 75 % (stability study).

Figure S13. PXRD patterns of the three co-crystals after 10 times and 100 times scale-up.
### Table S1. Hydrogen bond parameters for SMT-NIC co-crystal in (Å, °).

<table>
<thead>
<tr>
<th>D-H--A</th>
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<th>D--A</th>
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<td>N2B-H2B1--N7A</td>
<td>0.88</td>
<td>2.22</td>
<td>3.058(4)</td>
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<td>N2B-H2B2--O17A</td>
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<td>2.24</td>
<td>3.073(4)</td>
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<td>N3A-H3A--O1B</td>
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<td>1.83</td>
<td>2.699(4)</td>
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<td>N15A-H15A--O16A</td>
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<td>2.12</td>
<td>2.950(4)</td>
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<tr>
<td>N15A-H15B--N6B</td>
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<td>2.43</td>
<td>3.105(4)</td>
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</tr>
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<td>C14A-H14A--O16A</td>
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<td>2.46</td>
<td>2.865(4)</td>
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### Table S2. Hydrogen bond parameters for SMR-SAL co-crystal in (Å, °).

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<th>D--A</th>
<th>Å</th>
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<td>N8B-H8B1--O10B</td>
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<td>N8B-H8B2--O16A</td>
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<td>2.25</td>
<td>3.0506(16)</td>
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<td>N7A-H7A--N3A</td>
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<td>2.8989(18)</td>
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<td>O7B-H7B--O10B</td>
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<td>2.5139(17)</td>
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<td>N15A-H15A--O7B</td>
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<td>2.17</td>
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<td>N15A-H15B--O16A</td>
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<td>3.2183(19)</td>
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<td>C4A-H4A--O17A</td>
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<td>C10A-H10A--O16A</td>
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### Table S3. Hydrogen bond parameters for SMR-AA co-crystal in (Å, °).

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<th>D--A</th>
<th>Å</th>
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<td>2.723(2)</td>
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<tr>
<td>N10B-H10B--O17A</td>
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<td>2.29</td>
<td>3.030(2)</td>
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<td>N10B-H10C--O2B</td>
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<td>C8B-H8B--O16A</td>
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<td>2.56</td>
<td>3.340(3)</td>
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<td>C9B-H9B--O1B</td>
<td>0.93</td>
<td>2.42</td>
<td>2.742(3)</td>
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</table>
Figure S14. HPLC chromatograms of pure SMR, SMR-SAL and SMR-AA co-crystals.
Figure S15. HPLC chromatograms of pure SMT, and SMT-NIC co-crystal.
Figure S16. Hirshfeld surface plots of SMT form I (a), NIC (b), SMT molecule in SMT-NIC co-crystal (c) NIC molecule in SMT-NIC co-crystal (d).
Figure S17. Hirshfeld surface plots of SMR form I (a), AA (b), SMR molecule in SMR-AA co-crystal (c) AA molecule in SMT-AA co-crystal (d).
Figure S18. Hirshfeld surface plots of SAL (a), SMR molecule in SMR-SAL co-crystal (b) AA molecule in SMT-SAL co-crystal (c).
Figure S19. 2-D finger plots of SMT form I (a), NIC (b), SMT molecule in SMT-NIC co-crystal (c) NIC molecule in SMT-NIC co-crystal (d).
**Figure S20.** Hirshfeld surface plots of SMR molecule 1 (a), SMR molecule 2 (b) AA (c), SMR molecule in SMR-AA co-crystal (d) AA molecule in SMT-AA co-crystal (e).

**Figure S21.** 2-D fingerprint plots of SAL (a), SMR molecule in SMR-SAL co-crystal (b) AA molecule in SMT-SAL co-crystal (c).
Information for Tables S4- S11:

The interaction energies are in kJ/mol. ‘R’ is the distance between molecular centroids in Å. Total energies are the sum of four energy components, scaled appropriately as per the scale factors:

\[ E_{tot} = k_{ele}E_{ele} + k_{pol}E_{pol} + k_{disp}E_{disp} + k_{rep}E_{rep} \]  

Table S4. Interaction energy profile for SMT.

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<th>Symop</th>
<th>R</th>
<th>Electron Density</th>
<th>E_ele</th>
<th>E_pol</th>
<th>E_rep</th>
<th>E_tot</th>
</tr>
</thead>
<tbody>
<tr>
<td>x, y, z</td>
<td>7.43</td>
<td>B3LYP/6-31G(d,p)</td>
<td>0.8</td>
<td>-2.5</td>
<td>1.8</td>
<td>-6.6</td>
</tr>
<tr>
<td>-x+1/2, y+1/2, -z</td>
<td>12.41</td>
<td>B3LYP/6-31G(d,p)</td>
<td>0.2</td>
<td>-0.1</td>
<td>0.1</td>
<td>-1.7</td>
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<tr>
<td>x, y, z</td>
<td>9.32</td>
<td>B3LYP/6-31G(d,p)</td>
<td>-9.2</td>
<td>-4.3</td>
<td>-21.7</td>
<td>18.1</td>
</tr>
<tr>
<td>x+1/2, -y+1/2, z</td>
<td>10.29</td>
<td>B3LYP/6-31G(d,p)</td>
<td>-7.6</td>
<td>-2.9</td>
<td>-8.3</td>
<td>4.0</td>
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<tr>
<td>x+1/2, -y+1/2, z</td>
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<td>B3LYP/6-31G(d,p)</td>
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<td>-3.7</td>
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<td>x+1/2, -y+1/2, z</td>
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<td>-9.2</td>
<td>-47.9</td>
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<tr>
<td>-x, -y, -z</td>
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<td>B3LYP/6-31G(d,p)</td>
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<td>-2.0</td>
<td>0.0</td>
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<tr>
<td>-x, -y, -z</td>
<td>6.19</td>
<td>B3LYP/6-31G(d,p)</td>
<td>-33.6</td>
<td>-8.3</td>
<td>-45.6</td>
<td>44.3</td>
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<tr>
<td>-x, -y, -z</td>
<td>7.38</td>
<td>B3LYP/6-31G(d,p)</td>
<td>-33.2</td>
<td>-9.1</td>
<td>-58.0</td>
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<td>-4.6</td>
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<tr>
<td>-x, -y, -z</td>
<td>10.52</td>
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<td>-0.2</td>
<td>-4.6</td>
<td>1.8</td>
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Table S5. Interaction energy profile for NIC.

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<th>Symop</th>
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<th>Electron Density</th>
<th>E_ele</th>
<th>E_pol</th>
<th>E_rep</th>
<th>E_tot</th>
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<tbody>
<tr>
<td>x, y, z</td>
<td>3.88</td>
<td>B3LYP/6-31G(d,p)</td>
<td>5.6</td>
<td>-1.3</td>
<td>-29.6</td>
<td>15.8</td>
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<tr>
<td>-x, -y, -z</td>
<td>7.15</td>
<td>B3LYP/6-31G(d,p)</td>
<td>-3.9</td>
<td>-0.6</td>
<td>-12.0</td>
<td>11.2</td>
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<tr>
<td>-x, -y, -z</td>
<td>8.20</td>
<td>B3LYP/6-31G(d,p)</td>
<td>-9.8</td>
<td>-1.6</td>
<td>-10.2</td>
<td>12.7</td>
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<tr>
<td>x, -y+1/2, z+1/2</td>
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<td>B3LYP/6-31G(d,p)</td>
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<td>-9.0</td>
<td>-12.5</td>
<td>35.4</td>
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<tr>
<td>x, -y+1/2, z+1/2</td>
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<td>B3LYP/6-31G(d,p)</td>
<td>-36.1</td>
<td>-8.2</td>
<td>-12.7</td>
<td>31.9</td>
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<tr>
<td>-x, -y, -z</td>
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<td>B3LYP/6-31G(d,p)</td>
<td>-12.0</td>
<td>-2.5</td>
<td>-17.7</td>
<td>16.3</td>
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<tr>
<td>-x, y+1/2, -z+1/2</td>
<td>7.93</td>
<td>B3LYP/6-31G(d,p)</td>
<td>2.7</td>
<td>-1.0</td>
<td>-6.2</td>
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Table S6. Interaction energy profile for SMT-NIC co-crystal

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<th>E_pol</th>
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Table S7. Interaction energy profile for SMR.

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<th>E_ele</th>
<th>E_pol</th>
<th>E_dis</th>
<th>E_rep</th>
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Table S8. Interaction energy profile for AA.

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<th>E_pol</th>
<th>E_dis</th>
<th>E_rep</th>
<th>E_tot</th>
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Table S9. Interaction energy profile for SMR-AA.

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Table S10. Interaction energy profile for SAL.

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<th>E_dis</th>
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Table S11. Interaction energy profile for SMR-SAL.

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