Stabilization of the amorphous state of pharmaceuticals in nanopores

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Supplementary Information

Experimental Section

Materials. Acetaminophen (ACE) having a molecular weight of 151.16g/mol and a purity >99% was purchased from Sigma-Aldrich. Controlled porous glasses (CPGs) were obtained by leaching phase-separated sodium borosilicate glasses containing 70wt-% SiO₂, 23wt-% B₂O₃ and 7wt-% Na₂O. Thin CPG membranes having a thickness of about 300 µm were prepared in three steps: (i) generation of the desired shape by sawing, (ii) heat treatment in the temperature range between 530 and 720°C to induce phase separation, (iii) removal of the soluble phase by acids or combined acid/alkaline leaching treatment. The properties of the CPGs used in this work are summarized in Table SI. The samples have a sponge-like morphology as typical for materials produced by spinodal decomposition. The pore size distribution of the CPGs is narrow. Details of their preparation are described in Ref.(S1). A few additional experiments were performed on Vycor brand porous glass 7930 having an average pore diameter of 4 nm infiltrated with acetaminophen. Further information about this commercial porous glass sold by Corning Inc. are given in Ref.(S2).

Table SI. Textural properties of the CPG membranes used as host systems

<table>
<thead>
<tr>
<th>d in nm</th>
<th>μ in m²/g</th>
<th>v in cm³/g</th>
<th>P in %</th>
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</thead>
<tbody>
<tr>
<td>43</td>
<td>36</td>
<td>0.36</td>
<td>44</td>
</tr>
<tr>
<td>4.6</td>
<td>110</td>
<td>0.108</td>
<td>20</td>
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# Average pore diameter d, internal surface area μ, specific pore volume v and porosity P values are determined based on mercury porosimetry (43 nm) and nitrogen absorption (4.6 nm) measurements.

Sample Preparation. The CPG membranes were carefully dried in a vacuum oven at 180°C for 2 hours to remove entrapped moisture from the pores. Then, the pre-dried CPGs were infiltrated by immersing them in molten acetaminophen heated to 180°C for about 5 min. The samples were cooled to room temperature in the presence of a bulk acetaminophen surface layer, which was then carefully removed with a scalpel. Small pieces of the infiltrated CPGs with a mass of about 10mg were encapsulated in hermetically sealed aluminum pans (10µl) for subsequent DSC measurements. The chemical stability of ACE at 180°C has been tested by additional IR and Raman experiments indicating no detectable degradation effect consistent with high reproducibility of our DSC crystallization experiments on re-used samples.

DSC measurements. PerkinElmer Pyris Diamond and DSC 7 instruments were used for calorimetric measurements. All heating scans were performed at a heating rate of +10K/min.
Additional data for ACE in nanoporous host systems

**Figure S1.** Wide angle x-ray scattering data for acetaminophen in CPGs with 43 nm pores. The measurements are performed at room temperature. The samples are prepared in the DSC according to the programs described in the caption of Figure 1. Form I has been obtained for a sample having the thermal history as the sample used for the 1st heating scan, form III has been obtained using the isothermal crystallization program applied before measuring the 3rd heating scan. The amorphous halo is caused by the host system. Further information can be also found in Ref.[7a].

**Figure S2.** DSC heating scan for ACE confined in CPG with 4.6 nm pores measured after quenching the sample at a nominal rate of ~200K/min and isothermal crystallization at 35°C for 10 days.
Figure S3. DSC heating scans for ACE confined in Vycor brand porous glass 7930 showing the absence of a crystalline fraction and two distinct glass transitions. The scans are measured after different thermal treatments (1st heating: measured on a host-guest system crystallized while covered with a bulk ACE surface film; 2nd heating: measured after quenching the sample from 180°C to –40°C at a nominal rate of –200K/min after the removal of the ACE surface films; 3rd heating: measured after fast DSC quenching (-200K/min) and isothermal crystallization at 42°C for 120 min.) The curves are vertically shifted by 0.2 J/gK.

References