Supporting Information for "Rapid and Selective Crystallization of Acetaminophen using Metal-Assisted and Microwave-Accelerated Evaporative Crystallization" Mohammed et al.

Materials. Acetaminophen (< 99 %, USP grade), ethyl alcohol (190 proof), silver nitrate (>%99), D-glucose, ammonium hydroxide, sodium hydroxide and Silane-prep^{TM} glass microscope slides were purchased from Sigma-Aldrich Chemical Co. (Milwaukee, WI).
Methods. Deposition of Silver Island Films (SIFs): All glass ware were cleaned with piranha solution (3:7, 30 % hydrogen peroxide and conc. sulfuric acid, CAUTION: Piranha solution must be handled with care). SIFs were prepared by a modified Tollen's reaction scheme. In this regard, 390 ml of silver nitrate was taken in a 700 ml dish. While stirring at high speed, 1.4 ml of freshly prepared 5% (w/v) sodium hydroxide is added resulting in the formation of greenish-brown precipitate. Approximately 14 ml of 30% ammonium hydroxide solution is added to dissolve the precipitate, giving a clear solution. The solution is cooled down to 5^{o}C in an ice bath. The clean glass slides are introduced into the solution and after 2 minutes, a fresh solution of D-glucose is added. Subsequently, the temperature of the solution is raised to 30^{o}C. The solution changes color to yellowish-green and the silver is deposited onto the slides which turn green in approximately 2 mins. The slides are washed with deionized (DI) water, sonicated for 2 mins at room temperature; rinsed with deionized (DI) water several times and stored in deionized (DI) water until further used.
Characterization. Microscopic (optical) and timed images of the progression of crystals under all conditions were captured using Swift Digital M10L Monocular Microscope at 10X magnification. Images of the slides were taken with 12 MP digital camera. Raman spectroscopy was performed using *i*-Raman spectrometer (BW & Tek, Inc., Delaware, USA) and data was plotted with SigmaPlot software. Powder X-Ray Diffraction was done using Rigaku mini-XRD diffractometer.

Additional Results

Figure S4 shows the time progression of growth of acetaminophen crystals on blank glass slides and SIFs using microwave heating (PL 10). On glass slides (Figure S2-S3), a mixture of Form I and Form II acetaminophen crystals appear within 10 sec of microwave heating. As water completely evaporates in 25 sec on blank glass slides, the size of acetaminophen crystals increases up to 930 μm that is significantly larger than those grown on blank glass slides at room temperature (140-453 μm). It is important to note that there is a significant variation in the size of acetaminophen crystals grown on blank glass slides at all microwave heating levels studied here (Table 1). This is attributed to the fact that blank glass slides nucleation and growth of acetaminophen crystals occurs in a random fashion because there are no selective sites for these processes. On the other hand, the variation in crystal size on SIFs is less pronounced as compared to crystals grown on blank glass slides. Water is completely evaporated and crystal growth concluded in 15 sec on SIFs with microwave heating (PL 10). As shown in Figure S4-S5, the majority of the acetaminophen crystals is Form II crystals.

Figure S7 shows Raman spectra of acetaminophen crystals grown on blank glass slides and SIFs at room temperature and microwave heating (PL 10). The spectra were offset

for clarity and the peak names are reported in Figure S7-left. The Form I Raman spectrum exhibits five characteristic peaks in the 1200-1375 cm^{-1} range and three well-defined peaks in the 1500-1700 cm^{-1} range. The Form II Raman spectrum shows weak peaks at 1220 and 1245 cm^{-1} and a strong peak at 1329 cm^{-1}; the 1500-1700 cm^{-1} peaks shift closer to each other. Based on this information, the Raman spectra shown in Figure S7 imply that acetaminophen crystals grown on blank glass slides and SIFs at room temperature and microwave heating (PL 10) appear to be mostly of Form I. This is attributed to the mixed nature of acetaminophen crystals grown on these surfaces and the small sampling area of the laser spot from the Raman instrument.

Procedure for Quantitative Analysis of PXRD data:

Quantitative analysis of PXRD data for acetaminophen was performed using an open-access software, Materials Analysis Using Diffraction (MAUD) obtained from its developers (http://www.ing.unitn.it/~maud/). The CIF files for acetaminophen were obtained from Cambridge Crystallographic Data Center. Figure S8 shows the 2D plot for these two forms. In this regard, the following procedure was carried out using MAUD:

1. PXRD data is converted into ASCII format and uploaded into the program. (File new dataset).
2. The .CIF file for Form i and Form II are uploaded under the “Phases tab”. (Edit/Load an object from database Acetaminophen.CIF)
3. Each spectrum is computed with the actual values of the phases and a plot matching dataset and the standard is created. (Press the “Calculator” from the tool bar).
4. Run the quantitative analysis. (Analysis / Wizard Quantitative Analysis / GO!)
5. Rw and sig values, which are useful in assessing the goodness of fitting analysis, were extracted. Additional iterations with the last definable parameters were carried out to calculate the best fit.
6. MAUD plots the intensities in SQRT. (Select “SQRT” for the intensity mode) (Options / Plotting / Intensity scale mod/SQRT)
7. To view results select “Results” from the “Analysis” menu. (Analysis / Results)
8. The result of analysis is given under “Refined Parameters” as volume phase fraction complementary to the quantity to Form I and Form II of Acetaminophen (by default as 1.0).

Glass_DI_RT

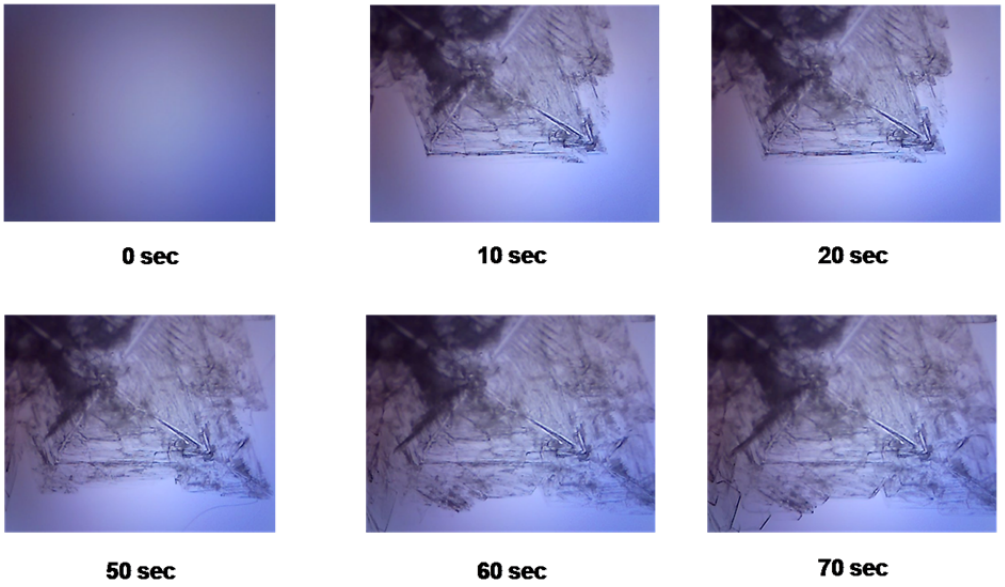

Figure S1. Timed images of acetaminophen crystallized from deionized (DI) water on glass at room temperature.

Glass_DI_MW-PL1

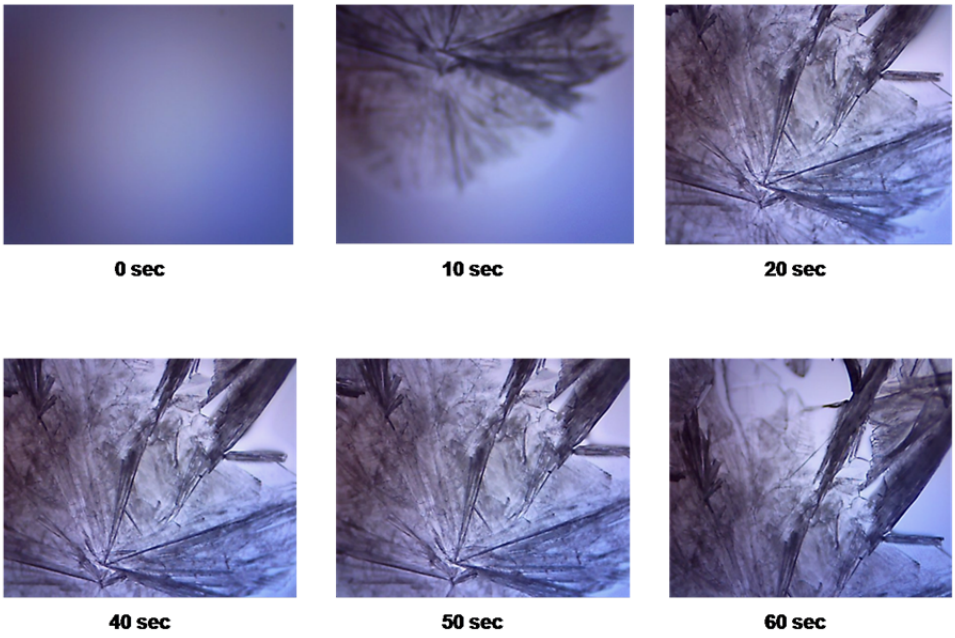

Figure S2. Timed images of acetaminophen crystallized from deionized (DI) water on glass at MW PL 1.

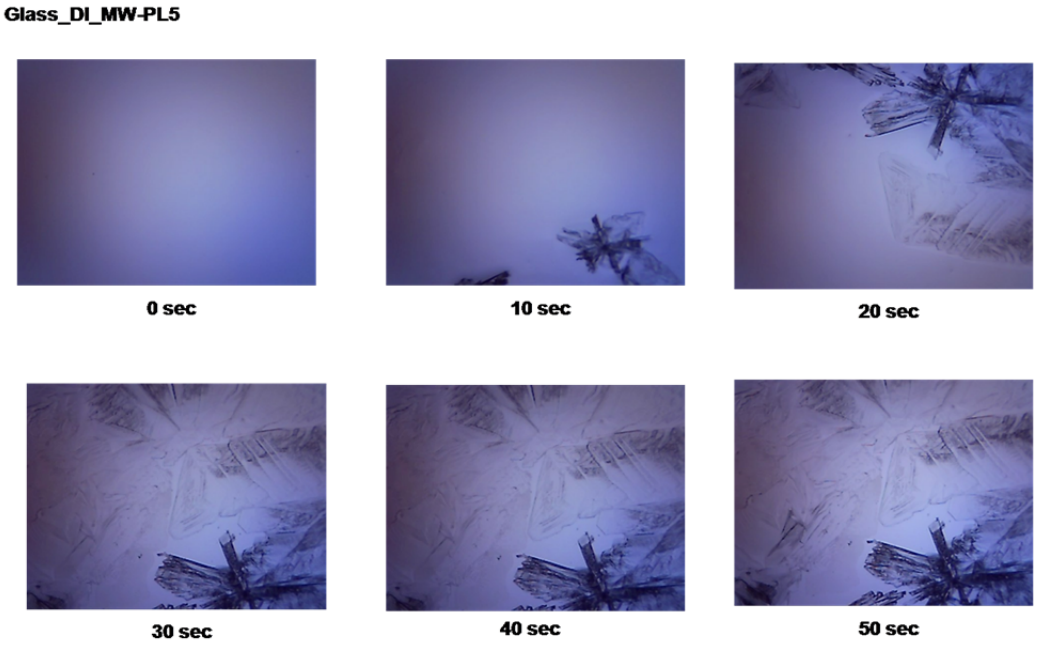

Figure S3. Timed images of acetaminophen crystallized from deionized (DI) water on glass at MW PL 5.

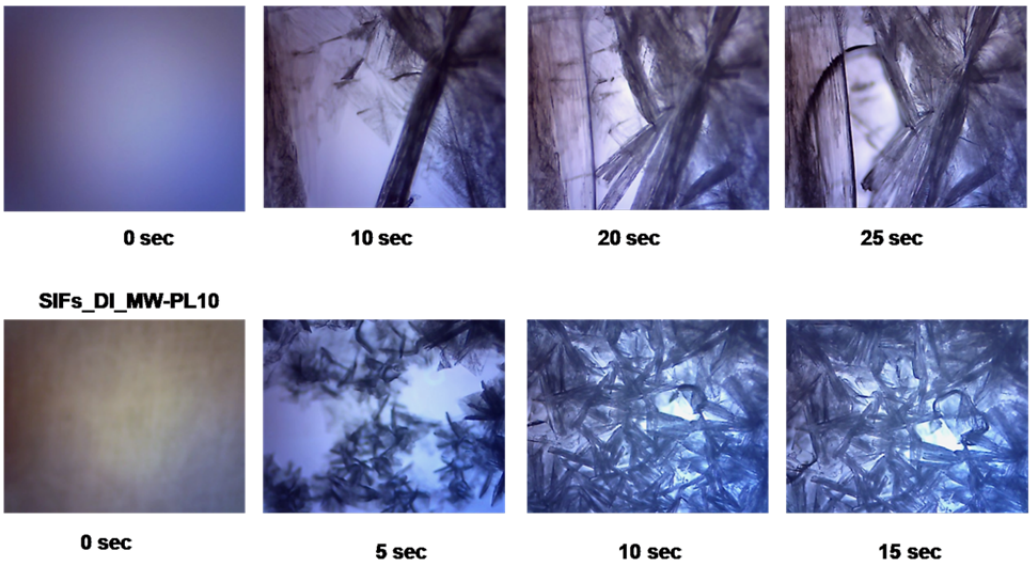

Figure S4. Timed images of acetaminophen crystallized from deionized (DI) water on (top) glass and (bottom) SIFs using microwave power level 10 (MW-PL 10).

SIFs_DI_MW-PL1

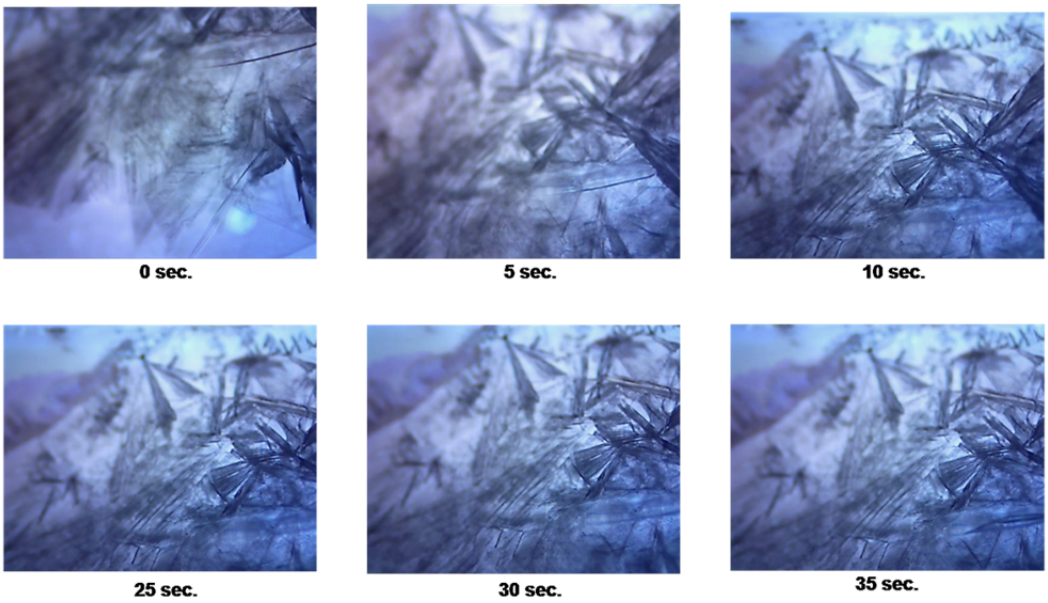

Figure S5. Timed images of acetaminophen crystallized from deionized (DI) water on SIFs at MW PL 1.

SIFs_DI_MW-PL5

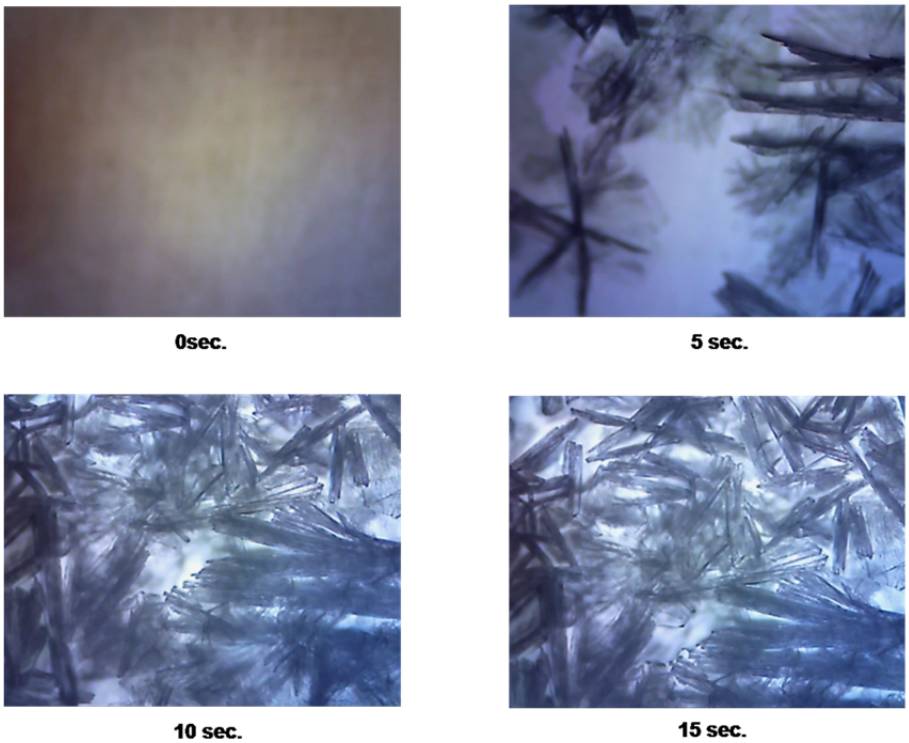

Figure S6. Timed images of acetaminophen crystallized from deionized (DI) water on SIFs at MW PL 5.

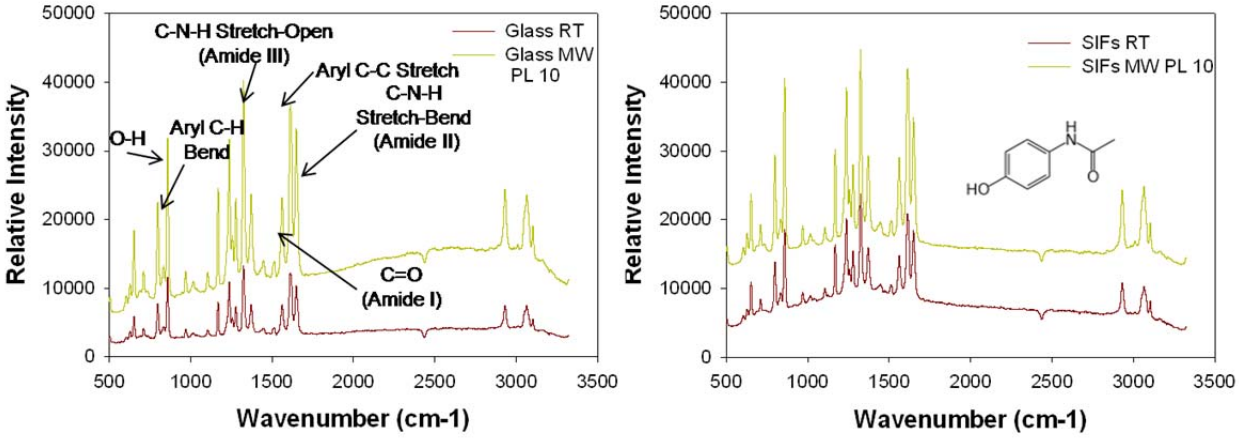

Figure S7. Raman spectra of acetaminophen crystallized from DI water on (left) glass slides and on (right) SIFs at room temperature and MW PL 10.

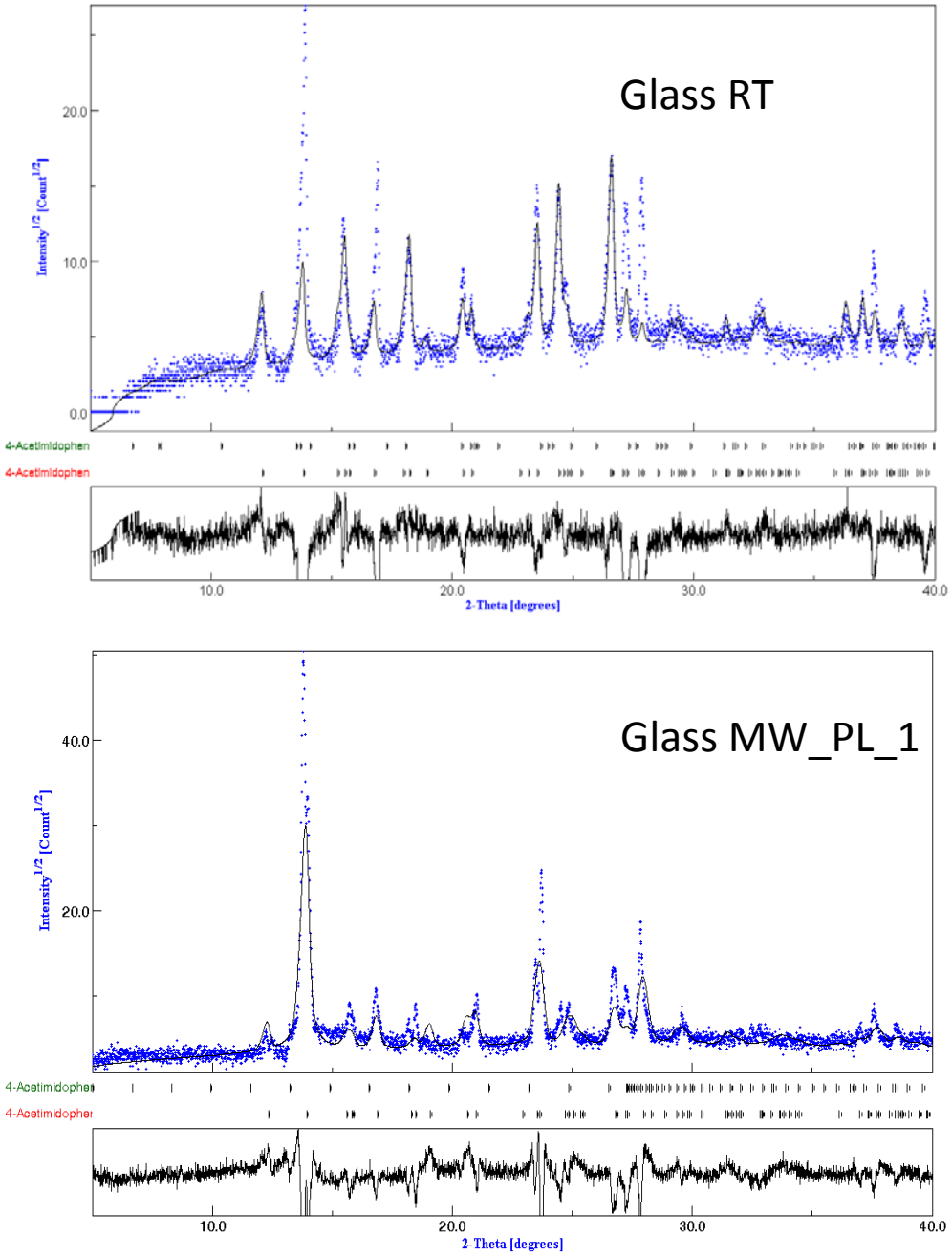

Figure S8. Quantitative analysis of experimental PXRD data (blue) using MAUD for Glass RT and Glass MW_PL1. These two examples show the matching of experimental data with standard data (black line) for acetaminophen.

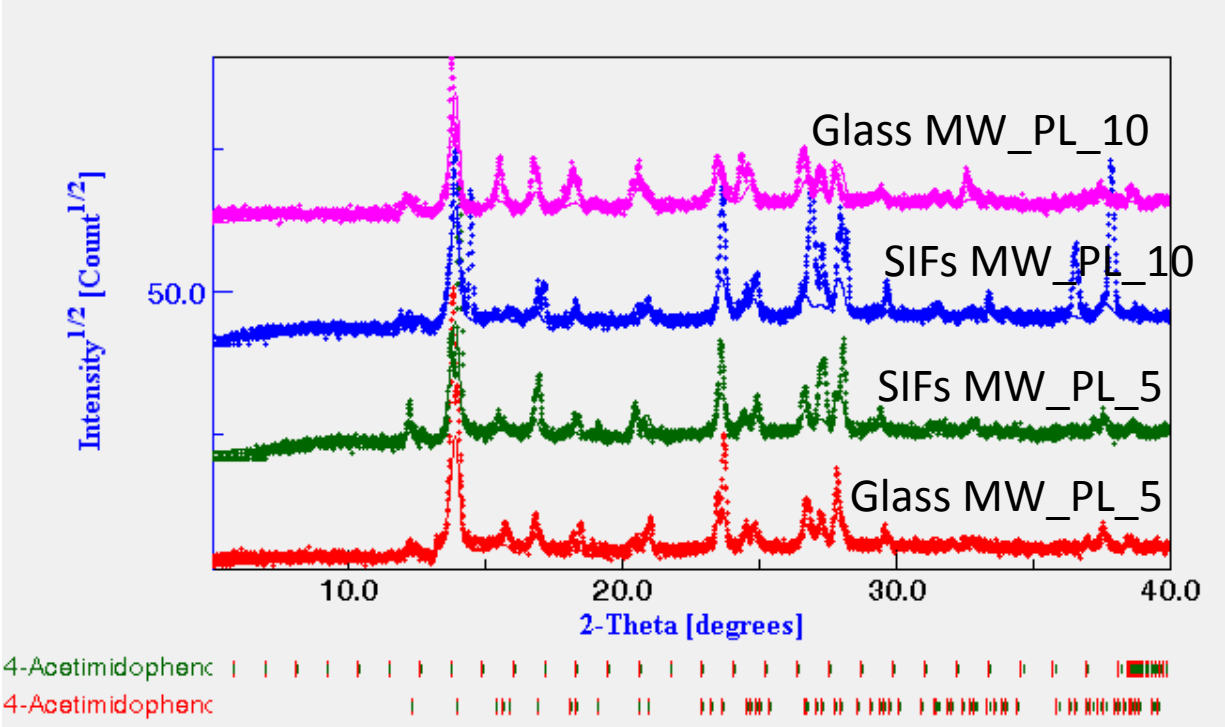

Figure S9. Quantitative analysis of PXRD data using MAUD for Glass MW_PL10. These two examples show the matching of experimental data with standard data for acetaminophen.