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Impact of method of preparation on the morphology and mechanical properties of Amorphous solid dispersion: Comparison of Co-precipitation and Spray Drying

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Purpose

Usage of the amorphous phase of compounds has become the method of choice to overcome oral bioavailability problems related to poor solubility. Due to the unstable nature of glasses, it is clear that the method preparation of the amorphous glass can have a profound impact on the morphology and mechanical properties of the amorphous phase. In order to understand the impact of method of preparation, we have explored the effect of co-precipitation and spray drying methods on the morphology and mechanical properties of the ASD powder using an in-house development compound (GDC-A) as an example. The effectiveness of acoustic mixing, a new technology, to generate co-precipitated ASDs was also studied.

Methods

Three methods were used to generate amorphous solid dispersions (ASD) of 50% GDC-A with HPMC-as: (i) Spray drying (SDD), (ii) Co-precipitation using overhead mixing (OHM), and (iii) Co-precipitation using resonant acoustic mixing (RAM). The microstructure of the ASDs were characterized using focused ion beam scanning electron microscopy (FIB-SEM). Phase mixing between components was studied using solid-state NMR. The compaction properties were studied using a Huxley Bertram Compaction Simulator and the flow of the ASDs was measured using a ring shear tester.

Results

All three methods were found to generate ASDs with good phase mixing and similar glass transition temperatures. SDD powders had a non-conformal geometry with no porosity with particles that were smaller than 15µm. OHM samples, in comparison, have large, irregular shaped aggregates that show uniform micro-porosity at 42%. LRM samples particles are mostly spherical in shape with dual porosity at 62%. Coprecipitated ASD powders (OHM and RAM) demonstrated superior tabletability and flow properties when compared to the SDD powder.

Conclusion

The differences observed in the tensile strength and the tabletability of the co-precipitated ASDs were attributed to their high particle porosity and therefore, high plastic deformation during powder compaction. Based on powder properties, the OHM material was found to be better suited for high drug load formulations. Acoustic mixing has been demonstrated as a scalable new method to make ASD through precipitation. FIB-SEM was found to be a powerful tool to quantitatively characterize microstructure differences between ASDs prepared using different techniques. Tuning the material properties of ASDs through appropriate selection of manufacturing process is expected to be a key factor in delivering high dose ASDs.

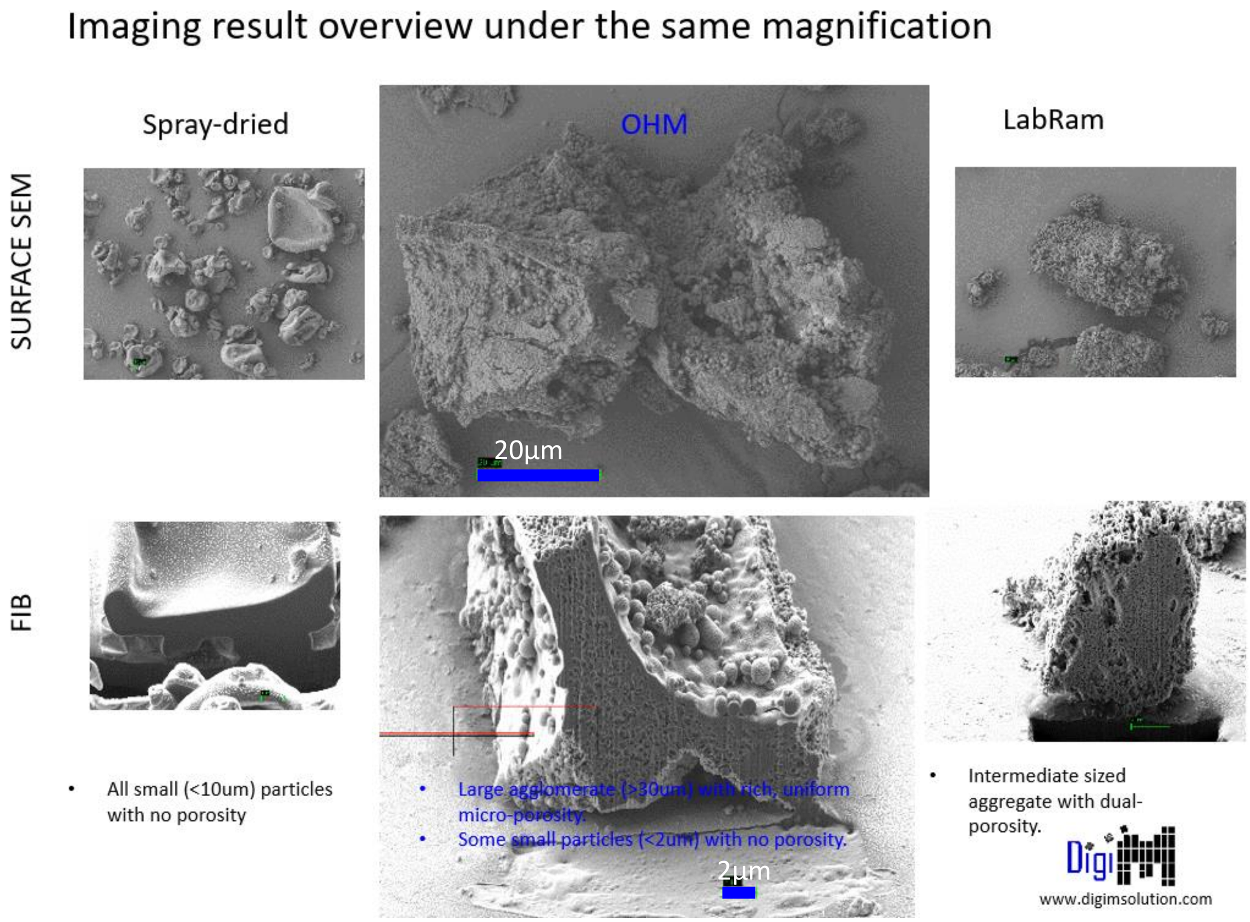

Figure 1. Comparison of sample external surface SEM overview at the same magnification, and the corresponding FIB cross section SEM at the same magnification (higher than the surface SEM magnification).

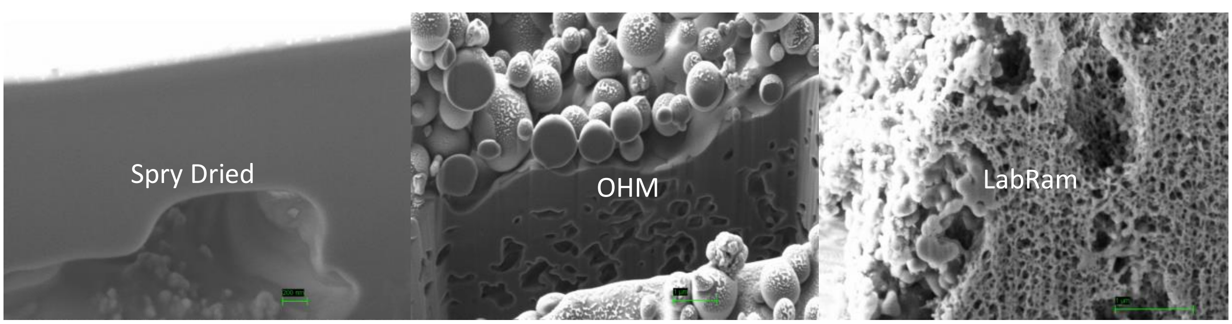

Figure 2. High magnification FIB-SEM cross section images.