Continuity of Solids between Amorphous and Crystalline States – insights from Synchrotron X-ray Pair Distribution Function (SXPDF) Studies

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Pharmaceutical and organic solid materials exist in a wide range of states including crystalline, amorphous, and liquid crystalline. For crystalline pharmaceutical materials, single crystal X-ray and powder XRPD are the gold standards for analysis and structure determination. Much less is known about the structures and order in amorphous and liquid crystalline materials even though these materials are present in medicines consumed by patients every day. Amorphous and liquid crystalline materials are produced during processing and manufacturing of both pure drugs and the composition ultimately given to patients. Processing/manufacturing steps include precipitation, desolvation (solvent removal), granulation, tablet compression, spray drying, melt extrusion, roller compaction, etc. Synchrotron X-ray Pair Distribution Function (SXPDF) is a powerful method for analysis of these materials. For example, for pure amorphous preparations of lapatinib, SXPDF shows nearest neighbor contacts out to the 5th order. For compositions of lapatinib and the cellulosic polymer HPMC only nearest neighbor contacts of the lapatinib molecules are present. For lapatinib and HPMCP (1:3) no nearest neighbor lapatinib contacts are present indicating the lack of domains. This composition was also the most stable indicating a correlation between the existence of domains and tendency to crystallize. This result is consistent with the fact that the lapatinib HPMCP dispersion (1:3) is a molecular mixture. Additional SXPDF studies and XRPD studies of calcium salts that form liquid crystals will also be discussed.