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Local structure of ion pair interaction in Lapatinib amorphous dispersions characterized by synchrotron X-ray diffraction and pair distribution function analysis

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For many years, the idea of analyzing atom-atom contacts in amorphous drug-polymer systems has been of major interest, because this method has always had the potential to differentiate between amorphous systems with domains and amorphous systems which are molecular mixtures. In this study, local structure of ionic and non-ionic interactions was studied by High-Energy X-ray Diffraction and Pair Distribution Function (PDF) analysis in amorphous solid dispersions of Lapatinib in Hypromellose Phthalate (HPMCP) and hypromellose (HPMC-E3). The strategy of extracting Lapatinib intermolecular drug interactions from the total PDF X-ray pattern was successfully applied allowing the detection of distinct nearest neighbor contacts for the HPMC-E3 rich preparations showing that Lapatinib molecules do not cluster in the same way as observed in HPMC-P, where ionic interactions are present. Orientational correlations up to nearest neighbor molecules at about 4.3 Å were observed for polymer rich samples; both observations showed strong correlation to the stability of the systems. Finally, the superior physical stability of 1:3 LP:HPMCP was consistent with the absence of significant intermolecular interactions in (Δ) in the range of 3.0 to 6.0 Å, which are attributed to C-C, C-N and C-O nearest neighbor contacts present in drug-drug interactions.

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