Investigating the Ionic Interaction in Lapatinib-HPMCP Amorphous Solid Dispersions Using Solid-State NMR Spectroscopy
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Purpose
The present work is to investigate the ionic interactions between Lapatinib (LB) with HPMCP in amorphous solid dispersions using solid-state NMR spectroscopy (SSNMR), and the effects of polymer selection on the dissolution and physical behavior of LB amorphous solid dispersions (ASD).

Methods
LB ASD were prepared using spray drying with four different polymers including Soluplus, PVP VA64, HPMCAS, and HPMCP, with various drug loadings from 10% to 80%. Powder X-ray diffraction (PXRD) was used to confirm the amorphous nature of the ASD. Modulated temperature differential scanning calorimetry (MDSC) was used to analyze the homogeneity of ASD and measure the glass transition temperature (Tg). SSNMR was used to investigate the nature of potential drug:polymer interactions in these systems at the molecular level. 1H T1 and T1ρ relaxation measurements were used to probe mobility and miscibility of the ASD. ASD in vitro dissolution was investigated under non-sink conditions. Physical stability under accelerated conditions was characterized by PXRD and MDSC.

Results
PXRD and DSC confirm the amorphous nature of all the lapatinib ASD. A large positive deviation between experimental Tg values of ASD and predicted values indicate relatively strong intermolecular interactions between LB and HPMCP. 15N spectra clearly show two distinct populations of the LB amine N, with a ~13 ppm chemical shift difference. The additional amine peak from the protonated species in the HPMCP dispersions has a chemical shift of -336 ppm, which aligns well with the ionized amine peak in the LB phthalate salt. Dissolution and stability testing also show significant benefits of the ionic interaction in LB-HPMCP ASDs.

Conclusion
15N SSNMR provided strong spectroscopic evidence of an ionic interaction between LB and HPMCP, which is likely the key driver in the ability of this polymer to stabilize amorphous lapatinib.