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Characterization of nanoscale spatial distribution of small molecules in amorphous polymer matrices RALM RICARTE, MARC HILLMYER, TIMOTHY LODGE, University of Minnesota — Hydroxypropyl methylcellulose acetate succinate (HPMCAS) can significantly enhance the efficacy of active pharmaceutical ingredients (APIs). Yet, the interactions between species in HPMCAS-API blends are not understood. Elucidating these interactions is difficult because the spatial distributions of HPMCAS and API in the blends are ambiguous; the polymer and drug may be molecularly mixed or the species may form phase separated domains. As these phase separated domains may be less than 100 nm in size, traditional characterization techniques may not accurately evaluate the spatial distribution. To address this challenge, we explore the use of electron energy-loss spectroscopy (EELS) for detecting the model API phenytoin in an HPMCAS-phenytoin blend. Using EELS, we directly measured with high accuracy and precision the phenytoin concentrations in several blends. We present evidence that suggests phase separation occurs in blends that have a phenytoin loading of approximately 50 wt percent. Finally, we demonstrate that this technique achieves a sub-100 nm spatial resolution and can detect several other APIs.

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