Characterization of Polymorphs, Amorphous Solid Dispersions, and Proteins in Lyophilized Formulations Using Solid-State NMR Spectroscopy

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Advanced analytical techniques such as solid state NMR can provide unique insight into the composition and properties of pharmaceutical formulations in both small molecules and lyophilized protein formulations. In this presentation, we will discuss how solid-state NMR spectroscopy can be employed to determine product stability in both small and large molecule formulations.

For the small molecule drugs, both structural and mobility information can be obtained about the formulations, but the challenge is to relate that information to functional properties such as physical and chemical stability, dissolution rate, and processing parameters. We are currently using solid-state NMR relaxation times to measure particle size, crystal defects, and chemical impurities in crystalline materials and their relation to stability. The relaxation times can also be used to determine phase separation and predict stability in amorphous formulations.

In addition, we have been using relaxation times to predict protein stability in lyophilized formulations, as well as measuring protonation states of probe molecules, which may be representative of the pH of the frozen solutions. Case studies will be presented on:

1. how different buffers change the micro-environmental pH during the freezing process and impacts the local protonation state.
2. how solid-state NMR can be employed to assess whether an IgG protein remains intimately mixed with the stabilizing agent, usually a sugar, and its impact on how stable the protein will be upon storage.
3. how the relative strength of the sugar matrix to inhibit mobility of the protein can impact protein stability in the matrix over time. The effect of additives that can increase the sugar matrix rigidity and reduce protein degradation will be discussed.

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