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Solid state mAbs and ADCs subjected to heat-stress stability conditions can be esterified with buffer and excipient molecules

We report that a unique type of chemical modification occurs on lyophilized proteins. Freeze-dried mAbs and antibody-drug conjugates (ADCs) can be covalently modified with buffer and excipient molecules on the side chains of Glu, Asp, Thr and Ser amino acids when subjected to temperature stress. The reaction occurs primarily via condensation of common buffers and excipients such as histidine, tris, trehalose and sucrose with Glu and Asp carboxylates in the primary sequence of proteins. The reaction was also found to proceed through condensation of carboxylate containing buffers such as citrate with Thr and Ser hydroxyls in the primary sequence of proteins. Based on the mass of the covalent adducts observed on mAbs and ADCs, it is apparent that the reaction produces water as a product and is thus favored in a low moisture environments such as a lyophilized protein cake. Herein, we present the evidence for the covalent modification of proteins drawn from case studies of in-depth characterization of heat-stressed mAbs and ADCs in the solid state. We also demonstrate how common charge variant assays such as imaged capillary isoelectric focusing and mass spectrometry can be used to monitor this specific class of protein modification.

Biography

Patsy Lewis is a Principal Scientist in Formulations and Drug Product Sciences Department at Seattle Genetics, USA. She has over 20 years of experience in Pharmaceutical Sciences ranging from mAb and ADC product development for FIH program efforts. Presently she is working as a Formulation and CMC Team Lead for several ADC programs providing hope for cancer patients.

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