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Formulating Monoclonal Antibodies as Powders for Reconstitution at High Concentration using Spray Drying: Models and Pitfalls

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Abstract

In anticipation of non-invasive routes capable of delivering adequately high, systemic monoclonal antibody (mAb) concentrations, subcutaneous (SC) injection is arguably the most patient friendly alternative administration route available for this drug class. However, due to the limited volume that can be administered through this route and mAbs' relatively low therapeutic activity, solutions for subcutaneous injection often need to be highly concentrated, making them inherently more prone to potentially detrimental protein (self-)interaction, which is why mAb formulations for SC injection and other highly concentrated mAb solutions are often dried to increase their stability. In this work we investigated spray drying (SD) as an drying technique for formulating mAbs as powders for reconstitution, assessing the influence of SD process parameters, as well as excipients present in the feed solution on both mAb stability and relevant powder characteristics for reconstitution using a model mAb. By employing a design of experiments approach we were able to provide statistically substantiated evidence for the reconstitution time reducing and stability improving properties of L-arginineHCl, L-histidineHCl, and L-lysineHCl and polysorbate 20 when combined with a disaccharide in

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