Dry powder therapeutic mAb formulations with enhanced temperature stability

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Purpose.

There is an increasing demand for differentiated strategies for formulating and delivering mAb in particulate form. The aim of this study was to investigate methods for optimising protein-coated microcrystal (PCMC) formulations of a human monoclonal antibody. PCMC technology provides a novel method of stabilising these important biopharmaceuticals in the form of dry powders

Methods.

Human monoclonal antibody coated microcrystals were prepared by coprecipitation of an aqueous mixture of PBS buffered human monoclonal antibody and concentrated glycine into propan-2-ol. The standard formulation contained mAb buffer salts and glycine and the effect of including potential precipitation stabilizing additives (PSA) was investigated e.g. Glu, Arg. Following coprecipitation, the PCMC particles were filtered and air-dried to form free-flowing dry powders. Protein integrity was assessed by comparing optical clarity of the reconstituted formulations, protein concentration by UV spectroscopy and monomer content by size-exclusion chromatography, using a Tosoh TSKgel G3000 SWXL 7.8 mm ID x 30 cm column.

Results.

The measured protein loadings were found to be within 5% of the target protein loading for all formulations. However, the optical clarity of reconstituted PCMC prepared with optimal PSA was significantly better. Protein particulates could be observed in reconstituted standard samples, whilst PCMC utilising PSA, such as Glu, Arg, were optically clear and free of particulates. Consistent with this, measurement of the degree of monomer conservation following coprecipitation showed that material produced without PSA generally had monomer retention of less than 90% whilst optimised samples incorporating PSA resulted in >98% of monomer conservation.

Conclusion.

Human monoclonal antibodies can be readily formulated using PCMC technology by incorporating precipitation stabilizing additives (PSA). PCMC coprecipitation leads to finely-divided dry powders, which can be rapidly reconstituted back into aqueous, to release the monoclonal antibody in monomeric form.