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Dry powder therapeutic mAb formulations with enhanced temperature stability

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Protein Coated Micro Crystal (PCMC) technology was used to process a human therapeutic monoclonal antibody into dry powder formulations, which were studied under accelerated stress conditions. Changes in protein integrity on reconstitution were measured by size exclusion chromatography and turbidity measurements. The effect of glutamic acid (Glu), L-arginine (Arg) and trehalose as precipitation stabilising additives was investigated.

Abstract

The measured protein loadings were found to be within 5% of the target protein loading for all chromatography, using a Tosoh TSKgel G3000 SW XL following coprecipitation, the PCMC particles were filtered and air-dried to form free-flowing dry microcrystal (PCMC) formulations of a human monoclonal antibody. PCMC technology provides a significantly better. Protein particulates could be observed in reconstituted standard samples, coprecipitation showed that material produced without PSA generally had monomer retention of Consistent with this, measurement of the degree of monomer conservation following precipitation stabilizing additives (PSA). PCMC coprecipitation leads to finely-divided dry powders, Human monoclonal antibodies can be readily formulated using PCMC technology by incorporating.

Methods.

Human monoclonal antibody, PFCP, was obtained from Pfizer Inc, St Louis, MO. PFCP is a fully human monoclonal antibody specific for human cytotoxic T lymphocyte–associated antigen 4. PFCP PCMC were prepared by coprecipitation of an aqueous mixture of histidine buffered antibody and concentrated glycine coprecipitant into GRAS solvent. The PCMC are formed by a rapid, self-assembly process, whereby the coprecipitant core (blue cubes) forms a support core and the biomolecule (yellow sphere) is immobilized on this crystal surface.

The ratio of active mAb to coprecipitant/PSA was varied between 17%w/w and 33%w/w, as shown in this table (Theoretical Protein Loading (%w/w).

Monomer Content after Coprecipitation

After drying, the PFCP PCMC material was reconstituted into histidine buffer at a target protein concentration of 1 mg/mL, and monomer content was measured by size-exclusion chromatography, using a Tosoh TSKgel G3000 SW 7.8 mm ID x 30 cm column.

Absorpmtion addit with aging

The measured protein loadings were found to be within 5% of the target protein loading for all chromatography, using a Tosoh TSKgel G3000 SW XL following coprecipitation, the PCMC particles were filtered and air-dried to form free-flowing dry microcrystal (PCMC) formulations of a human monoclonal antibody. PCMC technology provides a significantly better. Protein particulates could be observed in reconstituted standard samples, coprecipitation showed that material produced without PSA generally had monomer retention of Consistent with this, measurement of the degree of monomer conservation following precipitation stabilizing additives (PSA). PCMC coprecipitation leads to finely-divided dry powders, Human monoclonal antibodies can be readily formulated using PCMC technology by incorporating.

Discussion

PCMC coprecipitation preserves the activity of the mAb. The bioactivity of the PFCP samples was tested in a PFCP specific ELISA.

From the results it is clear that bioactivity has not been compromised by the PCMC coprecipitation process. Furthermore the protein loading measured is approximately equivalent to the theoretical composition, demonstrating that protein is not lost in the coprecipitation process, but is fully immobilized on the surface of the microcrystal.

Conclussion

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. Such PCMC mAb dry powders are attractive as a platform for alternate delivery applications.