

In light of the foregoing, there exists a need in the art for improved methods to more efficiently purify proteins, including therapeutic antibodies. The present invention addresses this need by incorporating improved simulated moving bed separation strategies into the purification of proteins.

3. SUMMARY OF THE INVENTION

In one aspect, there is provided a method for producing a host cell-protein (HCP) reduced target protein preparation from a sample mixture comprising a target protein and at least one HCP, said method comprising:

- (a) performing Raman spectroscopy analysis of said sample mixture;
- (b) contacting said sample mixture to an affinity chromatography resin such that the resin is loaded to about 50% -100% of its saturated binding capacity;
- (c) collecting a chromatographic sample; and
- (d) performing Raman spectroscopy analysis of said chromatographic sample to identify it as a HCP-reduced target protein preparation, wherein the target protein is an antibody or an antigen-binding portion thereof.

In certain embodiments the present invention is directed towards methods for producing a host cell-protein (HCP) reduced target protein preparation from a sample mixture comprising a target protein and at least one HCP. In certain embodiments, the methods of the instant invention comprise contacting a target protein-containing sample mixture to a chromatography resin such that the resin is loaded to about 50%-100%, including greater than about 50%, greater than about 60%, greater than about 70%, greater than about 80%, and greater than about 90%, of its saturated binding capacity, and collecting a chromatographic sample, wherein said chromatographic sample comprises said HCP-reduced target protein preparation. In certain of such embodiments, Raman spectroscopy is employed in order to monitor and/or determine the composition of one or more of the multi-component mixtures involved in the production of such HCP-reduced target protein preparations.

Certain embodiments of the present invention are directed to the production of HCP-reduced target protein preparations that comprise contacting a target protein-containing sample mixture to a chromatography resin such that the resin is loaded to between about 50%-100%, including greater than about 50%, greater than about 60%, greater than about 70%, greater than about 80%, and greater than about 90%, of its saturated binding capacity, and collecting a chromatographic sample, wherein said chromatographic sample comprises said HCP-reduced target protein preparation and the chromatographic resin selected from the group consisting of affinity chromatographic resin, ion exchange chromatographic resin, and hydrophobic interaction chromatographic resin. In certain of such embodiments, Raman spectroscopy is employed in order to monitor and/or determine the composition of one or more of the multi-component mixtures involved in the production of such HCP-reduced target protein preparations.

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