Tailor-Made Strategies for High-Capacity Chromatography Media and Their Applications in the Separation and Purification of Complex Biological Macromolecules (Postprint)

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Abstract

Chromatography technology occupies a crucial position in the field of bioseparation and purification. As the primary component of this technology, the structure and properties of chromatographic media profoundly influence the final separation and purification efficacy. Among these properties, binding capacity is a critical determinant of the separation and purification capability of the media, and enhancing media capacity has been a persistent focus in bioseparation engineering. This thesis targets high-capacity agarose chromatographic media and conducts tailor-made studies on both agarose hydrophobic interaction chromatography media and metal-chelate chromatography media. For agarose hydrophobic interaction chromatography media, spacer arms of varying lengths were introduced to achieve controlled preparation of hydrophobic properties, which was applied to the purification of hepatitis B surface antigen expressed in CHO cells. This approach significantly enhanced the vaccine binding capacity of the media, achieving a vaccine activity recovery rate exceeding 90% and a purification fold of 65.8, both surpassing traditional hydrophobic media. For agarose metal-chelate media, a dextran grafting strategy was adopted with simultaneous regulation of grafting degree to achieve controlled preparation of dextran grafting. This grafted metal-chelate media demonstrated a capacity for histidine-tagged recombinant proteins that was over 1.5 times higher than conventional media, far exceeding traditional alternatives. Tailor-made high-capacity chromatographic media hold broad prospects for large-scale separation and purification of recombinant proteins.

Full Text

Tailor-made High-capacity Chromatographic Media and Its Applications in Purification of Complex Biomacromolecules

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Abstract

Chromatography plays a crucial role in the separation and purification of biological products. Among its key components, the structure and properties of chromatographic media profoundly influence purification outcomes. Binding capacity, in particular, is a critical determinant of media performance, and enhancing this capacity has long been a central focus in bioseparation engineering.

This study investigates the development of tailor-made, high-capacity agarose-based chromatographic media, specifically examining both hydrophobic interaction chromatography (HIC) and immobilized metal ion affinity chromatography (IMAC) systems. For the HIC media, we introduced spacer arms of varying lengths to achieve controllable hydrophobic properties. When applied to the purification of hepatitis B surface antigen (HBsAg) expressed in CHO cells, this approach significantly enhanced antigen binding capacity, achieving a recovery of over 90% and a purification factor of 65.8—both substantially superior to conventional hydrophobic media.

For the IMAC media, we employed a controlled dextran grafting strategy to modulate the degree of grafting. This grafted metal-chelating medium exhibited a binding capacity for histidine-tagged recombinant proteins that was more than 1.5 times higher than that of traditional media. These tailor-made high-capacity chromatographic media demonstrate significant potential for large-scale purification of complex biomacromolecules, including recombinant proteins.

Note: Figure translations are in progress. See original paper for figures.