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What are protein therapeutics / monoclonal antibodies?

Protein therapeutics, specifically monoclonal antibodies (mAbs), have emerged as the most marketed biologic drug within pharmaceutical companies. These proteins are large in size (~150 kDa) and have many physical characteristics that require detailed characterization. This daunting physicochemical characterization combined with the long development timeline for a protein therapeutic to get approved has sparked a "fail-fast" mentality within the biopharmaceutical industry. From an analytical characterization perspective, the early stage development of new protein modalities is starting to rely on novel analytical technologies that are less common in the late stages in analytical laboratories.

Given the above movement, traditional analytical techniques, such as liquid chromatography, have a need to modify their approach for supporting this new industry necessity. Modernization of technique from HPLC to UHPLC is one straightforward way to speed up the analysis of proteins. As such, most of the methods for chromatographic analysis for new protein therapeutics are almost exclusively performed on UHPLC instruments.

One critical quality attribute that has lagged behind UHPLC capable methods is charge variant analysis (CVA) in order to determine protein charge heterogeneity. This fact has prompted laboratories to adopt black box solutions, such as imaging capillary isoelectric focusing (iCIEF), to perform charge variant analysis. While this technique is rapid and provides good charge heterogeneity data, it is limited in robustness and fractionation cannot be performed for any in-depth analyses. Therefore, liquid chromatography is preferred in most laboratories.

Phenomenex set out to develop a column technology that addressed the issue of rapid, robust CVA using liquid chromatography. Ion exchange chromatography (IEX) is the most common method for CVA, particularly mAbs, and have a higher isoelectric point (pI) which means cation exchange chromatography (CEX) should specifically be used. Whether strong cation exchange (SCX) or weak cation exchange (WCX), the chromatography has to be performed with a bioinert column hardware due to the "sticky" nature of proteins and their ability to adsorb onto stainless steel surfaces.

Our first technology advance to better suit protein therapeutics was to incorporate a bioinert metallic surface, namely titanium, so that it could avoid any secondary interactions with the protein analytes. Moreover, this titanium column hardware would allow high flow of the mobile phase and thus be able to withstand high pressure analysis. Ultimately, the total length of the analysis can be drastically reduced by using high flow CEX.

I recently co-authored an article that demonstrates our new WCX column with titanium hardware at high flows.

You can read more about our exciting development here:

http://www.chromatographyonline.com/high flow-weak-cation-exchange-charge-variant-analysis

Check out some of our other technology advances and co-authored articles below:

Biosimilars, Generic Drugs, and the Pharmaceutical Industry

Tips to Improve LC/MS Sensitivity in Your Lab