**Overcoming Gelling and Enhancing Filterability in PEGylated Intermediates**

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**Purpose:**

The filterability of PEGylated biotherapeutics is frequently challenged by gel formation, high hydration, and low wet cake density, which hinder efficient solid–liquid separation. This work aimed to mitigate gelling behavior, improve particle rigidity, and enhance filterability by modulating solvent precipitation conditions in the isolation of the PEGylated intermediate of a GalNAc ligand. A secondary objective was to correlate the thermal and physical properties of isolated solids—glass transition temperature (Tg), residual solvent content, bulk density, etc. —with observed filtration performance.

**Methods:**

PEGylated intermediates were precipitated under varying solvent systems, including changes in antisolvent, solvent content, and temperature. Filtration behavior was evaluated by measuring filtration rate, wet cake compressibility, and bulk density of wet and dry cakes. Isolated solids were analyzed using thermogravimetric analysis (TGA) to quantify residual solvent and differential scanning calorimetry (DSC) to determine thermal stability. Wet cake bulk density was measured and assessed for trends with filtration characteristics. Cake morphology was characterized by microscopy.

**Results:**

Solvent systems with lower polarity produced PEGylated solids with lower solvent retention and lower bulk density. Filtration rate improved by over 4-fold under optimized conditions on a multi-kilogram scale. Gelling was notably suppressed under solvent combinations that promoted sharp phase separation and reduced solvent retention in bulk solids.

**Conclusions:**

Solvent modulation during PEGylated product precipitation significantly affects the solid-state properties of the resulting filter cake. By tuning solvent composition to minimize solvent retention and increase solids’ thermal stability, it is possible to generate more rigid, less gel-like particles that exhibit superior filterability and lower cake compressibility. TGA proved to be an effective tool for rationalizing filtration performance based on the bulk characteristics of the solid product.

**Keywords:**

PEGylation, filtration, gelling, residual solvent, bulk density