

## CORE-SHELL VERSUS INERT POLYMER GRAFTED ADSORBENTS FOR THE NEGATIVE CHROMATOGRAPHY OF VIRUS-LIKE PARTICLE

Beng Ti Tey, Chemical Engineering Discipline, School of Engineering, and Advanced Engineering Platform,  
Monash University Malaysia, Malaysia  
tey.beng.ti@monash.edu

Micky Fu Xiang Lee, Chemical Engineering Discipline, School of Engineering, Monash University Malaysia,  
Malaysia.

Eng Seng Chan, Chemical Engineering Discipline, School of Engineering, and Advanced Engineering Platform,  
Monash University Malaysia, Malaysia.

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Core-shell and polymer grafted adsorbents are new generation media developed for the separation of virus-like particle (VLP) in a negative chromatography. The inert shell and grafted polymer chain are designed to exclude the big biomolecules such as VLP from adsorbing onto the ligands situated on the surface of the adsorbents. Meanwhile, these exclusion layers should be permeable for the smaller impurities which will be adsorbed by the ligands to prevent its presence in the flowthrough fractions. In this study, the performance of these negative chromatography media were compared in the purification of recombinant hepatitis B VLPs (HB-VLPs) from clarified *E. coli* feedstock. The core-shell adsorbents with different shell thickness (InertShell and InertLayer 1000) and poly[(ethylene glycol) methacrylate] grafted adsorbents (SQ) were studied in a packed bed mode. SQ adsorbed more impurities, thus achieving a higher purity in flowthrough while core-shell adsorbents recovered more HB-VLPs and recorded nearly 100% recovery in InertShell. This suggests the shielding effect of the core shell layer is higher than the inert polymer chain. For core-shell adsorbents, there was a trade-off between the purity and recovery of flow-through HB-VLPs due to the shell thickness. A thicker shell allows more HB-VLP exclusion but less impurities adsorption. Prolonging the residence time of the negative chromatography only resulted in a slight improvement in the impurities adsorption in all adsorbents, but the recovery of HB-VLPs in InertShell was reduced substantially. Atomic force microscopic (AFM) analysis revealed funnel-shaped pore channels on the shell layer which may contribute to the entrapment of HB-VLPs on core-shell adsorbents, thus decreasing the HB-VLP recovery. Overall, SQ performed better than the core-shell adsorbents in handling feedstock with high concentration.