341b Reducing Agents and Imidazole Protect Hsv-1 Vector from Inactivation during Immobilized Cobalt Affinity Chromatography

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Herpes simplex virus type 1 (HSV-1) based gene therapy vectors have been successfully utilized for treatment of numerous neurological diseases in animal models. An uncomplicated, cost-efficient and scaleable purification scheme would simplify production of vector stocks and provide high quality material for gene therapy clinical trials. We have successfully developed an immobilized cobalt affinity chromatography for selective purification of HSV vectors engineered to display cobalt affinity tag on viral envelope glycoprotein B. In this work, the infectivity loss of HSV on immobilized cobalt was studied and the buffer condition was optimized to achieve high vector yield during chromatography. We found: 1) loading clarified HSV harvest on IDA-Co2+ column resulted in low infectious virus recovery (<5%); 2) most virus infectivity was lost in the loading step by the mutual effects of cobalt ion and soluble substance from cell culture; 3) 20 mM of either ascorbic acid or sodium sulfite or imidazole in the loading, wash, and elution minimized HSV infectivity loss during chromatography and resulted in high infectious virus yield (>70%). An oxidation mechanism for HSV inactivation on IDA-Co2+ was proposed.