Concentration and purification of a baculovirus by ion exchange membrane chromatography

Tanja A. Grein [1], Ronald Michalsky [2], M. Vega López [2], Peter Czermak [1, 2, *]

[1] University of Applied Sciences Mittelhessen, Institute of Bioprocess Engineering and Pharmaceutical Technology, Wiesenstrasse 14, 35390 Giessen, Germany

[2] Kansas State University, Department of Chemical Engineering, Manhattan, Kansas, 66506, U.S.A.

Insect viruses are central components of current manufacturing processes producing recombinant proteins such as enzymes and human or animal vaccines at industrial-scale. This required the development of methods for virus purification and concentration. Application of adsorptive membranes based on the electric interaction between charged components of a liquid phase including viruses and ionic groups immobilized on the solid membrane matrix, ion exchange membrane chromatography (IEMC) is a potentially simple and efficient method for virus concentration and purification. To optimize process conditions, viral activity was measured as a function of pH ranging from pH 3-8 and ionic conductivity of electrolytes ranging from 0.77- 78.00 mS/cm in the eluate. Viral infectivity rapidly decreased when ionic conductivities fell below 5 mS/cm (i.e., water flux from the surrounding liquid into the viral particle equivalent to an osmotic pressure change of about 0.49 MPa) or at $H3O^+$ activities below pH 5.5 (rationalized with particle aggregation). Relative to the total amount of proteins present in the liquid volume processed IEMC excluded the major protein fraction in the eluate. The polyether sulfone-based membrane with quaternary ammonium ligand appears most promising for reduction of host cell protein and concurrent virus.

- Vicente T, Peixoto C, Carrondo MJ, Alves PM. 2009. Purification of recombinant baculoviruses for gene therapy using membrane processes. Gene Ther 16(6):766-75.
- Grein TA, Michalsky R, Vega López M, Czermak P. 2011. Purification of a recombinant baculovirus of AcMNPV by ion exchange membrane chromatography. J. Virol. Methods, submitted for publication 17.08.2011
- Michalsky, R., Pfromm, P.H., Czermaka, P., Sorensenb C.M., Passarelli, A.L.: Effects of temperature and shear force on infectivity of the baculovirus Autographa californica M nucleopolyhedrovirus, Journal of Virological Methods 153 (2008) 90–96.