ANTIBODY CHARGE HETEROGENEITY FORMATION IN A MAMMALIAN CELL CULTURE FED-BATCH PROCESS

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The charge heterogeneity of a monoclonal antibody (mAb) is as a sum factor of several post translational modifications and most of them are of high importance regarding product quality and efficacy. For this reason monitoring and controlling of this sum factor can be beneficial. The work presented here builds the basis for on-line monitoring and will help to achieve Quality by Control (Sommeregger et al., 2017). The aim of this work was to develop a method that allows fast and accurate determination of the charge profile of monoclonal antibodies directly from cell culture supernatants. We were able to circumvent a pre-purification step by adapting a cation exchange method (CEX) using a highly linear pH gradient (Lingg et al, 2013). The established method was then used to gain information about the formation of charge variants during a fed-batch process of an industrial relevant mAb produced by a Chinese Hamster Ovary (CHO) cell line. The achieved data suggested that glucose concentration was predominantly affecting the formation of acidic variants, at cost of the main ones. By assuming a second order reaction, the kinetics of the acidic variants formation and its temperature dependence have been elucidated. The presented analytical method was proven to be reliable, and can be regarded as a fingerprinting platform tool for any kind of basic mAb with a pI between 7 and 10.5. It will help to understand and to identify the key parameters of charge heterogeneity formation in cell culture processes. In a next step the gathered information will be incorporated in mathematical process models and may be used for advanced process control leading to consistent product quality.

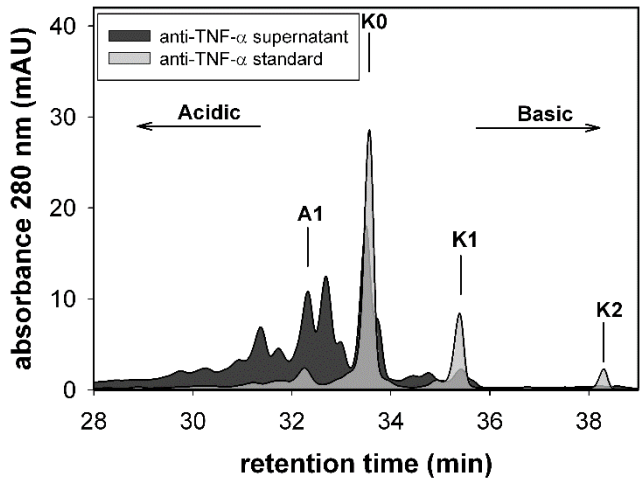

Figure: Charge heterogeneity chromatogram of anti-TNF-alpha determined directly from the supernatant and from the pharmaceutical standard.

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