Recent publications

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Amino acid-based advanced liquid formulation development for highly concentrated therapeutic antibodies balances physical and chemical stability and low viscosity

KEMTER K[1], ALTRICHTER J[1], DERWAND R[1], KRIEHUBER T[1], REINAUER E[1], SCHOLZ M[1]

1 LEUKOCARE AG, Am Klopferspitz 19, 82152 Martinsried/Munich, Germany
Email: info@leukocare.com

To develop highly concentrated therapeutic antibodies enabling convenient subcutaneous application, well stabilizing pharmaceutical formulations with low viscosities are considered to be key. The purpose of this study is to select specific amino acid combinations that reduce and balance aggregation, fragmentation and chemical degradation, and also lower viscosity of highly concentrated liquid antibodies. As a model, the therapeutically well-established antibody trastuzumab (25→200 $mgmL^{-1}$) in liquid formulation is used. Pretesting of formulations based on a stabilizing and protecting solutions (SPS®) platform is conducted in a thermal unfolding model using differential scanning fluorimetry (DSF) and accelerated aging at 37 and 45 °C. Pre-selected amino acid combinations are further iteratively adjusted to obtain stable highly concentrated antibody formulations with low viscosity. Size exclusion chromatography (SE-HPLC) reveals significantly lower aggregation and fragmentation at specific amino acid: sugar and protein: excipient ratios. Dynamic viscosities <20 mPa *s of highly concentrated trastuzumab (≥200 $mgmL^{-1}$) are measured by falling ball viscosimetry. Moreover, less chemical degradation is found by cationic exchange chromatography (CEX-HPLC) even after 6 months liquid storage at 25 °C. In conclusion, specifically tailored and advanced amino acid based liquid formulations avoid aggregation and enable the development.

Conflict of Interest
At the time of the study all authors were employees of LEUKOCARE AG, Martinsried, Germany.