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Formulations for subcutaneous administration: Exploring the influence of monoclonal antibody concentration and addition of excipients on their viscosity

Monika Prašnikar, Maja Bjelošević Žiberna, Pegi Ahlin Grabnar

Department of Pharmaceutical Technology, University of Ljubljana, Ljubljana, Slovenia

In the field of biopharmaceuticals, the current trend is oriented towards subcutaneous (SC) administration, which is faster, more convenient and comfortable for the patient thus, leading to increased compliance and cost-effectiveness. In contrast, the most limiting factor in SC application is the relatively small injection volume (≤2 mL) that requires highly concentrated protein formulations (above 100 mg/mL). The development of such formulations is associated with many challenges, such as ensuring protein stability and formulation injectability, where the latter is an obstacle resulting from increased viscosity of formulations for SC application [1].

The objectives of the study were: (i) to investigate the effect of monoclonal antibody (mAb) concentrations on sample viscosity; and (ii) to explore the potential of arginine as viscosity reducer agent in water-based mAb solutions.

First, the calibration curve of viscosity (m-VROC®, RheoSense, USA) as a function of mAb concentration was constructed and an exponential increasing trend was demonstrated. The lowest mAb concentration that exceeded the viscosity threshold for SC administration (i.e. 20 mPa·s) was 150 mg/mL. At this concentration potential viscosity reducing agent arginine (25mM) was tested and resulted in effective viscosity reduction for 0.46 factor. Then viscosity reducing effect of arginine was evaluated at different mAb concentrations where a relation was demonstrated. Namely, arginine lowered the viscosity more effectively with increasing protein concentration.

The main conclusion is that arginine is a promising candidate that enables viscosity reduction in mAb SC formulations, whereas further strategies to overcome this challenge of highly concentrated mAb formulations should be discovered.

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