Impact of the preparation of a clinical solution of rituximab 0.5 mg/mL on the particulates (aggregation) measured by dynamic light scattering: sodium chloride and glucose concentration, and agitation effect

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BACKGROUND

Rituximab (RTX) is a therapeutic monoclonal antibody used for the treatment of certain types of cancer. As a complex protein, routine handling or unintentional mishandling of its solutions may cause degradation that could remain unnoticed but could potentially compromise the clinical safety and efficacy of the drug product.¹

MATERIALS AND METHODS

RTX (Mabthera®, 10 mg/mL) was diluted to 0.5 mg/mL using different NaCl (from 0.5% to 1.5%) and glucose (from 1% to 10%) concentrations. Manual gentle shaking was performed for 10 minutes. Particulate was tracked by dynamic light scattering (DLS) and analytical signals were recorded in a protein solution DynaPro-99 system Dynamic Light Scattering module equipped with a temperature control micro sampler (Wyatt, Santa Barbara, California, USA) for obtaining the hydrodynamic radius (HR) and polydispersity values of the protein solutions studied.

RESULTS

In panels A to D, the DLS results of the different experiments are shown. 0.5 mg/mL RTX samples diluted in NaCl 0.9% and glucose 5% showed a single particulate population with a HR of 10.51 ± 2.210 nm and 10.72 ± 2.644 nm, respectively, attributed to monomers of RTX. No significant changes were observed for HR when the concentration of the diluents was changed (A and B): the size distribution by volume graphs show a single population that corresponds to the monomers. With regards to the samples stressed by manual agitation, no significant changes were observed in their HR (C and D). Values were placed in all cases within the interval of the size of the monomers. Polydispersity remained unchanged in all of the samples analyzed.

CONCLUSION

Variation in NaCl and glucose concentrations around clinical concentrations of 0.9% and 5% did not promote aggregation in a 0.5 mg/mL RTX solution detected by DLS (0.1nm-10nm). Also, manual shaking did not have an impact on aggregation in this clinical RTX solutions studied.

REFERENCE


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