

STABILITY OF INTRAVITREAL BEVACIZUMAB SOLUTION IN POLYPROPYLENE SYRINGES IN NEOVASCULAR MACULAR DEGENERATION

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BACKGROUND

Bevacizumab is used by intravitreal administration as an off-label drug to treat age-related macular degeneration and other ophthalmologic diseases.

PURPOSE

To analyse the physicochemical stability of bevacizumab repackaged in 1-mL polypropylene syringes for intravitreal injection.

MATERIAL AND METHODS

Bevacizumab syringes were repackaged under laminar flow. Each syringe contained 200 or 900 μL (25 mg/mL). For the stability assessment at 4°C, three storage groups of 2 repacked syringes and 2 original vials were constituted for each analysis time (0,3,7,14 days). For bevacizumab characterization a HPLC consisting of a Waters pump (600 E), an autosampler (717 plus), a dual UV detector (2487) to 214 nm, as stationary phase Shodex KW 804 (8.0mmx300mm) column and a mobile phase (25mM $\text{NaH}_2\text{PO}_4 \cdot 2 \text{H}_2\text{O}$ and 300mM NaCl pH 7) at a flow of 1ml/min. The size distribution of particles in the samples incubated in syringes was determined by a Zetasizer system.

RESULTS

The proposed HPLC method allowed us to separate two peaks for the bevacizumab control sample, corresponding to bevacizumab monomer (mean peak) and its oligomer, with retention times of 9.8 and 8.6 min respectively. We used the evolution of the monomer peak area value to indicate the stability. For the original vials the area values remained at 100% of their initial value for 7 days storage. For repacked bevacizumab this value was maintained for 3 days. The Zetasizer particles analyser detected submicron particles whose origin could be the repacking, for the vials mean particle size (17.8 ± 4.7) nm remained constant for 15 days. For repacked syringes this value remained constant for 3 days, at day 7 we found a small % of particles with size next to $5 \mu\text{m}$ indicating probable particle contamination of unknown origin.

CONCLUSIONS

Our results support the physicochemical stability for 3 days at 4°C of repackaged bevacizumab for intravitreal administration.

