Compatibility of Epirubicin-loaded DC Bead™ with different contrast media

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Introduction

Epirubicin hydrochloride is an anthracycline drug used in antitumour chemotherapy. Because of its cationic properties it can be loaded to negatively charged DC Bead™ which would be locoregionally administer the liver during transarterial chemoembolisation (TACE) procedures. Prior to administration via a catheter, the loaded beads are mixed with an equal volume of non-ionic contrast medium to guide the injection. The aim of this study was to determine the compatibility of epirubicin-loaded DC Bead™ with different non-ionic contrast media over a period of 7 days when stored light protected under refrigerated conditions.

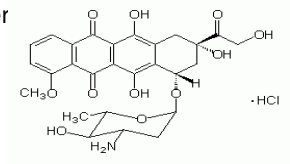

Fig. 1 Chemical structure of Epirubicin HCl

Material and Methods

2 ml DC Bead™ (Biocompatibles UK Ltd*) of the bead size 70-150 µm (=DC Bead*M1*™) or bead size 100-300 µm were loaded with 75 mg Farmorubicin® powder formulation (reconstituted with 3 ml water for injection to a concentration of 25 mg/ml) or 76 mg Epimedac® injection solution (2 mg/ml) within 2 h or 6 h, respectively. After removal of the excess solution, epirubicin-loaded beads were mixed in polypropylene (PP)-syringes with an equal volume (~1.5 ml) of contrast medium i.e. Accupaque™ 300 (Nycomed Inc.), Imeron® 300 (Bracco S.p.A), Ultravist® 300 (Bayer Pharma AG), Visipaque™ 320 (GE Healthcare) and agitated to achieve a homogenous suspension. Each combination was prepared in triplicate and samples were taken from the excess solution at predetermined intervals (before mixing, immediately after mixing, day 1, day 7) and injected 3 times to measure the epirubicin concentration by an HPLC assay.

HPLC-method

Waters HPLC system: 717 plus autosampler, 510 HPLC-pump, PDA detector 996, Detection wavelength: 479 nm
Column: Symmetry® C18 (250mm*4mm).
Mobile Phase: 72.5% phosphate buffer solution (0.05 mol KH_2PO_4 pH 4.6) + 27.5% acetonitrile.
Flow rate:1.5ml/min
Injection volume:10 µl
Run time:10 min
Software:
Waters Empower Pro
Calculation of the percentage rate of epirubicin remaining loaded before and after mixing

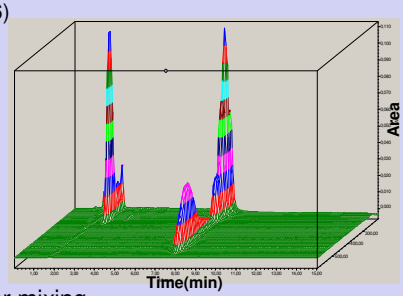

Fig.2 HPLC chromatogram of epirubicin

Results

Mixing of epirubicin-loaded beads with different non-ionic contrast media released 0.1-0.5% of epirubicin over a period of 24 h depending on the DC Bead™ size and type of contrast media. No further elution or degradation was observed after 7 days when the admixtures were stored protected from light under refrigeration.

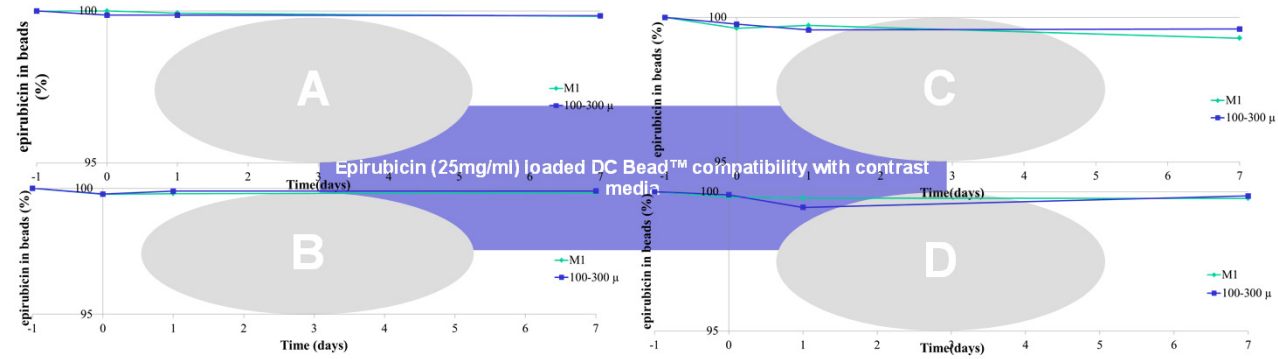

Figure 3 A-D: Percentage rate [%] of epirubicin remaining loaded in DC Bead™ (bead size 70-150µm=(DC Bead*M1*™),100-300 µm) after mixing with different contrast media: A: Accupaque™ 300; B: Imeron® 300; C: Ultravist® 300; D: Visipaque™ 320. The drug-device combination was prepared with 25 mg/mL epirubicin loading solution. Loading level before mixing was set as 100% (= -1 on the x-axis).

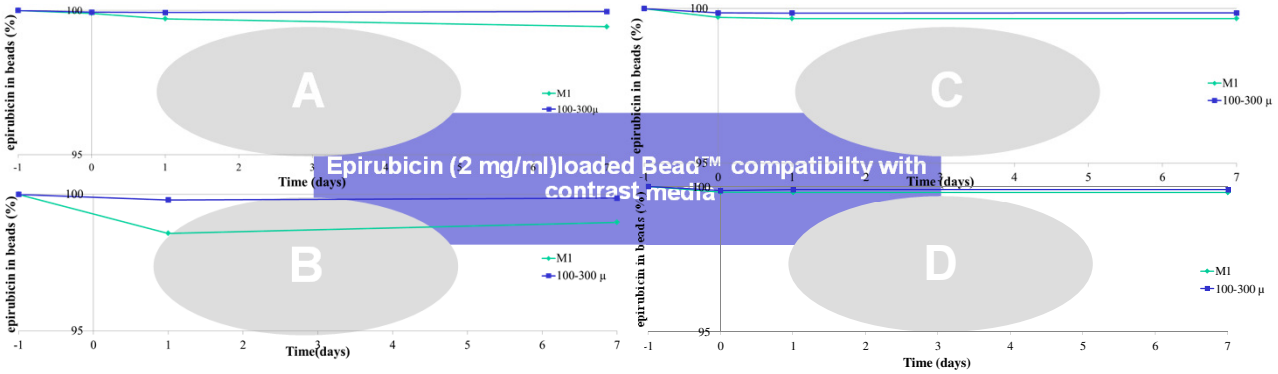

Figure 4 A-D: Percentage rate [%] of epirubicin remaining loaded in DC Bead™ (bead size 70-150 µm=(DC Bead*M1*™),100-300 µm) after mixing with different contrast media: A: Accupaque™ 300; B: Imeron® 300; C: Ultravist® 300; D: Visipaque™ 320. The drug-device combination was prepared with 2 mg/mL epirubicin loading solution. Loading level before mixing was set as 100% (= -1 on the x-axis).

Conclusion

Compatibility of epirubicin-loaded DC Bead™ with an equal volume of different contrast media in PP syringes is given over a period of 7 days. Due to a maximum elution of 0.1 - 0.5% of epirubicin from loaded DC Bead™ admixtures with contrast media can be prepared in advance in centralized cytotoxic preparation units . Microbiological aspects have to be considered when determining the expiration date of the product.

*Biocompatibles UK Ltd., a BTG International group company