

Chemical and Physical Stability of Dexrazoxane diluted in Ringer Lactate, in Polyvinyl Chloride and Polyethylene Containers

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OBJECTIVES

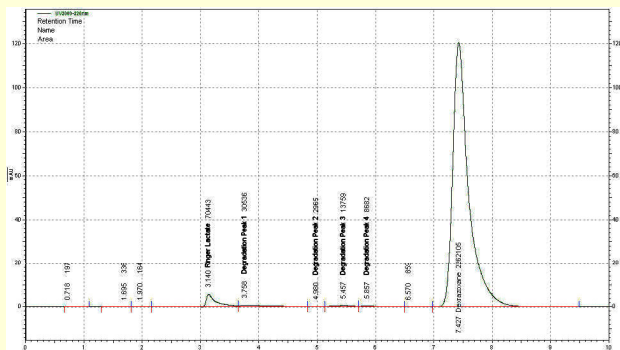
- ✓ Dexrazoxane (Cardioxane®) is known as a cardioprotective agent used prior to bolus of anthracyclins
- ✓ In France, the manufacturer recommends to dilute the drug in Ringer Lactate and indicates a 4 hours stability
- ✓ In other countries, it recommends to dilute the drug with NS or D5W and indicates a 6 hours stability
- ✓ The objectives were to evaluate the stability of dexrazoxane 4 mg/mL and 8 mg/mL in Ringer Lactate in either polyethylene or polyvinyl chloride containers

STUDY DESIGN

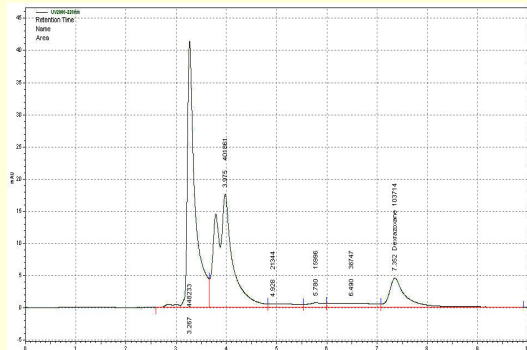
- ✓ Samples were prepared under a laminar airflow hood using aseptic conditions
- ✓ Samples concentrations : 4 mg/mL and 8 mg/mL in polyvinyl chloride (PVC) and polyethylene (PE) container
- ✓ Physical stability was performed by visual inspection (color and precipitation)
- ✓ Chemical stability was performed using a stability indicating high performance liquid chromatographic method (1) :
 - Flow rate : 1 mL/min
 - Column : C18, 250 x 4.6 mm
 - Detection wavelength : 220 nm
 - Injection volume : 10 µL
 - Mobile phase : 0.01 M phosphate buffer pH 4.7 + methanol (80/20)
 - Standard curves at 0.6, 0.8, 1, 1.2, 1.4 mg/mL
 - Within-day coefficient of variation : 1.66%
 - Between-day coefficient of variation : 3.10%
- ✓ Accelerated degradation of dexrazoxane was conducted with NaOH at room temperature
- ✓ Evaluations were performed at 0, 2, 4, 8, 12, 24 hours (storage at room temperature under ambient light)

RESULTS AND DISCUSSION

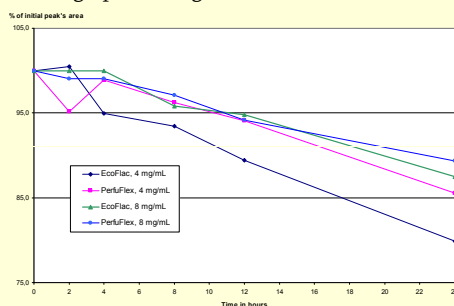
- ✓ After 8 hours, concentrations were higher than 95% of the initial one except the 4 mg/mL solution in PE
- ✓ After 12 hours, concentrations were all lower than 95% of the initial one
- ✓ No precipitate was observed but a yellow coloration appeared at 12 hours and maintained 24 hours
- ✓ Degradation peaks were present at T0 and increased throughout the study (graph 1 and 4)



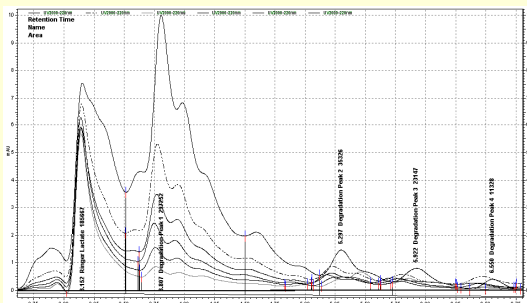
Graph 1 : Chromatogram of 4 mg/mL dexrazoxane solution freshly prepared



Graph 2 : Chromatogram of 4 mg/mL dexrazoxane solution mixed with NaOH 0.1 N at room temperature after 75 minutes



Graph 3 : Evolution of the concentrations of 4 mg/mL and 8 mg/mL dexrazoxane solutions in Ringer Lactate in either PE or PVC



Graph 4 : Zoom on main degradation peaks, superimposing of chromatograms, samples withdrawn at 0, 2, 4, 8, 12 and 24 hours

CONCLUSION

- ✓ Dexrazoxane 4 mg/mL solution in PE container was stable for 4 hours and 4 mg/mL solution in PVC container and 8 mg/mL solutions in PVC or PE were stable for 8 hours (concentrations > 95% of initial ones) at room temperature under normal ambient light

REFERENCE

1. Beijnen JH et al. Chemical stability of the cardioprotective agent ICRF-187 in infusion fluids. J Parenter Sci Technol. 1993 Jul-Aug; 47(4):166-71

Conflict of interest : Nothing to disclose



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