STABILITY OF 25 MG/ML AZACITIDINE SUSPENSIONS STORED IN POLYPROPYLENE SYRINGES AT -20°C

TCH017

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16th Congress of the European Association of Hospital Pharmacists
Vienna
30 march - 1 april 2011

OBJECTIVES

- Azacitidine is used for haematologic pathologies, essentially for myelodysplastic syndrome.
- The manufacturer indicates a 45 minutes stability at room temperature and 8 hours at 2-8°C.
- The purpose of the study was to investigate how freezing can affect the stability of azacitidine suspension 25 mg/mL in polypropylene syringes.

STUDY DESIGN

Sample preparation and storage

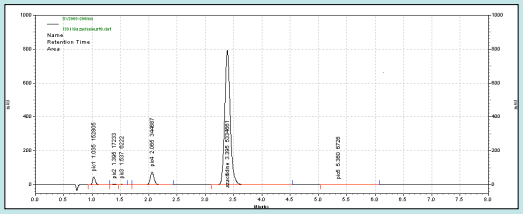
- Under a laminar airflow hood using aseptic conditions
- Concentration : suspension 25 mg/mL reconstituted with sterile water for injection
- Containers : polypropylene syringes
- Storage : -20°C

Analytical procedures

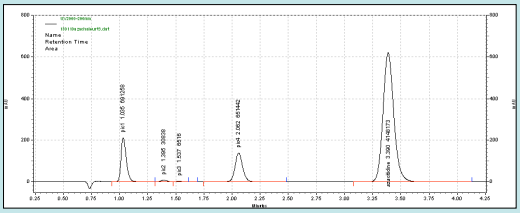
- Analysis : at days 0, 1, 2, 3, 4, 7 and 8
  - immediately after defrosting at room temperature
  - after storage for 8 hours at 2-8°C
- Material for reconstitution stored at 2-8°C or at room temperature
- Visual inspection
- Stability-indicating high-performance liquid chromatographic method adapted from [1]
  - Column : C18, 150mm x 4.6mm
  - Mobile phase : phosphate buffer 10 mM pH 6.5
  - Flow rate : 2 mL/min
  - Injection loop : 20 µL
  - Detection wavelength: 200 nm
  - Analysis time : 8 minutes
- Standard curve : 60, 80, 100, 120, 140 µg/mL
- Within-day coefficient of variation : 1.07 %
- Between-day coefficient of variation : 1.18 %
- Accelerated degradation was conducted with heat, HCl 0.1N and NaOH 0.1N.

RESULTS

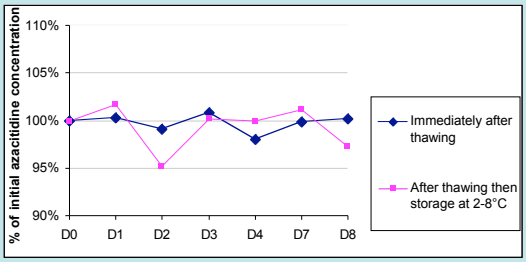
- No modification of suspension or coloration was visually observed in any syringe.
- Degradation peaks were observed after accelerated decomposition with HCl 0.1N.
- After 8 days, syringes retained a concentration higher than 95 % of initial azacitidine concentration (maximum difference 4.5 %).
- Three degradation products (DP) were observed. All were present at the beginning of the study and represented 5 % of the total of the peaks surfaces. But only DP 1 was increased during the study.
- Same results were observed when material for reconstitution was stored at 2-8°C or at room temperature.



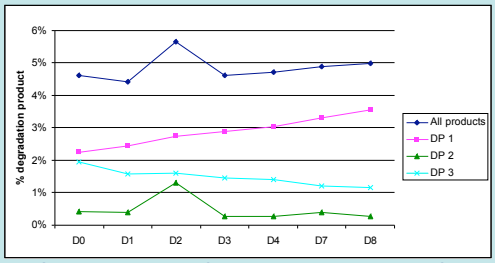
Graph 1 : Chromatogram of 100 µg/mL azacitidine solution in water for injection freshly prepared



Graph 2 : Chromatogram of 100 µg/mL azacitidine solution after storage for 3 hours at 37°C



Graph 3 : Evolution of concentrations of 25 mg/mL azacitidine suspensions after freezing at -20°C



Graph 4 : Evolution of degradation products (DP) after freezing, defrosting and storage for 8 hours at 2-8°C

CONCLUSION

- Azacitidine suspension 25 mg/mL, stored in polypropylene syringe, was stable for 8 days frozen at -20°C, and for 8 hours at 2-8°C after thawing at room temperature.
- Syringes can be prepared in advance and their freezing allowed to realize many savings of vials.

REFERENCE

[1] Den Harting J, Brandenburg HCR, Vermeij P. Stability of azacitidine in lactated Ringer's injection frozen in polypropylene syringes. Am J Hosp Pharm 1989 ; 46: 2500-2505.