Physicochemical Stability of Aztreonam in Polypropylene Syringes at High Concentration for Intensive Care Units.

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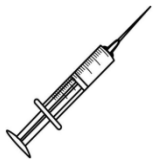
Introduction

Aztreonam: available stability data:
- Solution in PVC bag at 60 mg/mL in water for injection: 24 h at 37 °C
- Solution in polypropylene syringes at 20 mg/mL in NaCl 0.9 %: 48 h at 25 °C

In intensive care unit:
- Dose can vary from 2 g to 8 g per day
- Continuous administration and patient requiring fluid restriction
- → Concentration at 125 mg/mL

Purpose

To study the stability of aztreonam solutions :
- Concentration = 125 mg/mL
- Container: 50 mL polypropylene syringe
- Solvent: Dextrose 5 % (D5W) or NaCl 0.9 %
- Storage:
  - 20-25 °C
  - not protected from light
- Analyse time: H0, H6, H24 and H48



Materials and methods

Chemical stability

The method was validated according to the International Conference on Harmonisation Q2(R1).

Method: RP-HPLC with DAD detector at 270 nm
- C18 LiChrospher® 12.5 cm , particle size= 5 µm
- Mobile phase:
  Methanol (10 %) + potassium phosphate buffer (90 %)
- Flow rate: 1 mL/min
- Injection volume: 20 µL
- Forced degradation: HCl 5 M (2 h); NaOH 0.01 M (30 min); H_2O_2 0.3 %; UV (1 h at 254 nm); heat (16 h at 80 °C)

Physical stability

Visual inspection: colour, precipitation and gaz formation

Subvisual inspection: turbidimetry with a turbidimeter (Engineered systems & designs)

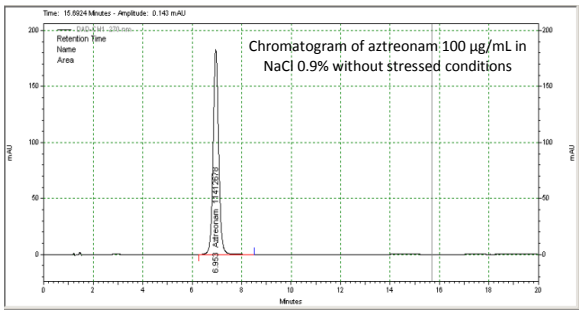
pH measurement (Bioblock Scientific pH meter)

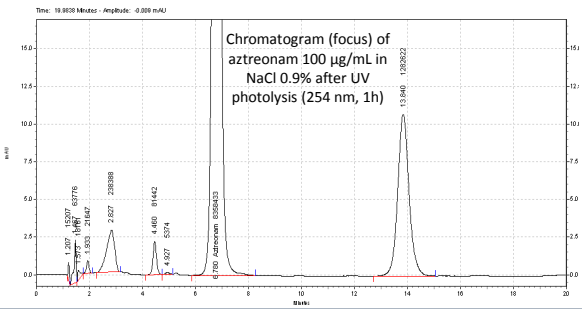
→ Three syringes for each condition (S1, S2, S3)

→ Stability = conservation of more than 95 % of the initial concentration, no visual change and no significative subvisual and pH variation

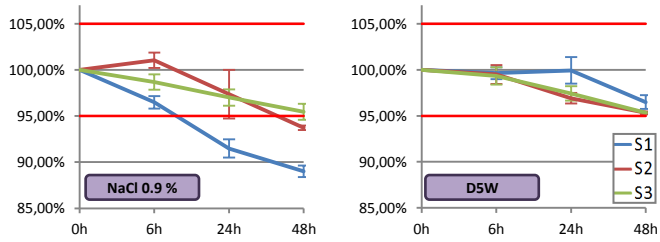
Results

Validation: RP-HPLC method
- Linearity: $r^2 > 0,999$ (5-point standard curve: 50-150 µg/mL)
- Repeatability and intermediate precision: CV < 2 %
- Retention time: 6.9 min
- Stability indicating capacity:



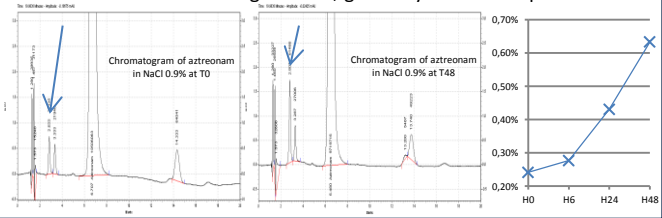


Room temperature (20-25°C) – Not protected from light



Physical Stability:
- Visual inspection: No colour change, no precipitate, no gaz formation
- Subvisual inspection: decrease of the turbidimetry from 1.67 NTU probably because of a progressive solubilization of aztreonam due to the high concentration used
- pH measurement: no significant modification (4.85 to 5.13)

Degradation product: A peak with a retention time at 2.83 min, also observed after the forced degradation, gradually increased up to 0.6%.



Discussion - Conclusion

Stability of aztreonam at 125 mg/mL in polypropylene syringe at room temperature:
- No significant physical modification → physically stable for 48 h
- Chemical stability: S1 in NaCl 0.9 % have a concentration less than 95 % at H24 but the concentration at H0 was higher than the other syringes for two point of three. That was probably due to a bad homogenization of the syringe S1.

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Aztreonam is stable diluted in NaCl 0.9% or D5W at 125 mg/mL in polypropylene syringe for 24 h at room temperature.
These stability data provide additional knowledge to assist ICUs in daily practice.

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