Physicochemical stability of CEFAZOLIN in Polypropylene Syringes and in Elastomeric Devices.

Introduction

CEFAZOLIN is an antibiotic used to treat methicillin-susceptible Staphylococcus aureus infections. The usual dose is 6 g per day. To the best of our knowledge, no stability data for cefazolin:

- 125 mg/mL (6 g in 48 mL) in syringes for continuous infusions
- 50 mg/mL (12 g in 240 mL) in elastomeric devices for infusions at home.

Objectives

Physicochemical stability studies of CEFAZOLIN solutions
Concentrations : 125 mg/mL (syringe) or 50 mg/mL (elastomeric) 
Container: polypropylene syringes or elastomeric devices 
Solvent: NaCl 0.9% - D5W 
Storage: 20-25°C (syringe) or 37°C (elastomeric devices)
Analysis after preparation, and after 6 , 24 and 48 hours.

Materials and Method

Chemical stability: defined as a concentration above 90% of the initial concentration

1. RP-HPLC with DAD detector at 272 nm
   - Column: C18 LiChrospher® 12.5 cm, 40 °C, particle size=5 µm
   - Mobile phase: isocratic 80% KH2PO4 buffer 0.005 M, pH=7.5 and 20% of methanol
   - Flow rate: 1.0 mL/min
   - Injector temperature: 20°C
   - Injection volume: 50 µL

Physical stability

- Visual examination: change of colour, precipitation, gas formation

3 syringes and 3 elastomeric devices (FOLFUSOR®, Baxter) for each condition (S1 – S2 – S3)

Materials and Method

2. Validation of the method as recommended by ICH Q2(R1)
   - Forced degradation
     | Acidic | Alkaline | Thermic | Photolysis |
     |--------|---------|---------|-----------|
     | HCl 5 M | NaOH 0.1 M | 80 °C | 20 min - under a sun-like spectrum lamp at 254 nm |
   - Linearity: standard curve with 5 points: 75-175 µg/mL
   - Repeatability and intermediate precision

3. pH measurement (Bioblock Scientific pH meter)

Results

Validation: RP-HPLC method
- Linearity: $R^2 > 0.999$
- Repeatability: [0.15-0.85%] - intermediate precision < 0.57%  

Chemical stability – HPLC

125 mg/mL – syringe – 20-25°C

Stability indicating capacity

Chromatogram of CEFAZOLIN 125 µg/mL in NaCl 0.9% after acidic stressed conditions (HCl 5 M, 5 min)

50 mg/mL – elastomeric – 37°C

Subvisual examination: turbidimetry by spectrophotometry at 350, 410 and 550 nm (Safas Monaco UV m²)

Chromatogram of CEFAZOLIN 125 µg/mL after alkaline stressed conditions (NaOH 0.1 M, 10 min)

Physical stability

Visual aspect: no modification in elastomeric device and in syringe

Subvisual aspect: of absorbances in elastomeric device and stable in syringe

Conclusion

Stability of cefazolin in syringes, diluted in NaCl 0.9% or in D5W at 125 mg/mL, for 24 hours at 20-25°C.

Cefazolin in elastomeric devices at 50 mg/mL is unstable after 6 hours. These preparations are not recommended.