



## 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 % KH<sub>2</sub>PO<sub>4</sub> buffer 0.005 M, pH=7.5 and 20 % of methanol
- **Flow rate** at 1.0 mL/min
- **Injector temperature** at 20°C
- **Injection volume**: 50 µL

### Physical stability



- **Visual examination** : change of colour, precipitation, gaz formation

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

### ② Validation of the method as recommended by ICH Q2(R1)

#### ▪ Forced degradation

Acidic	Alkaline	Thermic	Photolysis
HCl 5 M 5 min	NaOH 0.1 M 10 min	80 °C 2 hours	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)

- **Subvisual examination** : turbidimetry by spectrophotometry at 350, 410 and 550 nm (Safas Monaco UV m<sup>2</sup>)

## Results

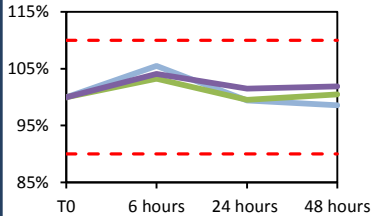
### ① Validation – RP-HPLC method

- **Linearity** : R<sup>2</sup> > 0.999
- **Repeatability** : [0.15-0.85%] - intermediate precision < 0.57%

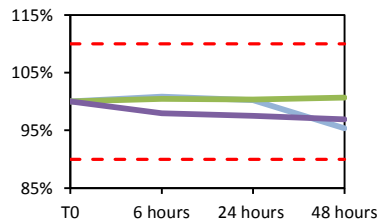
### ② Chemical stability –HPLC

125 mg/mL – syringe – 20-25°C

NaCl 0.9%

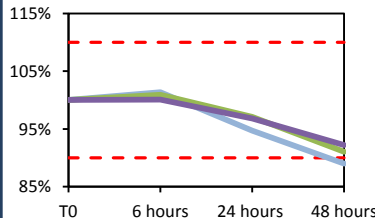


D5W

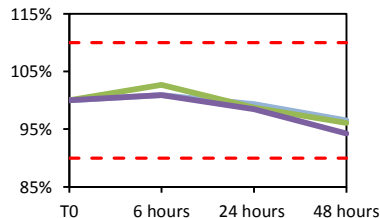


50 mg/mL – elastomeric – 37°C

NaCl 0.9%



D5W



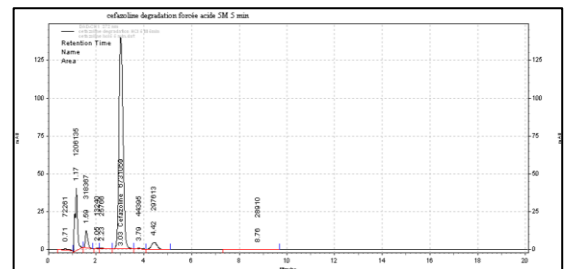
### pH measurement

- **Syringes** : ↗ of one pH unit after 48 h
- **Elastomeric devices** : ↗ of one pH unit after 6 h

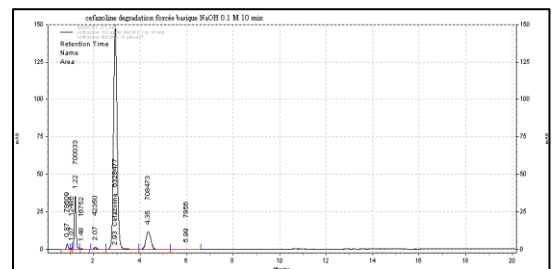
### ③ Physical stability

**Visual aspect**: no modification in elastomeric device and in syringe

### ▪ Stability indicating capacity



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



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

**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**.

