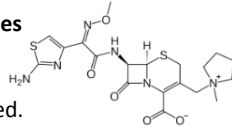




Introduction

CEFEPIME is a 4th-generation cephalosporin used to treat severe infectious. To the best of our knowledge, no stability data for cefepime solutions at

- **110 mg/mL in polypropylene syringes** for continuous infusion.
- **50 mg/mL in elastomeric devices** for infusion at home have been published.



Objectives

Physicochemical stability studies of CEFEPIME solutions

	NaCl 0.9% - D5W	110 mg/mL	20-25°C 	Times of analysis : 0, 6, 24, 48 h
	NaCl 0.9%	50 mg/mL	37°C 	

Materials and Method

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

① RP-HPLC with DAD detector at 257 nm

- **Column**: C18 LiChrospher® 12.5 cm, 40°C, particle size= 5 µm
- **Mobile phase**: isocratic
90% KH₂PO₄ buffer 0.005 M, pH=7.5 and 10% of methanol
- **Flow rate** : 1.0 mL/min
- **Injector temperature** : 10°C
- **Injection volume**: 10 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	Oxydative	Photolysis
HCl 1 M 30 min	NaOH 0.2 M 1 min	H ₂ O ₂ 3.0%	2h - under a sun-like spectrum lamp at 254 nm

- **Linearity** : standard curve with 5 points : 60-140 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 m²)

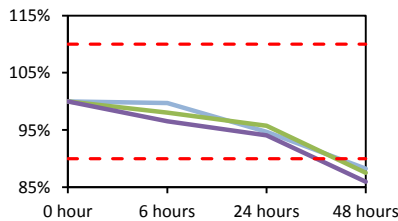
Results

① Validation : RP-HPLC method

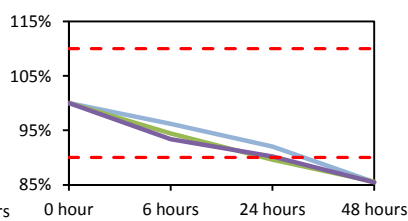
- **Linearity** : R²>0.999
- **Repeatability** : [0.04-0.83%] - intermediate precision < 1.7%

② Chemical stability –HPLC

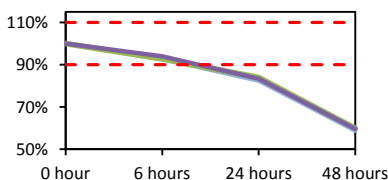
110 mg/mL – NaCl 0.9%
Syringe – 20-25°C



110 mg/mL – D5W
Syringe – 20-25°C



50 mg/mL – NaCl 0.9% - Elastomeric devices – 37°C



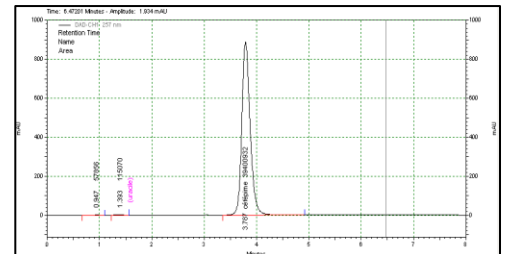
pH measurements

↗ of one pH unit after 48 hours in elastomeric devices.

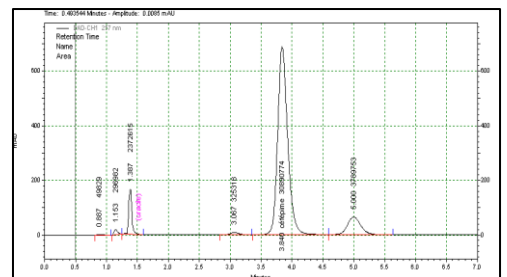
③ Physical stability

- **Stability in syringes** : no visual modification and no turbidity
- **Stability in elastomeric devices** : colour modifications and particulates formation after 6 hours

▪ Stability indicating capacity



Chromatogram of CEFEPIME 100 µg/mL in NaCl 0.9% without stressed conditions, freshly prepared.



Chromatogram of CEFEPIME 100 µg/mL after alkaline stressed conditions (NaOH 0.2 M, 1 min)

Conclusion

Physicochemical stability of **CEFEPIME 110 mg/mL** in **NaCl 0.9%** and **D5W** in **syringes** for **24 h** ➔ Administration by **continuous infusion**
Minimal volume of solution



In **elastomeric devices**, **CEFEPIME 50 mg/mL** was **unstable** at **37°C**