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

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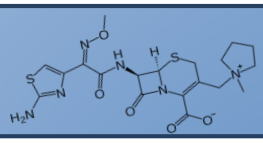
Göteborg (Sweden)
25-27th, March 2020

3PC-004

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** or at **50 mg/mL in elastomeric devices** have been published.



Objectives

Physicochemical stability studies of CEFEPIME solutions

	NaCl 0.9% - D5W	110 mg/mL	20-25°C	T=0, 6, 24 – 48 h
	NaCl 0.9%	50 mg/mL	37 °C	

Materials and Method

Chemical stability

① **RP-HPLC with DAD detector at 257 nm**
- **Column**: C18 LiChrospher® 12.5 cm, particle size=5 µm at 40°C
- **Mobile phase**: isocratic 90 % KH_2PO_4 buffer 0.005 M, pH=7.5 and 10 % of methanol
- **Flow rate** at 1.0 mL/min
- **Injector temperature** at 10°C
- **Injection volume**: 10 µL

Physical stability

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

② **Validation of the method as recommanded by ICH Q2(R1)**
- **Forced degradation**

Acidic	Alkaline	Oxydative	Photolysis
HCl 1 M 30 min	NaOH 0.2 M 1 min	H_2O_2 3.0 %	2h

- **Linearity :** standard curve with 5 points : 60-140 µg/mL
- **Repeatability and intermediate precision**

③ **pH measurement** (Bioblock Scientific pH meter)

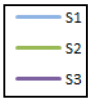
➢ **Subvisual examination** : turbidimetry by spectrophotometry at 350, 410 and 550 nm (Safas Monaco UV m²)

➡ **3 syringes for each condition (S1 – S2 – S3)**

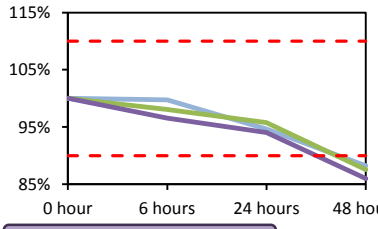
Results

① **Validation : RP-HPLC method**
- **Linearity** : R^2>0.999
- **Repeatability and intermediate precision demonstrated**

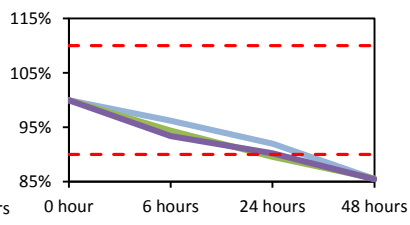
② **Chemical stability –HPLC**



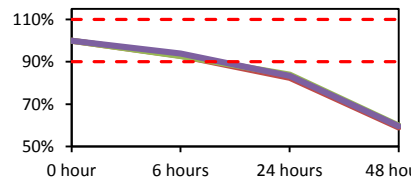
110 mg/mL – NaCl 0.9%



110 mg/mL – DW5



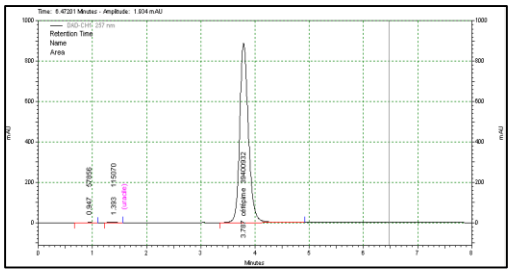
50 mg/mL – NaCl 0.9%



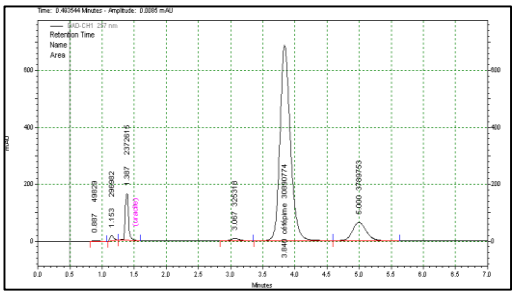
pH measurement
↗ of one pH unit after 48 hours in elastomeric devices.

③ **Physical stability**
- *Stability in syringes :* no visual modification and no turbidity.
- *Stability in elastomeric devices :* visual colour modifications after 6 hours.

- **Stability indicating capacity**



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



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

Conclusion

Physicochemical stability of **CEFEPIME at 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** at **50 mg/mL** was **unstable** at 37 °C.