



Introduction

In ICUs, the dose of cefotaxime can vary from 3 g to 24 g per day and continuous administration is the preferred mode of administration.

Patients with fluid restriction

Minimum volume and high dose

High concentrations of cefotaxime

Objectives

Physicochemical stability studies of cefotaxime sodium solutions

- **Concentrations** : 83.3 and 125 mg/mL
- **Container**: polypropylene syringes
- **Solvent**: sodium chloride 0.9% (NaCl 0.9%) - glucose 5% (G5%)
- **Storage** : 20-25°C, unprotected from light
- **Analysis** after preparation, and after 6 and 12 hours.

Materials and Method

Chemical stability

① RP-HPLC with DAD detector at 235 nm

- **Column**: C18 LiChrospher® 12.5 cm, particle size=5 µm at 30°C
- **Mobile phase**: gradient mode

Phase A : 86 % Na₂HPO₄ buffer 0.05 M, pH=6.25 and 14 % of methanol

Phase B : 60 % Na₂HPO₄ buffer 0.05 M, pH=6.25 and 40 % of methanol

- **Flow rate** at 1.3 mL/min
- **Injector temperature** at 15°C
- **Injection volume**: 10 µL

Physical stability



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

➔ 3 syringes for each condition (S1 – S2 – S3)

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

▪ Forced degradation

Acidic	Alkaline	Oxydative	Heat
HCl 0.05 M 3h	NaOH 0.01 M 5 min	H ₂ O ₂ 0.30 %	40°C 7h

- **Linearity** : standard curve with 5 points : 50-150 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

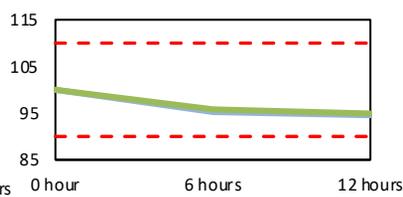
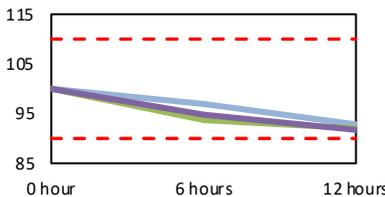
① Validation : RP-HPLC method

- **Linearity** : R²>0.999
- **Repeatability and intermediate precision** : CV < 1.81 %

② Chemical stability –HPLC

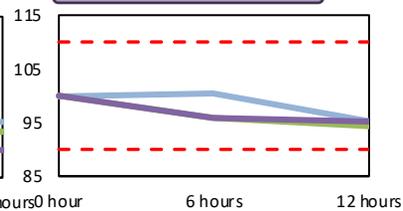
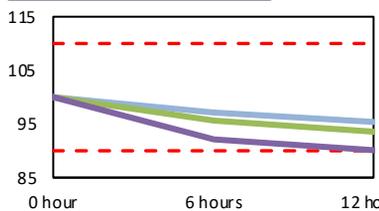
83.3 mg/ mL – NaCl 0.9%

125 mg/ mL – NaCl 0.9%

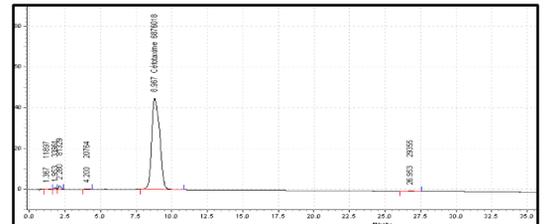


83.3 mg/ mL – G5%

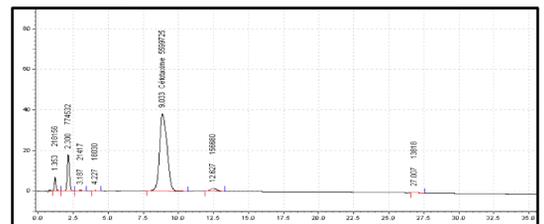
125 mg/ mL – G5%



▪ Stability indicating capacity



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



Chromatogram of cefotaxime sodium 100 µg/mL after alkaline stressed conditions (NaOH 0.01 M, 5 min)

Additional peak (Relative retention = 3.01)
 ↗ Up to 4.01% in NaCl 0.9% } at T=12 hours
 ↗ Up to 3.17% in G5% } of the total surface area of the peaks.

pH measurement

- ➔ decreased slightly
- Maximum variation** : T0 → T12h : 0.5 pH unit [5,32 → 4,82]

③ Physical stability

- **Visual aspect** : ↗ of the intensity of the yellow colour
- **Sub-visual aspect** : ↗ of the absorbance values progressively of each wavelength and each condition.

Conclusion

Chemical stability of cefotaxime solutions for each condition

➔ Physical modification of cefotaxime after a 12-hour storage

➔ Limitation of the stability for cefotaxime at 83.3 and 125 mg/mL at 6 hours for G5% and NaCl 0.9%.