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

CEFEPIME is a 4th-generation cephalosporin used to treat severe infections. 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.

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, gas formation

2. Validation of the method as recommended by ICH Q2(R1)
   - Forced degradation

<table>
<thead>
<tr>
<th>Acidic</th>
<th>Alkaline</th>
<th>Oxidative</th>
<th>Photolysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCl 1 M 30 min</td>
<td>NaOH 0.2 M 1 min</td>
<td>H₂O₂ 3.0%</td>
<td>2h - under a sun-like spectrum lamp at 254 nm</td>
</tr>
</tbody>
</table>

- 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

<table>
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<tr>
<th>Chemical stability</th>
<th>Stability indicating capacity</th>
</tr>
</thead>
<tbody>
<tr>
<td>110 mg/mL - NaCl 0.9% Syringe - 20-25°C</td>
<td>Chromatogram of CEFEPIME 100 μg/mL in NaCl 0.9% without stressed conditions, freshly prepared.</td>
</tr>
<tr>
<td>110 mg/mL - DSW Syringe - 20-25°C</td>
<td>Chromatogram of CEFEPIME 100 μg/mL after alkaline stressed conditions (NaOH 0.2 M, 1 min)</td>
</tr>
</tbody>
</table>

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

Conclusion

Physicochemical stability of CEFEPIME 110 mg/mL in NaCl 0.9% and DSW in syringes for 24 h → In elastomeric devices, CEFEPIME 50 mg/mL was unstable at 37 °C

DSW: dextrose 5% - NaCl 0.9% - sodium chloride 0.9%