Physicochemical stability of Vancomycin Hydrochloride in Polypropylene Syringes at High Concentrations for Intensive Care Units

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Introduction

In some severe infections, the dose of vancomycin may be 60 mg/kg/day. By manufacturers, the final concentration of vancomycin solutions should not exceed 10 mg/mL.

- Body weight: 65 kg
- Daily dose of vancomycin: 4 g
- Dilution in 400 mL of solvent

For patients requiring fluid restrictions, this volume is not adequate.

Materials and Method

1. Impact of an electric syringe pump on the physical stability
2. Physicochemical stability studies of vancomycin solutions
   - Concentrations: 62.5 and 83.3 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, 24 and 48 hours.

Validation of the method as recommended by ICH Q2(R1)
- Forced degradation
  - Acidic degradation
  - Alkaline degradation
  - Heat degradation

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<th>Acidic degradation</th>
<th>Alkaline degradation</th>
<th>Heat degradation</th>
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<td>HCl 1.0M 16 hours</td>
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<td>NaOH 1.0M 60 min</td>
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<td>80°C 4 hours</td>
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- 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 \(m^2\))

For patients requiring fluid restrictions, this volume is not adequate.

Results

1. Validation: RP-HPLC method
   - Linearity: \(R^2=0.999\)
   - Repeatability and intermediate precision: CV<2.5 %

2. Chemical stability – HPLC
   - 62.5 mg/mL – NaCl 0.9%
   - 83.3 mg/mL – NaCl 0.9%
   - 62.5 mg/mL – G5%
   - 83.3 mg/mL – G5%

   Chromatogram of vancomycin 100 µg/mL without stressed conditions.

   Chromatogram of vancomycin 100 µg/mL after alkaline stressed conditions (NaOH 1.0 M, 1h)

3. Physical stability
   - No modification
     - No impact of the action of an electric syringe pump
     - Visual aspect: precipitation for solutions at 83.3 mg/mL after 48 hours.
   - Sub-visual aspect: no modification

Conclusion

Vancomycin at 62.5 mg/mL and 83.3 mg/mL in G5% are stable for 48 hours at 25°C
- Unprotected from light
- For high concentrations of vancomycin, G5% as solvent is recommended.