Physicochemical stability of MEROPENEM in Polypropylene Syringes at 41.7 mg/mL for intensive care units

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INTRODUCTION

Meropenem is a broad-spectrum antibiotic used to treat severe infectious. The maximum dose recommended is 6 g per day. A stability not exceeding 24 h has been demonstrated by many research teams in different publications. Only 2 studies were performed at 40 mg/mL in polypropylene syringes with conflicting stability results: 4h and 8h. [1] [2] Meropenem is a time-dependent antibiotic, its continuous administration improves its efficiency.

METHODS

CHEMICAL STABILITY

Method: RP-HPLC with DAD detector at 297 nm [3]

- C18 LiChrospher® 12.5 cm, particle size = 5 µm
- Mobile phase: isocratic: ammonium acetate buffer (10 mM) / acetonitrile 95/5 (v/v), pH = 3.0 adjusted with HCl 0.1M
- Flow rate: 1 mL/min
- Injection volume: 20 μL

- Forced degradation: HCl 0.1M (10 min); NaOH 0.01 M (20 min); UV (1h at 254 nm); heat (1h at 50°C)
- Linearity: standard curve with 5 points: between 50 to 250 µg/mL
- Repeatability and intermediate precision: 50, 150, 250 µg/mL
- pH measurement (Bioblock Scientific pH meter)

PHYSICAL STABILITY

Visual inspection: search for colour change, precipitation and gaz formation
Subvisual inspection: turbidimetry by spectrophotometry at 350, 450 and 550 nm (Safas Monaco UV m²)

RESULTS

1. Validation: RP-HPLC method

- Linearity: R² > 0.9999
- Repeatability and intermediate precision: CV < 2%
- Retention time: 7.9 min
- Stability indicating capacity:

2. Chemical stability HPLC:

- pH measurement: decreased slightly with maximum variation: 0.2 unit
- pH variation: 7.8 → 7.6, T0h → T8h in D5W and 0.15 pH unit in 0.9% NaCl

3. Physical stability:

- Subvisual inspection: no significative variation in 0.9% NaCl.
- In the D5W at 410 and 550 nm, major increase in absorbance between T0h and T8h.
- Visual inspection: major colour change in D5W (yellowing +++) at T4 h and T8h. In 0.9% NaCl only slight intensification in colour was observed.

CONCLUSION

Meropenem was stable at 41.7 mg/mL in polypropylene syringes diluted in 0.9% NaCl for 8 hours. This new stability data allows a continuous administration.

In D5W meropenem was unstable, with chemical and physical instability.