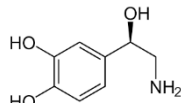




Introduction

Norepinephrine is usually used in emergency situations as in intensive care units (ICUs) for the restoration of blood pressure. High doses at 3 to 5 µg/kg/min can be used in the treatment of septic or hemorrhagic shock.



Objectives

Physicochemical stability studies of norepinephrine solutions

- **Concentrations** : 0.5 and 1.16 mg/mL
- **Container**: polypropylene syringes
- **Solvent**: Glucose 5 % (G5%)
- **Storage** : 20-25°C, protected and unprotected from light
- **Analysis** after preparation, and after 6, 24 and 48 hours.

Materials and Method

Chemical stability

① RP-HPLC with DAD detector at 280 nm

- **Column**: C18 LiChrospher® 12.5 cm, particle size=5 µm at 25°C
- **Mobile phase**
Mixture of acetonitrile and 0.05 M phosphoric acid containing 1 mg/mL of heptane sulfonic acid sodium salt
- **Flow rate** at 1 mL/min
- **Injector temperature** at 20 °C
- **Injection volume**: 10 µL

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

▪ Forced degradation

Acidic degradation	Alkaline degradation	Heat degradation
HCl 0.5M 6 hours	NaOH 0.01M 5 min	100 °C 6 hours

- **Linearity** : standard curve with 5 points : 80-160 µg/mL
- **Repeatability and intermediate precision**

③ pH measurement (Bioblock Scientific pH meter)

Physical stability



- **Visual examination** : change of colour, precipitation, gas formation
- **Subvisual examination** : turbidimetry by spectrophotometry at 350, 410 and 550 nm (Safas Monaco UV m²)

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

Results

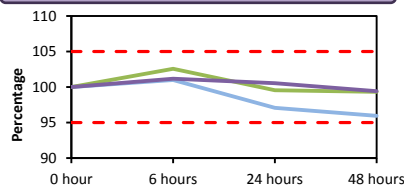
① Validation : RP-HPLC method

- **Linearity** : R²>0.999
- **Repeatability and intermediate precision** : CV<3 %

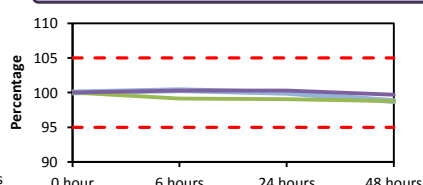


② Chemical stability –HPLC

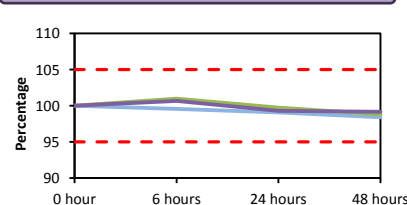
0.50 mg/ mL – unprotected from light



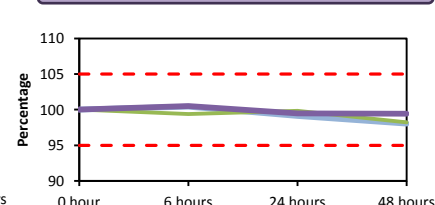
0.50 mg/ mL – protected from light



1.16 mg/ mL – unprotected from light



1.16 mg/ mL – protected from light

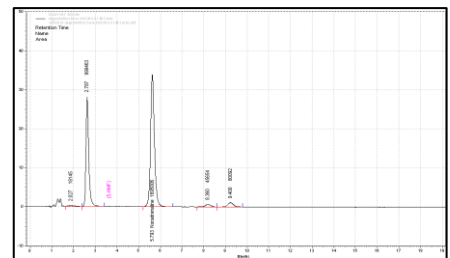


pH measurement : no modification
[8.78-9.06]

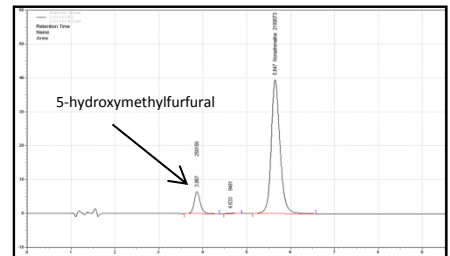
③ Physical stability

- Visual aspect : no modification
- Subvisual aspect : no modification

▪ Stability indicating capacity



Chromatogram of norepinephrine 120 µg/mL in ultrapure water after alkaline stressed conditions.



Chromatogram of a norepinephrine solution diluted in glucose 5% after preparation.

Conclusion

Norepinephrine at **0.50 mg/mL** and **1.16 mg/mL** in G5%



Stable for **48 hours at 25°C**
Protected or not from light



Additional knowledge to assist ICUs in daily practice