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18th Congress of the EAHP

Paris 2013

TCH-033

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Physicochemical stability of ready-to-administer epinephrine injection solutions 20 µg/ml, 50 ml

Background and Purpose

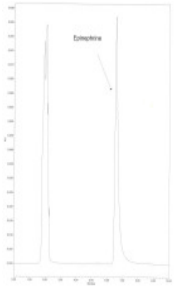
In the University Medical Center Mainz standard concentrations are defined for medicinal products to be adminstered by continous injection with syringe pumps in adult intensive care patients. Patient individual doses are provided by adjusting the injection rate. Various medications are aseptically prepared in the pharmacy department as ready-to-administer products. Batch wise preparation of the products and keeping them in stock is only possible if stability of the products is tested using a validated stability indicating method.

The aim of the study was to test the stability of ready-to-administer epinephrine injections solutions 20 µg/ml in 50 ml plastic syringes.

Materials and Methods

Epinephrine bulk solution 20 µg/ml was prepared aseptically by diluting Suprarenin® 25 mg/ 25 ml Sanofi-Aventis with 5% glucose infusion solution in empty infusion bags (PP/PE). The solution was filled with the NeoCare Compounder into 50 ml opaque BD Perfusion Syringes Luer Lock Tip. The products were stored refrigerated at 2-8 °C for 6 months. Another batch of epinephrine syringes was stored for two days at 2-8 °C and then at room temperature for 14 days.

Epinephrine concentration was determined by using a validated HPLC method with UV detection at 280 nm and an innovative HPLC column Nucleodur which contains sulfonyl groups.



Column: Nucleodur HILIC® 5 µm, 250 x 4.6 mm

Mobile phase: 25% ammonium acetate buffer
75% Acetonitril

Injection volume: 100 µl

Flow rate: 1.5 ml/min

UV/Vis-Detection : 280 nm

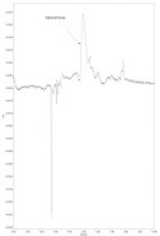
Linearity: 0.9997

Accuracy: 100% ± 1,87

Intraday Precision [RSDr]: 1.87%

Interday Precision [RSDt]: 2.88%

Fig. 1: HPLC Chromatogram of Epinephrine 20 µg/ml, UV/VIS- Detection at 280 nm



Following alkaline forced degradation (adjustment with NaOH to pH 8 or pH 11) was conducted to detect adrenochrome.
Resulting chromatograms are shown in Fig.2 – Fig.4.
The specific detection wavelength of adrenochrome is 480 nm. [1]

Fig. 2: pH 8, UV/VIS 480 nm

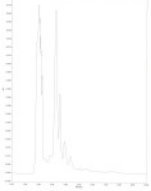


Fig.3 pH 8, UV/VIS 280 nm

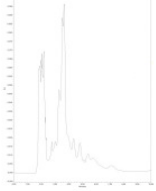


Fig.4 pH 11, UV/VIS 280 nm

Results

The concentration of epinephrine in the 50 ml syringes and stored under refrigeration remained unchanged over a period of 6 months. After 28 days, 3 months, and 6 months of storage the concentration amounted to 100.0%,100.1% and 97,6% of the nominal concentration, respectively. After 7 months of storage the concentration of epinephrine declined to 92.2% of the nominal concentration (s. Fig.5)

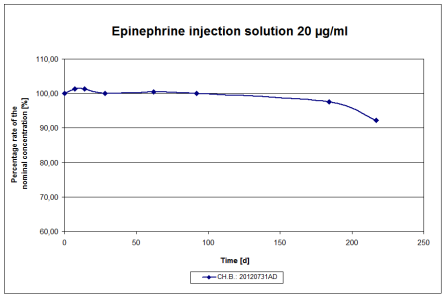


Fig.5: Stability of epinephrine injection solution 20 µg/mL over 6 months under refrigeration

After 14 days at RT the concentration of epinephrine had declined to 91 % of the nominal concentration (s. Fig.6)

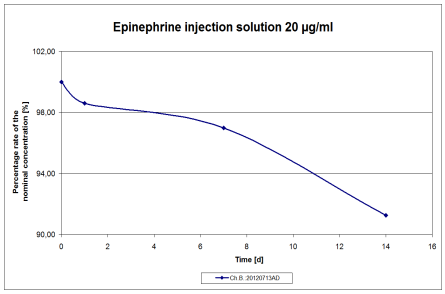


Fig.6: Stability of epinephrine injection solution 20 µg/mL over 14 days storage at RT

Neither adrenochrome nor any other degradation product was detected during the storage periods.

Conclusions

The ready-to-administer epinephrine injection solution 20 µg/ml, aseptically prepared by diluting the marketed injection concentrate with 5% glucose infusion solution in 50 ml light protected plastic syringes, is stable under refrigerated conditions for at least 6 months. At room temperature, the epinephrine injection solution is stable for a maximum of 14 days.

The Nucleodur column revealed a simple and more precise HPLC method for the quantification of epinephrine than commnon methods using SDS in the mobile phase.

Literature

[1] Bindoli, A. Deeble, D.J. Et al; Direct and respiratory chain-mediated redox cycling of adrenochrome; Biochimica et Biophysica Acta 1990; 1016: 349-356