

REPLACEMENT OF A DISCONTINUED COMMERCIAL BRAND OF PREFILLED ATROPINE SYRINGES BY A HOSPITAL PHARMACY PRODUCTION : SHELF LIFE DETERMINATION

W Griffiths, H Ing, B Matthey, F Sadeghipour, P Bonnabry
Pharmacy, University Hospitals of Geneva (HUG), Switzerland

Background and Objective

Atropine is a potent parasympatholytic agent used to increase heart rate in life-threatening bradycardias. According to resuscitation guidelines, it is given in doses of 0.5 to 1 mg IV repeated every 3 – 4 minutes (total: 0.04mg/kg)^{1,2}. In Geneva, atropine has been present in the Cardiomobile (CMB), a mobile intensive care unit, and also in hospital emergency kits as two piece ready-to-use (RTU) syringes. Since 2002 they are no longer commercialised in Switzerland and only ampoules were available as replacement. The objective of the study was to develop an RTU syringe prepared in the pharmacy and to determine its chemical stability for at least 6 months.

Commercial product :
Gone off the market



"Ready to use" syringe



Method

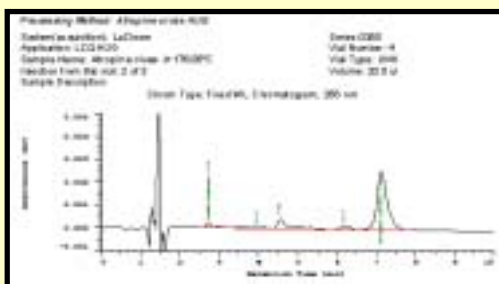
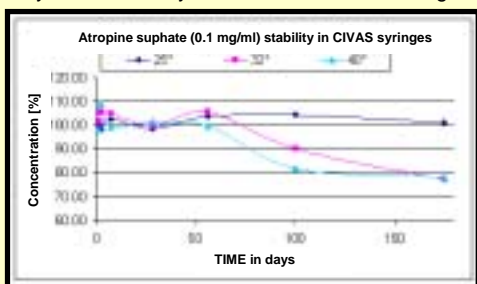
An atropine sulphate solution (in 0.9% sodium chloride and pH adjusted to 4.0 ± 0.5 with 0.1 M sulphuric acid) was prepared (1mg/10ml) and filled under aseptic conditions into polypropylene syringes (Plastipak^R, Becton Dickinson) and individually packed in sterile light-proof plastic sachets and stored at 25±2°C, 32±2°C and 40±2°C. Analysis was not carried out at 4°C due to the impossibility to maintain the cold chain in the CMB. Samples were analysed according to ICH guidelines at 0, 1, 2 and 7 days, and 1, 2, 3 and 6 months using an HPLC method validated for stability testing. The pH was controlled and sterility testing was performed during the study to determine integrity of the syringes. Visual inspection for the eventual presence of particles was also carried out.

HPLC Parameters

Merck Hitachi System with high pressure pump L-7100 and D7000 interface.
Column: Nucleosil (Macherey Nagel) C18 (5microns) 250/8/4mm.
Mobile Phase: Ammonium acetate buffer 0.05M pH 4.0 Acetonitrile R 87:13
Flow rate: 2.0 ml/min.
Injection Volume: 20 µl
Detection: UV 256 nm
Internal standard: Phenol 0.2 mg/ml
Atropine standard: Atropine sulphate 2 mg/ml

Results

The HPLC method was stability indicating as no degradation peaks were detected. The drugs levels showed no significant losses (< 5% of their original concentration) at 25±2°C after 6 months. However, at the higher temperatures some losses occurred after 3 months. The pH did not vary significantly and all sterility tests were found to be negative. No particulate matter was detected.



Conclusions

Syringes of RTU atropine for use in the CMB and emergency room are stable for at least 6 months at room temperature with no significant loss of potency. The administration delay is notably diminished when compared with ampoule and vial forms.

References

- 1 C. Gleason, E. Molle-Matthews, D Washburn; <http://nsweb.nursingspectrum.com/ce/ce83.htm>
- 2 Resuscitation Guidelines 2000; <http://www.resus.org.uk/pages/als.htm>
- 3 ICH Guidelines Q1A (R2); <http://www.ich.org>
- 4 Modified assay method of USP Atropine Monography