PALL Medical

Technical Report

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Filterability of Amiodarone Through Pall ELD Family and AEF1E Filters

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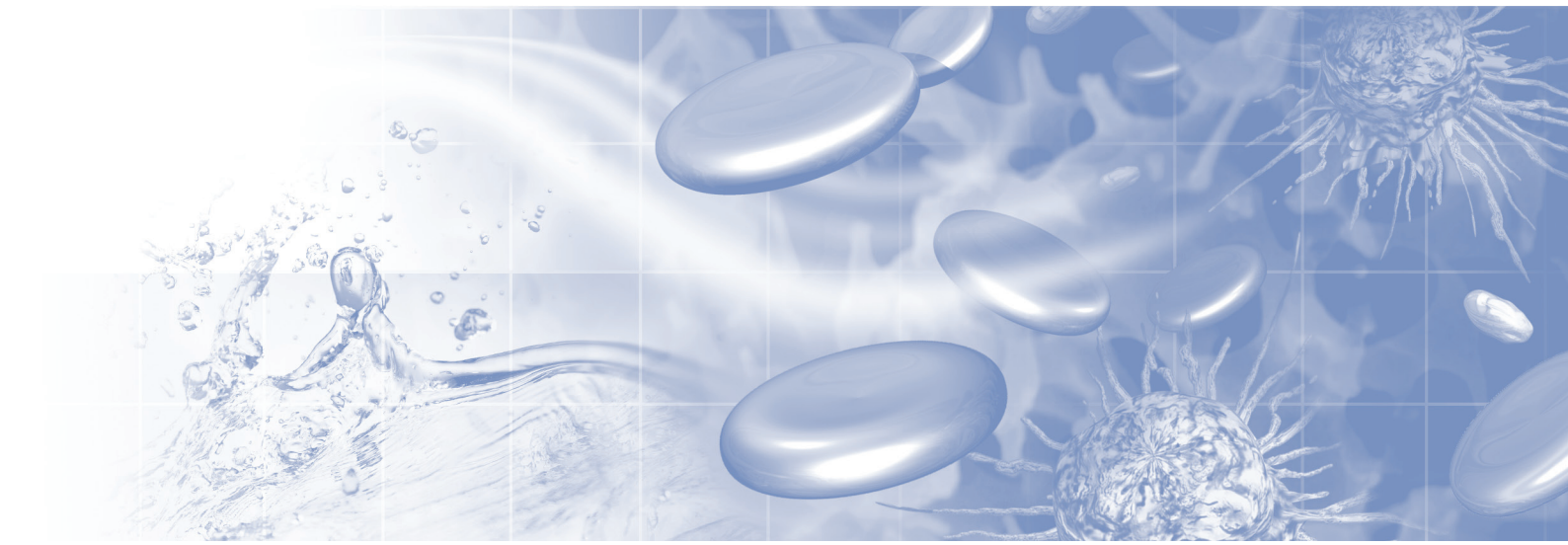

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Abstract

Amiodarone, a commonly used pharmaceutical drug, was analyzed for filterability through Pall AEF1E and ELD96LLCE filters. Amiodarone Carino (Carinopharm) was assayed using UV spectrophotometry before and after passage through the filters using a drug concentration of 0.6 mg/mL and a flow rate of 20 mL/h.

Incorporation of Pall AEF1E or ELD96LLCE filters during simulated infusion of Amiodarone did not significantly alter the infusion or flush kinetics when compared to the negative control (no filter). No obvious binding or retention of the drug to the filters was detected.

Introduction

Use of in-line filtration for intravenous (IV) infusions protects patients against inadvertent particulates, air, and microbial contamination that may be present in the fluids administered during infusion therapy.

In order to deliver the clinically required dose to the patient it is important to ensure that in-line filters do not cause a significant change in the concentration of the infused drug due to binding. Additionally, it is also important that they do not impair the ability to flush residual amounts of drug that may be present in the infusion system when more than one drug is administered in sequence, particularly if they are incompatible.

The aim of this study was to evaluate the filterability of Amiodarone under simulated infusion conditions.

Materials and Methods

Materials

- Amiodarone 150 mg i.v. Carino (Carinopharm)
- 5 % glucose (B.Braun)
- B. Braun Perfusor◆ Space pump (B.Braun)
- B. Braun Perfusor Compact pump (B.Braun)
- Pall Supor™ AEF1E filters, lot 14-666, (Pall)
- Pall Nanodyne™ ELD96LLCE filters, lot 15-658
- Disposables (IV-lines, 3-way-valves, adapters, non-return valve) (B.Braun)
- Photometer Ultrospec III, s/n 52199 (Pharmacia)
- Flow cell (fused silica, 0.25 cm pathlength) (Pharmacia)

Methods

The filterability of Amiodarone through Pall AEF1E filters and Pall ELD96LLCE filters was analyzed. Measurements of drug concentrations were made using an Ultrospec III Photometer equipped with a flow cell (fused silica glass with 0.25 cm path).

Preliminary tests were carried out to determine the settings required to obtain signals within the detection range based on a linear correlation (R2 = 0.9969). The used analytical method, based on UV absorption at a wavelength of 240 nm, was validated showing no interference by other ingredients beside the active pharmaceutical ingredient Amiodarone.

Flow rates were regulated by two perfusor pumps; a diagrammatic representation of the test apparatus is shown in Figure 1.

5% glucose was used as a carrier (Perfusor Compact pump, 99 mL/h) to dilute the drugs to ensure that the drug concentration was within the detection range, and also as a solvent for the drug for all tests. Prior to any drug being added, the system was completely flushed with 5 % glucose. The Amiodarone in 5% glucose was then run through the system (0.6 mg/mL, 20 mL/h) until a stable UV absorption level was reached (infusion phase). Once a stable UV measurement had been obtained the pumps were both stopped and the drug solution in the Perfusor Space pump was replaced with 5% glucose. The pumps were then restarted using the same flow rates as before and the drug flushed from the system (flush phase). Analytics by spectrophotometry were carried out using a wavelength of 240 nm at a sample rate of 1/(5 s).

The three way valves shown in Figure 1 were used to switch between filtration through the test filter and no filtration through the bypass circuit. This allowed comparison of the level of UV-VIS-light-absorption when the test solution passed through the test filter to the level when the solution flowed through a similar infusion line without filter.

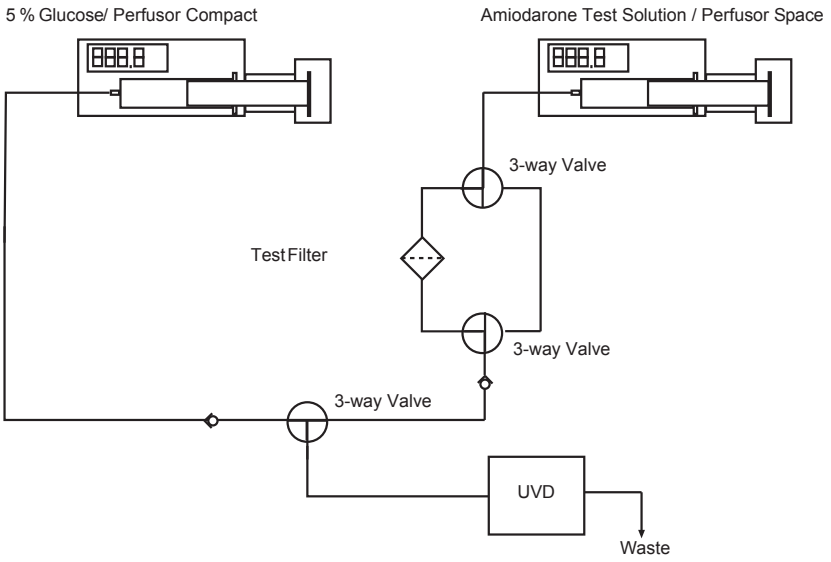
Tests were performed three times for each filter and for the bypass.

Percentage UV absorption for the drug at the maximum plateau was calculated as follows (AU= Absorption Unit):

$$\text{Absorption rate [\%]} = \frac{AU_{unfiltered} - AU_{filtered}}{AU_{unfiltered}}$$

Figure 1

Diagrammatic representation of the test apparatus

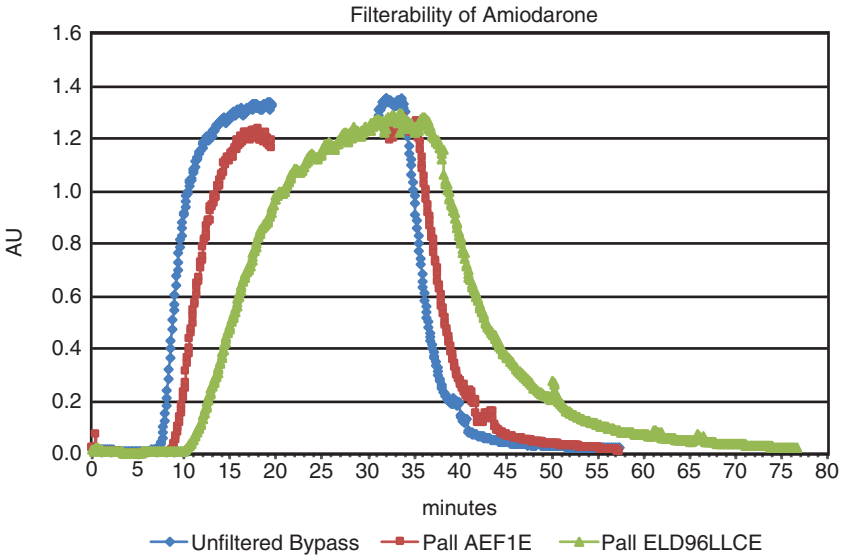


Results

Figure 2 shows the infusion (left) and flush (right) phases of the experiments for the bypass (no filter) and the AEF1E and ELD96LLCE filter respectively (average of 3 runs).

Figure 2

Application of Amiodarone solution (0.6 mg/mL) at 20 mL/h (Average of 3 runs)



Discussion

The kinetics of the inflow phases (left side of the graphs) and flush phase (right side of the graphs) in the presence of the AEF1E filters were similar to those achieved in the unfiltered (bypass) controls. For the ELD filters the time for inflowing and as well for flushing were approx. 20 minutes longer, mainly driven by the slow flow rate in combination to the higher hold-up volume of the ELD filter.

UV absorptions of the tested drug using the AEF1E filter or the ELD96LLCE filter compared to the unfiltered bypass showed both a constant maximum plateau at heights within the analytical specification of the method.

Conclusion

The presence of AEF1E and ELD96LLCE filters during simulated infusion of Amiodarone did not significantly alter the inflow kinetics or flush kinetics of the drug when compared to the unfiltered (bypass) control. There was no obvious irreversible binding or retention of the drug to any of the filters.

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