Stability study of 20 mg/mL paediatric amiodaron oral suspension in syrspend

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BACKGROUND/PURPOSE

Amiodaron is a class 3 antiarrhythmic drug with a narrow therapeutic range. The lack of pediatrics marketed available formulation leads the pharmacist to product preparation.

Laboratory data show that the oral suspension of amiodaron at 5 mg/mL in syrspend® is stable, but this concentration is too low for important posologies, that's why a 20 mg/mL suspension could be useful.

The aim of this study is to determine the physico-chemical stability of amiodaron oral suspension in order to set a shelf life for the preparation in a maximum of 60 days.

MATERIALS/METHODS

Three batchs of oral suspension are prepared, using amiodaron hydrochloride powder and Syrspend® SF-PH4, packaged in amber vials, to protect from light and stored at room temperature.

Study design :

Physical stability (visual inspection, osmolality measurement), chemical stability (pH measurement, concentrations analysed by a Liquid Chromatography - High Resolution - Mass Spectrometer (LC-HR-MS)) studied at different days : 0, 3, 5, 8, 10, 15, 30, 60 **(n=3)**

Liquid Chromatography - High Resolution - Mass Spectrometer (LC-HR-MS) :

The chromatographic separation of the analytes was performed with an Accela pump equipped with a Thermo Fisher C18 Accucore column (100 x 2.1 mm , 2.6 µM) using a gradient of 10 mM ammonium acetate buffer containing 0.1% (v/v) formic acid and of acetonitrile with 0.1% (v/v) formic acid. Data were acquired in positive Full Scan mode and quantification was performed by extracting the exact mass value of protonated amiodaron (681.8 m/z) using a 5 ppm mass window. Amiodaron concentration at day 0 was considered as 100%.

Data analysis was performed on the software Xcalibur® 2.1.

Microbiological stability were observed by the test uses colony counts on media platings at 36°C.

RESULTS

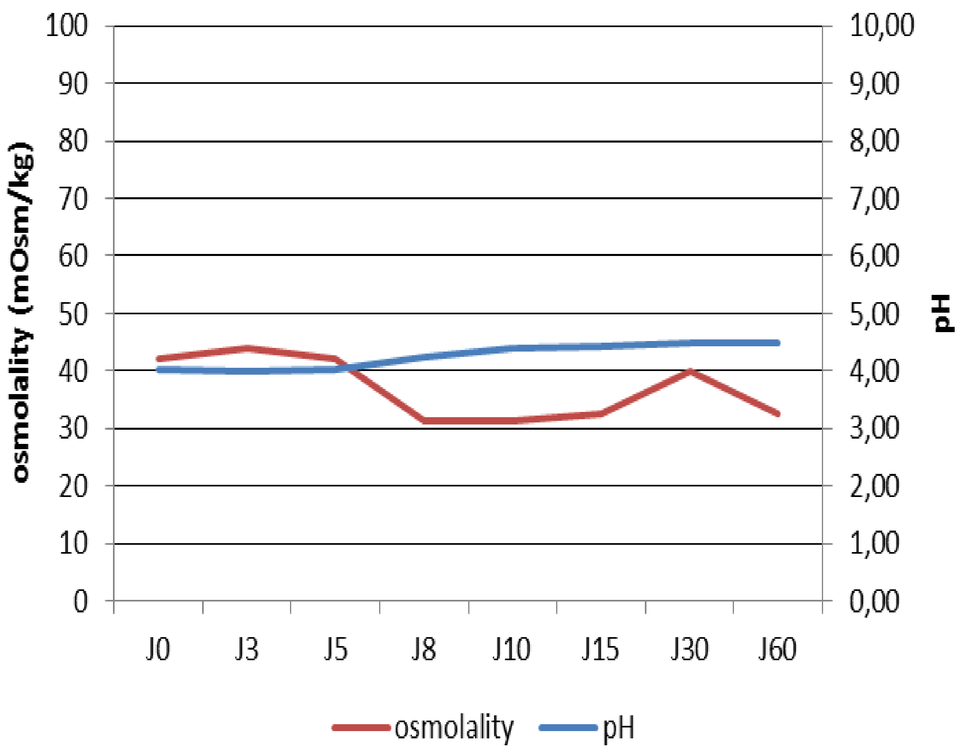

Figure 1. Osmolality and pH value during the study time

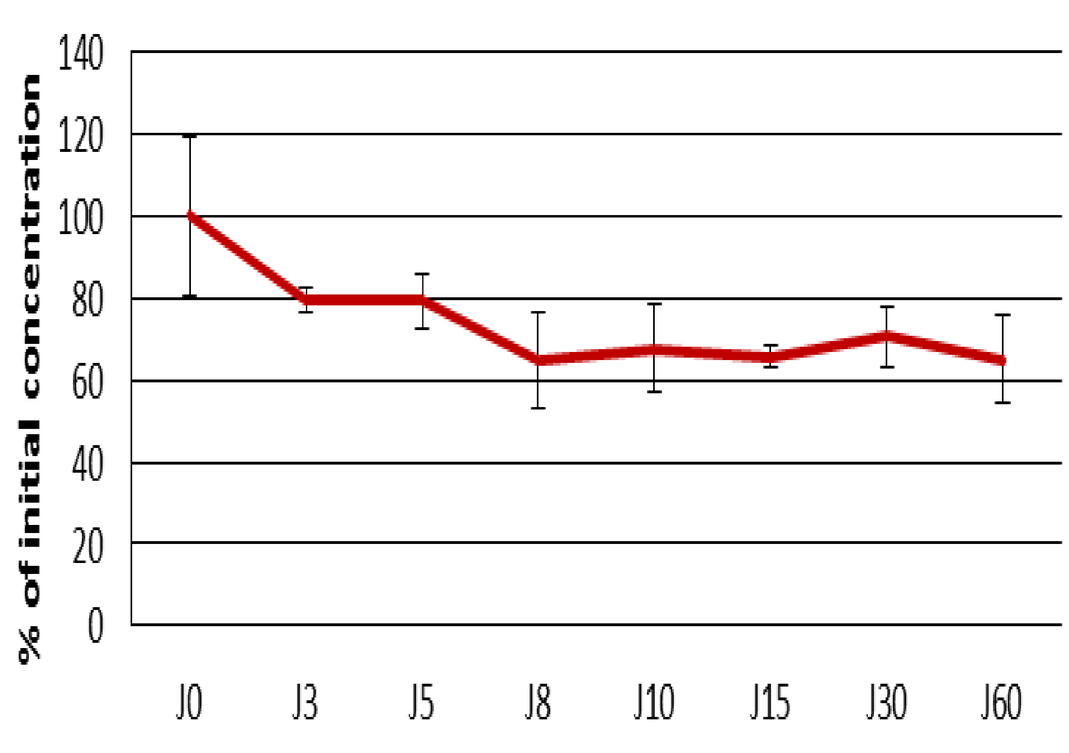

Figure 2. Dosage results of amiodaron oral suspension (20 mg/mL)

No culture were observed and a viscosity increased after 10 days is noted.

After 60 days, no significant variation of pH (slight increase of 10% < 1 pH unity) and osmolality (30% difference between the highest and lowest value). *(Figure 1)*

An important concentration decrease (20%) was observed between J0 and J3. After J3 there is no more than 10% difference between the highest and lowest concentration. *(Figure 2)*

CONCLUSION

This study showed that the microbiological and physical stability were acceptable.

Regarding chemical stability, preliminary study showed that 20 mg/mL amiodaron oral suspension was stable for at least 10 days.

However, during the main study, these results weren't confirmed. The causes of bias were assessed : freezing sample, experiment, very important dilution could explained these disputed results.

Another study, using HPLC system with DAD detector is underway. The preliminary results are rewarding and showed a shelf life of 8 days. Further studies will be conducted such as forced degradation study.

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