

## Isolation and Characterization of Degradation Products of Amiodarone HCl Associated with Microcrystalline Cellulose

Craig Carrell, PharmD Candidate; Marcelo Nieto, PhD; Timothy McPherson, PhD

### Abstract

**Background:** Amiodarone HCl is a commonly used antiarrhythmic medication dating back to the 1960's. Used both in adults and pediatric populations, it is a safe treatment of supraventricular (SVA) and ventricular arrhythmias (VA). However, dosage forms available for amiodarone are not readily available for pediatric populations and often must be compounded. Challenges arise with stability of liquid formulations. A previous study (Brun, D. et al. 2021) tested stability of amiodarone with common excipients (microcrystalline cellulose, mannitol, and lactose). They demonstrated an unidentified degradation product in mixtures containing microcrystalline cellulose.

**Objective:** The goal was to isolate and characterize the degradation product that was formed in mixtures of amiodarone with microcrystalline cellulose.

**Methods:** A forced degradation study of amiodarone HCl was performed with microcrystalline cellulose, mannitol, and lactose. These powder mixtures were incubated in an oven for several months to determine if degradation would occur. High performance liquid chromatography with mass spectroscopy (LCMS) was used to identify the presence of degradation product. These results were compared to controls ( $t_0$ ) consisting of samples analyzed immediately after preparation in the same manner as the forced degradation samples. Proton ( $^1\text{H}$ ) and carbon ( $^{13}\text{C}$ ) nuclear magnetic resonance (NMR) spectroscopy was used to analyze the chemical structure of degradation products.

**Results:** No degradation products were detected in  $t_0$  samples. Degradation products were found in the highest amounts in mixtures of amiodarone and microcrystalline cellulose. LCMS identified two degradation products, which were labeled Product 1 with molecular weight of 546 and Product 2 with molecular weight of 618. NMR analysis was consistent with molecular formula of  $\text{C}_{19}\text{H}_{16}\text{I}_2\text{O}_3$  for Product 1. Further characterization of Product 2 is underway.

**Conclusion:** Amiodarone HCl coupled with microcrystalline cellulose showed a predominant degradation product of an O-dealkylation to the ether group of the parent compound amiodarone. Further evaluation of amiodarone compounded formulations should be explored.