Isolation and Characterization of Degradation Products of Amiodarone HCl Associated with Microcrystalline Cellulose
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BACKGROUND
- Amiodarone HCl is a common anti-arrhythmic drug dating to the 1960’s.\(^1\)
- Dosage forms for amiodarone are not readily available for pediatrics.\(^2\)
- Challenges come from stability of drugs when compounding, directly related to excipients.
- Previous study evaluated 3 common excipients: mannitol, lactose, and microcrystalline cellulose.\(^2\)
- They identified an unknown degradation of amiodarone when paired with cellulose.

OBJECTIVE
- Isolate and characterize the unknown degradation product from the reaction of amiodarone and cellulose

METHODS
- A forced degradation study (labeled t=120) was prepared using amiodarone HCl with each of the following excipients: microcrystalline cellulose, mannitol USP powder, and lactose monohydrate.
- These powder mixtures were allowed to incubate in an oven for several months to determine if degradation would occur.
- High performance liquid chromatography with mass spectroscopy (LCMS) was used to identify presence of degradation product and to aid characterization.
- Control samples (t\(\_0\)) were compared to forced degradation samples.
- To analyze the chemical structure, nuclear magnetic resonance (NMR) proton (\(^1\)H) and carbon (\(^{13}\)C) was used
- A pH study was also evaluated of the excipients and amiodarone.

RESULTS
- Two degradation products were found with amiodarone and microcrystalline cellulose with LCMS.
- Molecular weights were used to identify the two products
- Named Product 1 and Product 2.
- NMR analysis showed consistency with molecular formulas (see Figure 1)
- Product 1 is the predominant degradation product and is an O-dealkylation of the ether group.
- Product 2 is N-dealkylation of one of the ethyl groups (Product 2) was not isolated in pure form and currently working to purify to finalize characterization.
- Product peaks can be seen in Figure 2.

CONCLUSION
- Amiodarone HCl coupled with microcrystalline cellulose showed a predominant degradation of Product 1, an O-dealkylation of the ether group.
- Further evaluation of amiodarone compounded formulations should be explored.
- Product 2 needs further work up to fully characterized.

REFERENCES