R14. Amikacin extended release nanoliposomes using the ethanol injection method: development and characterization

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Amikacin extended release nanoliposomes using the ethanol injection method: Development and characterization

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RATIONALE, HYPOTHESIS AND AIM
Mycobacterium avium complex (MAC) lung disease is a serious condition, that in some cases can cause severe, even permanent damage to the lungs1. Amikacin is a polycationic, semisynthetic, bactericidal aminoglycoside. The entry of the moiety is mediated by binding of the antibacterial moiety to the negatively charged components of the bacterial cell wall. The primary mechanism of action involves the disruption and inhibition of protein synthesis in the target bacteria by binding to the 30S ribosomal subunit. Arikayce® approved by FDA in 2018 and generic of Arikayce® is not available at the moment. Due to the complex NLs dosage form, the development of generics takes a longer time compared to the conventional dosage form. The aim is to develop and characterize the Amikacin (Amk) loaded extended release nanoliposomes (NLs) by ethanol injection method.

Central Hypothesis: Inhaled Amk-NLs will produce a robust and consistent quality inhaled Amk-NLs for the treatment of MAC lung disease.

FORMULATION DEVELOPMENT

- Prepare 20mL 0.99%w/v solution of Sodium Chloride and add 50 mg Amikacin to it to form 1.10mg/ml drug concentration of final formulation. Let it dissolve completely at 50°C.
- Prepare 1.3mL 90%V/V ethanolic solution. Add 17.29mg DPPC and 8.65mg Cholesterol.
- Stir well for the lipids to completely dissolve in the ethanolic solution giving clear solution at 50°C.
- Using a syringe pump, the ethanolic lipid solution was injected into 0.9%w/v Tween 80 to prevent browning of particles during nebulization and were thereafter weighed. A filter paper was placed on the last collector stage.
- Stir the solution continuously at 600 rpm for 30 min after the injection is complete.
- A compressor nebulizer, Sami the Seal (Philips Respironics, NJ) was operated at a flow rate of 18.3±0.1 L/min as recommended by United States Pharmacopeia (USP) and the formulation was nebulized for 20 minutes.
- After nebulization, the impactor was disassembled and all the plates were again weighed. The mass median aerodynamic diameter (MMAD), geometric standard deviation (GSD) of the formulation were calculated according to the formula given in USP chapter <601>.

RESULTS

<table>
<thead>
<tr>
<th>ACI components</th>
<th>Cumulative % deposition</th>
<th>Effective cut off diameter (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plate 1</td>
<td>Plate 2</td>
<td>Plate 3</td>
</tr>
<tr>
<td>Plate 4</td>
<td>Plate 5</td>
<td>Plate 6</td>
</tr>
<tr>
<td>Plate 7</td>
<td>Paper</td>
<td>Mouthpiece</td>
</tr>
</tbody>
</table>

Graph 4: % Deposition in ACI components

The MMAD and GSD for the Amikacin were found to be 4.13±0.134 µm and 1.82±0.064 respectively.

CONCLUSION(S)
The Amikacin loaded nanoliposomes were successfully formulated with characteristics similar to Arikayce® with particle size range of less than 300nm.

FUTURE WORK
The future optimization of Ethanol injection method (formulation and process parameters), in vitro, and preclinical in vivo testing are needed to test the developed Amk-NLs.

REFERENCE
2) Patrick T. O'Shaughnessy, B-Stage Non-Viable Impactor Data Reduction Spreadsheet and Supporting Information, BGI, Waltham, MA, September 2006.