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Synergistic Effect of Co-Spray Dried Colistin & Azithromycin for Treatment of Lower Respiratory Infections

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Background
An ongoing focus of pharmaceutical research is enhancing the efficacy of inhaled drugs intended to treat lower respiratory infections. To achieve this, an inhaled drug must exhibit a high aerosolisation performance, or the ability of fine particles to disperse and reach the target site in the lower respiratory passageways. Proper deposition of the aerosol particles at the site of action is dependent upon chemical properties and the aerodynamic diameter. Preliminary data demonstrated that the aerosolisation performance of colistin, a hydroscopic antibiotic, notably decreased when stored at a relative humidity (RH) of 75% due to moisture absorption. To prevent moisture absorption, my aim is to combine two antibiotics, colistin and azithromycin, into one formulation to improve the combination drug’s delivery to the target site of action and produce a synergistic effect. The use of azithromycin, an antibiotic that exhibits hydrophobic properties, would minimize water absorption and increase the drug’s efficacy. A better understanding of colistin and azithromycin’s aerosolisation properties is important in strengthening therapeutic methods to treat individuals with specific pulmonary disorders.

Methods
1) Spray Drying (Colistin:Azithromycin, 1:1)
Spray drying is a dehydration process in which a liquid is converted to a powder form. Compressed air atomizes the solution into fine droplets, followed by a rapid drying process by hot gas, resulting in a fine powder.\[1\]

2) Next Generation Impactor (NGI)
The NGI measures in-vitro aerosol performance and is used to classify aerosol particles into size fractions for testing dry powder inhalers. Essentially, this device mimics the human respiratory system and consists of 8 stages, with the early stages representing the upper airways (stage 1: human throat) and the latter stages mimicking the lower airways (stage 8: alveoli of lungs). Air passes through the impactor, and particle sizing is achieved by forcing the air stream through a series of nozzles containing progressively reducing jet diameters. The fine particles from each stage are collected in a series of collection cups.\[2\]

3) High-performance liquid chromatography (HPLC)
HPLC is performed to separate, identify, and quantify the mixture of azithromycin and colistin. A pump forces the mixture through a column under high pressure. Azithromycin and colistin are separated from one another due to different interactions with the stationary phase or column material. Each component possesses a distinct retention time, or the time it takes for a solute to pass through the column. The computer output displays a series of peaks, each one representing a component in the mixture passing through the detector and absorbing UV light.\[3\]

Results
The graphs suggest azithromycin in combination with colistin successfully prevented moisture absorption due to no significant changes in FPF values as RH increased. In other words, the combination of azithromycin and colistin improved drug stability at higher humidity levels and overall aerosolisation performance. Furthermore, the data suggest that rather than coating colistin, azithromycin acts to minimize the interfacial tension between colistin and water particles, ultimately preventing aggregation.

Discussion
The graphs suggest azithromycin in combination with colistin successfully prevented moisture absorption due to no significant changes in FPF values as RH increased. In other words, the combination of azithromycin and colistin improved drug stability at higher humidity levels and overall aerosolisation performance. Furthermore, the data suggest that rather than coating colistin, azithromycin acts to minimize the interfacial tension between colistin and water particles, ultimately preventing aggregation.

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References