An aerosolized antimicrobial combination for the treatment of pulmonary Pseudomonas aeruginosa infections

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Abstract

During the last decades, multiple approaches have been developed to combat bacterial resistance. One of them involves combination therapies of existing antibiotics with potentiating adjuvants, empowering the activity of the antibiotic against resistant strains.

In the respiratory system, Pseudomonas aeruginosa is known as a frequent and virulent pulmonary pathogen and one of the leading causes of morbidity and mortality in cystic fibrosis (CF) patients.

In this context, the antibiotics pulmonary administration has become a precious tool in the management of respiratory infection.

The aim of our study is to develop a new potent pharmaceutical form intended for pulmonary administration, based on a combination of an antibiotic (Doxycycline) with an adjuvant: a polyaminoisoprenyl derivative NV716 allowing restoration of doxycycline efficacy against P. Aeruginosa strains naturally resistant to doxycycline. The proof of concept of such a combination has been previously verified in vitro on various P. aeruginosa strains. (PlosOne, 2016)

Here we report the characterization of three different aerosols: doxycycline alone, NV716 alone and doxycycline/NV716 combination, using the Next Generation Impactor. Aerosols evaluation was carried out according to different concentration, duration of nebulization and nebulizers: The droplet size distributions and aerosol efficiency were expressed in terms of Mass Median Aerodynamic Diameter (MMAD) and Fine Particle Fraction (FPF).

Results showed MMADs (3,4-4,4 μm) in accordance with the standards recommended for therapeutic aerosols (< 5 μm) suitable for deep lung deposition, with a high FPF (> 50 %) required to maintain drug level above its Minimum Inhibitory Concentrations (MIC) at the infection site

Biography:

Hana Douafer was born in Guelma, Algeria. In 2017, she obtained her diploma from the Faculty of Medicine, Annaba (Algeria) and went to Marseille (France), where she is currently working on her doctoral thesis at the Faculty of Pharmacy (UMR-MD1, U1261 INSERM) under the supervision of Dr V. Andrieu and Dr J. M. Brunel