



TITOLO  
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ANTIMICROBIAL SPRAY-DRIED MICROPARTICLES BASED ON CHITOSAN/HYDROLYSED COLLAGEN FOR RESPIRATORY TRACT INFECTIONS

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Riassunto

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The pulmonary administration route is one of the most popular for drug delivery because it has a high surface area that promotes faster and more efficient drug absorption. It has been widely used to treat local lung diseases like respiratory infections, asthma, and chronic obstructive pulmonary diseases<sup>1,2</sup>. The aim of the current study was to develop microparticles (Mps) using the spray-drying process. With the purpose of treating bacterial infections of the respiratory tract, insoluble Mps were prepared exploiting the interaction between hydrolyzed collagen (HC; Kelisema, I) and chitosan (Cs; medium MW, Sigma Aldrich, I).

Regarding the preparation process, aqueous solutions containing several concentrations of HC (1%, 2%, 4% w/w) were prepared and combined with 2% w/w Cs solution in 0.5M acid acetic at a weight ratio of 1:1. Mixtures of Cs/HC0.5, Cs/HC1, and Cs/HC2 were spray-dried at various inlet temperature settings, ranging from 120 to 200°C (100% aspirator, 0.6 L/h flux).

Mps were characterized using the following techniques: i) scanning electron microscopy (SEM) to determine their size and morphology; ii) Fourier-Transform Infrared Spectroscopy (FT-IR) and Thermal Gravimetric Analysis/Differential Scanning Calorimetry (TGA/DSC) to investigate the formation of interaction products (IP) between HC and Cs; iii) Next Generation Impactor (NGI) to assess their aerodynamic performance and particle size distribution. *In vitro* cytotoxicity test using adenocarcinomic human alveolar basal epithelial cells (A549) was also performed. Moreover, the antibacterial properties and the capability to prevent bacteria from adhering to A549 (*S. aureus* BH1CC strain and *P. aeruginosa* PAO1 strain) were investigated.

Mps had a perfectly spherical shape and a size ranging from 1 to 10 µm, depending on the polymer concentration and the inlet temperature set. For example, in the case of Mps Cs/HC0.5 obtained at 120°C, 95% of Mps had a mean diameter lower than 5 µm, making them suitable for pulmonary drug delivery. The formation of IP between Cs and HC, which is responsible for the formation of insoluble and biodegradable Mps, was confirmed by FT-IR and TGA/DSC analysis. *In vitro* cytotoxicity test towards A549 cells proved Mps biocompatibility. Regarding antimicrobial assays against Gram + and Gram - bacteria, Mps were characterized by higher antibacterial properties with respect to those of the raw ingredients and their physical mixture. Lastly, Mps demonstrated the ability to prevent bacteria adhesion to A549 cells.

In conclusion, spray drying process has proven to be an effective method for producing water insoluble Mps based on CS and HC IP. They were characterized by a size functional to pulmonary administration. The IP demonstrated enhanced antibacterial properties and the capacity to prevent bacterial adhesion to cells.

#### References:

[1] B. Mishra, J. Singh, Academic Press, 2020, 57-95

[2] H. Jain, A. Bairagi, S. Srivastava, S.B. Singh, N.K. Mehra, Drug Discovery Today, 202, 25 (10), 1865-1872.

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