

Drug solubility and aerodynamic properties of dry powders prepared by spray drying: clarithromycin versus its chlorohydrate salt.

Michele Dario Manniello, Alessandra Simonetti, Pasquale Del Gaudio, Rita P. Aquino, Paola Russo.

Department of Pharmacy, University of Salerno, Fisciano (SA).

Purpose

The antibiotic therapy for a direct administration to the lung in cystic fibrosis patients has to provide suitable availability, possibly in the lower respiratory tract, characterized by the presence of thick secretions. Because of this problem, one of the crucial step in the therapeutical management of the respiratory disease could be the drug solubilization directly in this site of action. The aim of the study was to obtain respirable powders of clarithromycin, while improving drug aqueous solubility.

Methods

Several batches of micronized particles were prepared by spray drying different feed solutions, varying the solvent composition (water/isopropyl alcohol ratio), the drug concentration and pH of the liquid feeds. Particle size distribution of raw materials and engineered particles was determined using a light-scattering laser granulometer while particle morphology was assessed by scanning electron microscopy. The in vitro deposition of the micronized clarithromycin powders was evaluate by means of a Single-Stage Glass Impinger (SSGI; apparatus A, European Pharmacopoeia 8.0), using a Turbospin® as device for the aerosolization. True density measurements were performed by a helium pycnometer (Accupyc II 1340). Solubility measurements of raw and spray-dried drug were carried out at 37°C in phosphate buffer (0.05 M, pH 6.8).

Results

Morphology and aerodynamic properties of spray-dried particles were strongly influenced by organic solvent concentration and pH of the liquid feeds processed, both modifying drug solubility. Spherical particles and crystals were obtained at higher pH and lower organic solvent content, while wrinkled particles were obtained at lower pH values. Moreover, thanks to their shape, spray-dried powders from hydro-alcoholic solutions containing clarithromycin in its salt form, showed better aerodynamic properties.

Conclusions

The clarithromycin inhalable powders containing the drug in its salt form, showed high water solubility and good aerodynamic properties, thanks to a fine-tuning of the process parameters and liquid feed composition, with no need to add any excipients.