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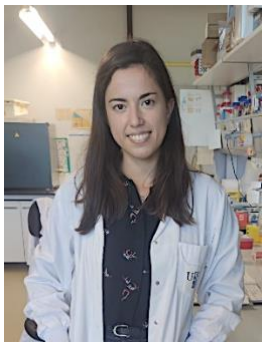

Development of rifabutin-loaded protamine nanocarriers for pulmonary drug delivery with improved aerodynamic properties

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Tuberculosis is an infectious respiratory disease that constitutes a significant public health challenge. The extended administration of high doses of drugs in its oral antibiotic therapy has difficult patient compliance and has promoted resistance to these treatments [1]. Therapeutic strategies based on microparticle administration in the form of dry powder inhalers (DPIs) constitute a promising alternative for pulmonary delivery and patient adherence. The controlled agglomeration of nanoparticles into micron-sized particles allows their transport to the alveoli, where redispersion and release of the nanoparticles take place. [2]. In this work, rifabutin-loaded protamine nanocapsules (NCs) were prepared by solvent displacement method and were physicochemical, *in vitro,* and aerodynamic characterized after their spray-drying procedure. Protamine NCs presented a size of around 200 nm, positive surface charge, and drug association of up to 54%. They were stable as a suspension under storage, as well as in biological media and as a dry powder after lyophilization in the presence of mannitol. The developed NCs presented a strong capacity to internalize and activate alveolar macrophages and showed good compatibility with red blood cells. Moreover, rifabutin-loaded protamine nanoparticles could be successfully incorporated in microparticles by co-spray drying with mannitol for the obtention of a dry powder with adequate aerodynamic properties. The developed ready-to-use pulmonary dry powder system holds great promise of interest for inhalable therapy of pulmonary tuberculosis.

References:

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