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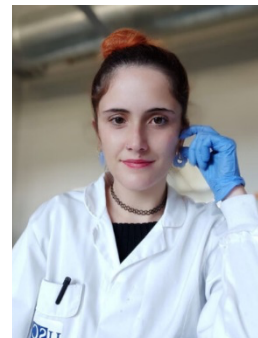
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A multi-stage pulmonary drug delivery system based on pollen grains

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In this work, we aim to develop a micro/nano system to improve antibiotic delivery to the lung. For this, we explored different chitosan-based nanocapsule compositions for their further microencapsulation in pollen grains. These nanocapsules were characterized in terms of size, PDI, surface charge, morphology, encapsulation efficiency and biological stability. In addition, in vitro studies in different static and dynamic cell culture models (A549 lung epithelial cells and Raw 264.7 macrophages) demonstrated the safety of the nanocapsules, as well as their efficient internalization. The presence of pollen grains further enhanced cellular interaction and retention of the nanosystems.

An antimicrobial susceptibility test was performed to evaluate the effectiveness of the developed system against two species of Mycobacterium, *M. phlei* (fast-growing strain) and *M. smegmatis*, a (slow-growing strain), using rifabutin as a model drug. This study indicated complete inhibition of antibiotic concentrations within the expected susceptibility range (≤ 0.25 –16 mg/L) for rifabutin. Further studies confirmed high biofilm dispersal activity for the nanocapsules in suspension and for those that were associated with pollen grains. These inhibition values were greater than those achieved with the model drug, rifabutin. Overall, this micro/nano system could be an interesting candidate as a pulmonary mucosal delivery system for the local treatment of infectious diseases.

References:

1. Valverde-Fraga, L. et al. Design and in vitro assessment of chitosan nanocapsules for the pulmonary delivery of rifabutin.
2. Ageitos, J.M. et al. *Polymers* 2021, 13, 2094.