Design and characterization of emulsified spray dried alginate microparticles as a carrier for the dually acting drug roflumilast.

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Abstract

Roflumilast is a selective inhibitor of phosphodiesterase-4 isoenzyme in lung cells. Having psychiatric adverse reactions when administered orally affects negatively the patients' adherence to the drug. This work aimed to prepare emulsified spray dried alginate microparticles for the pulmonary delivery of roflumilast. Sodium alginate was used as microparticle-forming material, isopropyl myristate as an oil, TweenÈ80 as surfactant and calcium beta-glycerophosphate as cross-linking agent to enhance the mechanical properties of the particles. The prepared particles were evaluated for their encapsulation efficiency, particle size and in-vitro drug release. From the studied carriers, beta-cyclodextrin (CD) was the best regarding giving formulation with smaller particle size and more sustained drug release. The inhalation profile of CD-based microparticles was investigated using Anderson cascade impactor. The aerosolization profile of CD-based microparticles suggested their efficiency to deliver the drug deep in the lung. The CD-based microparticles possessed more inhibitory effects on the viability of A549 cells and on the pro-inflammatory cytokines (TNF-Ů, IL-6 and IL-10) compared to the pure drug. Hence, CD-based microparticles could regulate the tumorigenesis besides tumor-associated inflammation. Finally, CD-based microparticles showed more sustained bronchodilatation properties in healthy human volunteers when compared to VentolinÈHFA. CD-based microparticles proved to be a promising carrier for inhaled roflumilast in human.

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