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Development of a combined nanosystem as a dry powder inhaler for the treatment of pulmonary inflammations

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Many pulmonary diseases are listed as major death-causing diseases in the world, therefore, developing new treatments is a mounting need. Local delivery of drugs by inhalation has shown higher effectiveness with less systemic side effects. Mannitol is an osmotic agent used as a mucolytic to improve the clearance of mucus, and it is available in the market as a dry powder inhaler. Since respiratory inflammations are mostly engaged with mucus accumulation, we aimed to develop a combined nanosystem for inhalation by combining mannitol with a well-known non-steroidal anti-inflammatory drug (NSAID) that can be administered to fight pulmonary inflammation. This nanosystem can be used to target mucusobstructive pulmonary diseases such as cystic fibrosis, bronchitis, and bronchiectasis. The formulation process was in two stages: (i) a top-down method (wet-media milling) was used to produce nanosuspension containing NSAID, (ii) followed by co-spray drying with mannitol. During the formulation, different mannitol ratios were studied. The powder characterizations were investigated in terms of particle size, zeta potential, distribution index and morphology. Moreover, powder yield and drug content were calculated. Physical, structural, and thermal analyses were carried out. Also, in vitro release test and in vitro lung deposition characterization were assessed. The resulting powder was roughly spherical in shape and nano in size which enabled a high lung deposition and showed an enhanced release profile. Hence, we successfully developed two active agents loaded in a single nanosystem as a promising combination therapy that has the potential to increase mucus clearance while simultaneously treating inflammation and improving patient adherence.

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