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DissolvIt: An In Vitro Method for Simulating the Dissolution and Absorption of Inhaled Dry Powder Drugs in the Lungs.

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Abstract

The main purpose of this work was to develop an in vitro method for simulating the dissolution and absorption of inhaled dry powder drugs that also mimics systemic pharmacokinetic data. A second purpose was to evaluate this method. DissolvIt® was developed as a simulation of the air-blood barrier of the upper airways, constituting: "airborne" particles deposited on a glass cover slip, a mucus simulant, a polycarbonate (basal) membrane, and a pumped albumin buffer simulating the pulmonary blood flow. The PreciseInhale® exposure system was used to aerosolize and deposit test formulations onto cover slips. The particle dissolution was observed by optical microscopy as particle disappearance, and it was started directly when the particles came into contact with the mucus simulant. Solute from the dissolving particles diffused through the barrier and was absorbed into the perfusate. The drug concentration in the perfusate over time and the remaining drug in the barrier at the end of the experiment were quantitated by using liquid chromatography-tandem mass spectrometry. Budesonide and fluticasone propionate generated different pharmacokinetic dissolution/absorption profiles in DissolvIt. This study indicates that DissolvIt simulates dissolution and absorption of drugs in the lung, and that DissolvIt also mimics pharmacokinetic profiles and parameters.

KEYWORDS:

aerosol generation; dissolution testing; dry powder; in vitro dissolution method; inhalation; lung dissolution