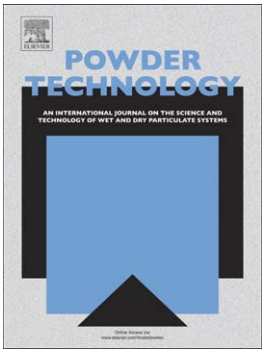

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Mechanistic Approach in Powder Blending PAT: Bi-Layer Mixing and Asymptotic End Point Prediction

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Abstract

We derive a simple first order kinetics model for the powder mixing in a bin blender and adapt it to fit the NIR spectra obtained during the real-time mixing. The model is tested on a full drug product formulation mixing consisting of API and multiple excipients. It allows to extract a quantitative mixing rate for individual ingredients, which may be used in the drug development and production scale-up design. We further propose an algorithm for a calibration-free blending end-point determination from the NIR data, which allows for a robust and easily transferable blending process control.

Keywords: Powder Mixing, Convection, Blend Uniformity, NIR, Process Analytical Technology, Quality by Design

1. Introduction

Blending is one of the most widely performed material processing operation across a wide range of industries, including pharmaceutical, chemical,

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