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Characterization of the hydrodynamics in a miniaturized dissolution apparatus

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Abstract

The hydrodynamics of a miniaturized dissolution apparatus was characterized using computational fluid dynamics (CFD) simulations and analyzed in relation to the biorelevance and robustness of measurements of drug dissolution and precipitation kinetics from supersaturated drug solutions. The effect of using three different agitator geometries operated at 50, 100, 150 and 200 RPM as well as different positioning of an UV probe in the vessel was systematically evaluated. The CFD simulations were validated using a particle streak velocimetry experiment. The results show that the choice of agitator geometry influences the hydrodynamics of the system and indicates that an off-center probe position may result in more robust measurements. Furthermore, the study shows that the agitator geometry has a significant effect on supersaturation studies due to differences in the hydrodynamic shear produced by the agitator.

Keywords

In silico modeling; Dissolution; Mathematical model; Precipitation; In vivo models

Abbreviations used

CFD, computational fluid dynamics; RPM, rounds per minute; PSV, particle streak velocimetry; IDR, intrinsic dissolution rate;

Introduction

Dissolution studies are an essential part of development of new oral drug products[1]. In order to achieve results that can predict *in vivo* performance, it is important to conduct experiments that simulate the *in vivo* conditions, such as controlling pH, bile salt and phospholipid concentrations. In recent years, there has been an increasing interest in using *in silico* modeling as a tool for predicting the pharmacokinetic profile of a compound based on *in vitro* experiments[2]. In order to do this, the *in vitro* models need to be well-characterized and one important aspect of *in silico* modeling of dissolution is the hydrodynamics of the *in vitro* model. The hydrodynamics of a dissolution experiment have previously been shown to have an effect on both dissolution[3,4] and precipitation kinetics[5], but because the agitation of the dissolution medium is typically kept constant within experiments this factor is often disregarded. However, hydrodynamic