76f Quantitative Determination of the Role of Geometric and Operating Variables on the Hydrodynamics of the Usp Dissolution Apparatus II

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In the pharmaceutical industry, dissolution testing is routinely conducted to determine the rate of dissolution of solid dosage forms. In-vitro dissolution testing is used to assist with formulation design, process development, and the demonstration of batch-to-batch reproducibility in production. The device typically used to conduct dissolution testing is the USP Apparatus II. Despite its widespread use, limited information is available on the hydrodynamics of this dissolution apparatus, and the effects of operating and geometric variables on the velocity distribution in the apparatus.

In this work, the velocity distribution inside a USP Apparatus II was experimentally determined via Laser-Doppler Velocimetry (LDV) and numerically predicted using Computational Fluid Dynamics (CFD). Results were obtained for a variety of conditions, i.e., under the USP-prescribed standard conditions (fill level: 900 mL; agitation speed: 50 rpm; impeller off-bottom clearance: 25 mm), as well as under other less commonly used operating conditions such as reduced fill level (500 mL), increased agitation speeds (75 and 100 rpm), non-standard, within-specification impeller locations, presence and absence of dissolving tablet.

The flow was found to strongly dominated by the tangential component of the velocity. The velocities in the zone below the impeller were generally small in magnitude and varied considerably in direction with location, even at small distances. This phenomenon was especially relevant in the zone just under the impeller center and along the vessel bottom. The dimensionless velocity components were observed to be nearly independent of the impeller speed and liquid height.

The nearly quiescent zone below the shaft is likely to be responsible for the coning phenomenon that is often observed as the tablet becomes fragmented during dissolution, and the fragments accumulate below the impeller in the shape of a cone. The velocity profiles in this nearly quiescent zone and the size of this zone do not appear to change appreciably with increasing agitation speeds. However, the velocities surrounding this zone, as well as the velocity profiles in all other regions of the vessel do change in direct proportion to the impeller speed. Therefore, particles outside the nearly quiescent zone are likely to experience very different fluid dynamic conditions which can possibly result in their transfer out of the quiescent region, their suspension, and the elimination of coning with increasing impeller speed.