FUTURE DIRECTION

With advances in technology and increased understanding of in vivo absorption, often dissolution methods that have clinical or in vivo relevance can be developed such that the method may provide more mechanistic information lending to greater product understanding. Implementation of Quality-by-Design principles into drug development efforts and availability of the FDA/ICH Quality guidance documents support advancing in vitro methods into reliable benefit/risk assessment tools linking in vitro and in vivo product performance and patient benefit.

Computer modeling can be effectively used to enhance the understanding of the in vitro and in vivo dissolution of a target oral dosage form. The desired attributes of the product can be studied and sensitivity of different physicochemical and physiologic parameters affecting the in vivo release could be ascertained a priori. A model such as Advanced Compartmental Absorption and Transit can be coupled with the regular compartmental or physiologic model [54] to map the drug lifecycle from its in vitro release to the in vivo input, absorption, distribution, metabolism, and elimination phases. Computer modeling and simulations can be targeted to cover aspects such as deconvolution, in vitro/in vivo relationship, drug transport, and bioavailability.

SUMMARY

During early discovery, and various stages of drug development, reliable in vitro dissolution testing may provide significant product information and, if shown to have in vivo relevance, could be used for guiding product development and may even replace some in vivo clinical trials. However, use of in vitro dissolution methods and leveraging of the information gained from in vitro studies vary greatly. In vitro dissolution testing has been evolving over the years from use as a product quality characterization tool to serving as a link between in vitro and in vivo product performance. When applicable, dissolution testing serves as a surrogate for bioequivalence demonstration as well as an indicator of a well-controlled, robust, and reliable manufacturing process, delivering products with established batch-to-batch consistency.

From the product quality perspective and for adequate assurance of in vivo performance of a solid dosage form, a detailed in vitro characterization is essential. In vitro dissolution testing of the solid oral dosage form can be conducted using various tests and techniques. This type of evaluation is useful during product development, for quality assurance and control, for product stability testing, and during assessment of comparability. In vitro dissolution testing may also be useful for getting waivers of in vivo bioavailability or bioequivalence studies, particularly when the dosage form exhibits formulation proportionality to the biostudied lot, or when the drug meets the criteria for BCS Class I and exhibits rapid dissolution, or when a meaningful in vitro/in vivo relationship is established. The modern frontiers in developing efficient in vitro performance testing include areas such as fiber optics for monitoring of drug concentration in the dissolution medium [55], application of artificial neural network for dissolution prediction [56], and process analytical technology [57].