molecular pharmaceutics

editorial

BCS in Drug Discovery, Development, and Regulation

Mention BCS at a cocktail party and you are much more likely to end up discussing football than drug permeability. In point of fact, the Biopharmaceutics Classification System (BCS) has been around longer than its sports namesake and, more importantly, has proven to be an invaluable tool for predicting the extent of drug absorption after oral administration. In 1995, Amidon and his colleagues published a theoretical basis for drug classification based on a drug's permeability and solubility. This system groups drugs into four categories: class 1, high permeability and high solubility; class 2, high permeability and low solubility; class 3, low permeability and high solubility; and class 4, low permeability and low solubility. Since its inception, the BCS has provided a simple and facile scientific framework for drug development and, as a result, has been incorporated into a number of regulatory guidances worldwide, not the least of which is the FDA guidance titled *Waiver of In Vivo Bioavailability and Bioequivalence Studies for Immediate-Release Solid Oral Dosage Forms Based on a Biopharmaceutics Classification System,* that was finalized in August of 2000. This guidance provides recommendations for those sponsors who wish to request a waiver of *in vivo* bioavailability and bioequivalence studies for immediate release solid oral dosage forms containing class 1 drugs. In this featured topic issue of *Molecular Pharmaceutics*, we examine the use of BCS in drug development and explore new potential extensions of BCS into the regulatory realm. Starting with permeability, Knutson et al. provide a unique and in-depth look at the clinical measurement of drug permeability using the single pass perfusion technique, LOC-I-GUT. Thiel-Demby et al. give an instructive lesson on the validation of an in vitro permeability method using a Madin-Darby canine kidney type II cell line that heterologously expresses the human P-glycoprotein (P-gp) efflux transporter. Dahan and Amidon explore the role of P-gp efflux in the intestinal absorption process of BCS class III drugs that are substrates of the efflux transporter, using a combination of *in vitro* and *in vivo* permeability methodology. On the dissolution front, Sheng et al. link theoretical considerations of dissolution and practical methodology to illustrate the dependence of buffer differential on biopharmaceutical properties of BCS II weak acids. Using simulation tools and *in vitro*−*in vivo* correlation, Kovačević et al. examine a possible extension of biowaiver criteria to BCS class II drugs. In an analysis of risk factors in bioequivalence studies, Yamashita and Tachiki provide convincing evidence that BCS classification can be useful in efficient planning of BE studies, particularly for generic drug products. For controlled release drug candidates, Tannergren and colleagues emphasize the importance of understanding in vivo colonic absorption, stressing early biopharmaceutical assessment of potential controlled release candidates and offering practical guidelines based on the candidate's BCS classification. Finally, Chen and Yu analyze preclinical and clinical data of 51 high permeability drugs, examining drug metabolism as a tool for supporting and extending current BCS classification. These articles represent the interface of academic research, industrial development, and regulatory thought that has developed around the Biopharmaceutics Classification System. With continued industry emphasis on more efficient processes and decreasing drug development timelines, it is likely that BCS will remain an invaluable tool for the foreseeable future.

John M. Hilfinger
Guest Editor

TSRL Inc., 540 Avis Drive, Suite A, Ann Arbor, Michigan 48108

E-mail: jhilfinger@tsrlinc.com

MP900003F

10.1021/mp900003f CCC: $40.75
Published on Web 02/02/2009