MODERN BIOPHARMACEUTICAL CLASSIFICATION SYSTEM: A COMPLEX CLASSIFICATION SYSTEM TO PREDICT PHARMACOKINETIC FAILURES

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Dear Editor,

The present letter is focused on the re-classification of Biopharmaceutical Classification System (BCS), which is adopted by United States Food and Drug Administration (USFDA)[1]. Bioavailability (BA) and Bioequivalence (BE) studies of drug products not only assure the safety of drug products but also assure the efficacy and allow inter-changeability of drug products, which is important in cost reduction of drug therapy. The traditional biopharmaceutical classification system[2], appeared in literature a decade before, is effectively implemented by pharmaceutical companies for designing BA/BE studies, *in-vitro in-vivo* correlation (IVIVC), optimization of dissolution media and formulation research[3]. BCS is based on the two important rate-determining steps in BA known as drug solubility and drug permeability[4]. However, few other parameters like dose, dissolution volume and pH were equally considered for classifying the drugs based on BCS[2]. Even though BCS made a great impact on discovery and development of drugs in pipeline, BCS is mainly focused on bioavailability and IVIVC[3]. Moreover, BCS serve as a guideline for formulators in selection of excipients and processes. On the other hand, advent of biotechnology, pharmacology, High Through Put (HTP) screening, combinatorial chemistry and drug delivery research encouraged the invention of highly potent synthetic drug substances as well as protein and peptide molecules[5]. The future molecules may face conventional pharmacokinetic problems such as poor solubility, poor permeability and shorter half life. In addition to that unconventional problems like high first pass effect, low *in vitro* and *in vivo* stability, (Pgp) mediated efflux transport, lack of sensitivity to analyze the drug in biological matrices and lack of sensitivity to detect the polymorphs in dosage forms will appear in front of pharmaceutical scientist while developing a drug and/or dosage forms. It is really very difficult and most of the time not necessary to consider all the parameters to classify the drugs. Our Proposed Biopharmaceutical Classification System (PBCS) allows classifying the drugs not only based on drug solubility and permeability but also considering drug stability in GIT and first pass effect. Highly stable drugs should be 90% stable in GIT for the time required to absorb 90% of unchanged drug in GIT. First pass effect of more than 60 % is considered as high first pass effect of drugs. Proposed biopharmaceutical classification system is presented in Table No 1. The main aim of PBCS is to predict the BA of dosage form from the results obtained from Phase I clinical studies. PBCS will give the clue for formulation scientist to optimize the BA by the addition of enzyme inhibitors, change in micro environmental pH and addition of buffers to improve the BA. PBCS will also allow addition of some enzymes in dissolution media that will give the trend of first pass effect in *in-vivo* conditions.

Table 1. Modern Biopharmaceutical Classification Systems

MBCS Class	Solubility	Permeability	First pass effect	Stability
Class I	High	High	-	-
Class I_A	-	-	High	High
Class I_B			Low	High
Class I_C			High	Low
Class II_D			Low	Low
Class II	Low	High	-	-
Class II_A			High	High
Class II_B			Low	High
Class II_C			High	Low
Class II_D			Low	Low
Class III	High	Low	-	-
Class III_A			High	High
Class III_B			Low	High
Class III_C			High	Low
Class III_D			Low	Low
Class IV	Low	Low	-	-
Class IV_A			High	High
Class IV_B			Low	High
Class IV_C			High	Low
Class IV_D			Low	Low

BA/BE studies are conducted in healthy human subjects. The unnecessary exposure of drug in healthy human volunteers needs ethical justification. Moreover, human trails are costly affairs and time consuming process. The main goal of PBCS is to reduce the human trails for BA/BE studies. If at all effective *in vitro* dissolution technologies are invented in future on the basis of PBCS that will serve as surrogate marker in BA and BE of drug products. PBCS conventionally be termed as Modern Biopharmaceutical Classification System (MBCS).

Reference

1. Guidance for industry, waiver of in vivo bioavailability and bioequivalence studies for immediate release solid oral dosage form based on biopharmaceutics classification scheme. Food and Drug Administration, Center for Drug Evaluation and Research, Rockville, Maryland, USA. August 2000.
2. Amidon G, Lennernas H, Shah VP. A theoretical basis for a biopharmaceutic drug classification: the correlation of invitro drug product dissolution and invivo bioavailability. Pharm Res., 12, 1995, 413-420.
3. Dressman J, Johannes K. Pharmaceutical dissolution testing, 1st ed. Taylor and Francis, Boca Raton, 2005, p 206.
4. D.M. Brahmankar, Sunil B. Jaiswal, Biopharmaceutics and pharmacokinetics A treatise, 1st ed. Vallabh Prakashan, New Delhi, 1995, p 19.
5. Gregory AN, Daniel BK. Existing and emerging strategies for the analytical characterization and profiling of compound libraries, Annul reports in medicinal chemistry. Academic press, London, 2001, 36, 27, p 277.

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