2. AIM AND OBJECTIVES

Establishing a correlation between the in vitro dissolution profile of a Modified Release (MR) formulations and the in vivo plasma concentration profiles have been of great interest for a number of years. Modified release (MR) of drugs in the gastrointestinal (GI) tract following oral administration is the intended rate-limiting factor in the absorption process. It is, therefore, desirable to use in vitro data to predict in vivo bioavailability parameters for the rational development and evaluation process for extended release dosage forms.

The ultimate goal of an in vitro–in vivo correlation (IVIVC) should be to establish a meaningful relationship between in vivo behavior of a dosage form and in vitro performance of the same, which would allow in vitro data to be used as a surrogate for in vivo behavior. A meaningful IVIVC for extended release dosage forms would be of benefit as a surrogate for bioequivalence studies which might typically be required with scale up or minor post-approval changes (SUPACs) in formulation equipment, manufacturing process or in the manufacturing site. A meaningful IVIVC could lead to improved product quality and decreased regulatory burden.

It is well known that in vitro dissolution testing is a powerful and useful method for determining product quality. The utility of in vitro dissolution as a surrogate for in vivo bioavailability is very attractive and has been demonstrated for several products. Furthermore to utilize this dissolution test, the IVIVC must be predictive of in vivo performance of the product. Levels A, B, C and multiple level C correlations have been described in the US Food and Drug Administration (FDA) IVIVC guidance. The most useful of these is a level A correlation, which is described as a point-to-point correlation, in which the in vivo percentage absorbed curve is compared to in vitro percentage dissolved curve. Generally, these correlations are linear and are considered most informative and very useful from a regulatory view point.
Numerous IVIVC studies of modified release formulations have been previously reported. There are no reports, however, of such studies for the drugs of Zolmitriptan and Rizatriptan. The purpose of this study was, therefore, to develop IVIVCs for the selected modified release formulations of these drug candidates.