

Research Paper Review:

A Technique to Estimate In Vivo Dissolution Profiles Without Data from a Solution

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Jack Cook from Pfizer recently published a research paper in *The AAPS Journal* (1). The topic of the paper was a starting point for developing a dissolution in vitro method using a profile generated by deconvolution of a synthesized in vivo profile. This approach works best for BCS Class 2 or 4 where dissolution is the rate-limiting step.

The author asserts that dissolution testing ideally is a surrogate to ensure quality and is expected to ensure adequate in vivo product performance. The dissolution test is typically developed around the time human studies are initiated, at which point the in vivo product performance is usually not known. The lack of solution in vivo data can preclude the use of traditional deconvolution techniques to assess in vivo dissolution. This lack of in vivo solution data may be because a solution is not possible or feasible either because of resource constraints or compound solubility.

There has been recent progress in predicting human permeability. It is possible to synthesize the plasma drug concentration–time profile from human permeability predictions and first-in-human trial results and to use these data to synthesize a pharmacokinetic profile for a solution and provide an initial estimate of the in vivo dissolution profile.

Cook examined plasma metoprolol concentration–time data from a previously published study of pharmacokinetics of three metoprolol formulations and an oral solution (2). This study included an in vivo–in vitro correlation (IVVC) that allowed a comparison of predicted in vivo dissolution profiles with the dissolution profiles from the in vitro method. The most appropriate in vitro method for the correlation was determined to be Apparatus 1 at 150 rpm using pH 6.8 media.

A one-compartment unit impulse function was used, and the absorption rate was estimated from animal permeability data. The results were compared with those obtained using a unit pulse function estimated from the oral solution data. The results from deconvolution using the synthetic unit impulse function were in good agreement with those derived using the modeled solution.

The mean in vitro dissolution profile for the three solid oral formulations used in the clinical trial of the metoprolol study was very similar to the in vivo dissolution profile derived using the synthetic method. This suggests that estimation of the in vivo dissolution profile may greatly facilitate IVVC development.

In conclusion, the paper states that for poorly soluble compounds where a solution is unavailable, a synthetic solution method offers a way to estimate in vivo dissolution profiles through deconvolution.

This is an important tool for dissolution method development in the early phases of product development. This profile could be used as a target for the product dissolution rate as the dissolution test method is developed.

REFERENCES

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