Evaluation of Viscosity Effects on Drug Dissolution and Permeation across Caco-2 Monolayers Using In Vitro Dissolution and Absorption Systems (IDAS)

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PURPOSE

1. Determining the effect of medium viscosity (food viscosity [1]) on diffusion and permeation of API across Caco-2 cell monolayer [2] using a novel In-vitro Dissolution Absorption System, IDAS1
2. Delineating the role of oral drug product dissolution, and API diffusion on permeation across Caco-2 cell monolayer in low and high viscosity medium using IDAS2

METHOD

IDAS1 and IDAS2 (Figure 1) are comprised of a dissolution chamber/vessel and permeation chamber(s), separated by human Caco-2 cell monolayers. Both systems enable simultaneous measurements of drug dissolution and permeation in vitro, while IDAS2 permits evaluation of intact oral solid dosage forms (tablets or capsules). Dissolution media were formulated to possess low viscosity (LV) and high viscosity (HV). Test drugs were selected from four BCS classes, i.e. propranolol (Class I), carbamazepine (II), atenolol or ranitidine (III), and acetazolamide (IV). Viscosity effect on API permeation was evaluated using IDAS1. Intact drug tablet dissolution and drug permeability in LV or HV medium was evaluated using IDAS2 by LC-MS/MS analysis.

RESULTS

IDAS1

There was NO apparent effect of medium viscosity on the permeation of all four compounds (propranolol, carbamazepine, atenolol, and acetazolamide) tested in IDAS1 (Figure 2).

IDAS2

High viscosity caused an apparent reduction in the dissolution and permeation in all tested compounds with more profound effects on low soluble drugs, carbamazepine BCS II and acetazolamide BCS IV (Figure 3).

CONCLUSION

- Medium viscosity has predominant effect on the dissolution and permeation of intact oral solid dosage forms of poorly water-soluble API, presumably by delaying dosage form disintegration/dissolution
- Combination of IDAS1 and IDAS2 enables distinguishing between the roles of intrinsic drug properties and product-related factors that may affect drug dissolution and/or permeation, a critically important for drug formulation development

REFERENCE

1. Radwan et al., Biopharm & Drug Disposition 2012; 33: 403-416