Prediction of the EG of midazolam and its variability in 10 groups of 5 individuals selected randomly from a population of 50 virtual subjects.

The ADAM model outputs regional fractions of the dose absorbed and metabolised in different segments of the gut. The results indicate that the absorption of midazolam is not solubility-limited, and that the dose is completely absorbed.

The ADAM model was repeated assuming an even distribution of CYP 3A along the small intestine. The pattern of regional absorption of midazolam was unchanged but the predicted mean value of EG decreased to 0.33.

Conclusions

The ADAM model is capable of predicting spatial and inter-individual variability in intestinal drug absorption and metabolism along the gut. Its use exemplifies the value of physiologically-based mechanistic models, with incorporation of realistic population variability, in the drug development process.

References