In vitro dissolution testing and in silico modeling for orally administered drug products

Created on: 08-04-2020 - Last modified on: 08-04-2020

Contact person

Bart Hens

Organisation

Name of the organisation Katholieke Universiteit Leuven (KUL)

Department Department of Pharmaceutical and Pharmacological Sciences

Country Belgium

Geographical Area Flemish Region

SCOPE OF THE METHOD

The Method relates to	Human health
The Method is situated in	Basic Research, Education and training, Regulatory use - Routine production, Translational - Applied Research
Type of method	In silico

DESCRIPTION

Method keywords

PBPK modeling

in vitro dissolution testing

intestinal absorption

oral absorption

Scientific area keywords

Biopharmaceutics
drug products
pharmacometrics
pharmacokinetics
pharmacodynamics

Method description

Performing biopredictive dissolution tests in *in vitro* models that are frequently used in pharmaceutical and academic institutions and using these *in vitro* dissolution data as input for PBPK models to predict the systemic exposure of the drug in humans/patients.

Lab equipment

Dissolution beakers ;
Stirrers ;
Sampling material ;
Biorelevant media ;
PBPK software packages.

Method status

Published in peer reviewed journal

PROS, CONS & FUTURE POTENTIAL

Advantages

3R principle for sure! Also, these tests are much faster and less expensive compared to clinical trials as traditionally done during the drug development process.

Challenges

Not all physiological variables are integrated in *in vitro* dissolution methods which may result in sometimes false predictions in the end!

Modifications

Doing more clinical studies in the hospital with the focus on exploring human GI physiology so we have more information to optimize *in silico* and *in vitro*

models.

Future & Other applications

Especially in regulatory science, this approach may lead to easier and faster drug product approvals. In the current setting, the time from drug discovery until marketing access takes about 12 years on average. This could significantly reduced if regulatory authorities revise their guidelines.

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

References

Hens B, Masuy I, Deloose E, Mols R, Tack J, Augustijns P. Exploring the Impact of Real-Life Dosing Conditions on Intraluminal and Systemic Concentrations of Atazanavir in Parallel with Gastric Motility Recording in Healthy Subjects [published online ahead of print, 2020 Feb 27]. Eur J Pharm Biopharm. 2020;S0939-6411(20)30055-2. doi:10.1016/j.ejpb.2020.02.014

Bermejo M., Hens B., Dickens J., Mudie D., Paixão P., Tsume Y., Shedden K., Amidon G.L.A Mechanistic Physiologically-Based Biopharmaceutics Modeling (PBBM) Approach to Assess the In Vivo Performance of an Orally Administered Drug Product: From IVIVC to IVIVP, 2020, Pharmaceutics, 12 (1)

Cristofoletti R., Hens B., Patel N., Esteban V.V., Schmidt S., Dressman J.. Integrating drug- and formulation-related properties with gastrointestinal tract variability using a product-specific particle size approach: case example ibuprofen. J Pharm Sci. 2019

Hens B., Kataoka M., Ueda K., Gao P., Tsume Y., Augustijns P., Kawakami K., Yamashita S. Biopredictive in vitro testing methods to assess intestinal drug absorption from supersaturating dosage forms. JDSST. 2019

Yu A.M., Koenigsknecht M., Hens B., Baker J.R., Wen B., Jackson T.L., Pai M.P., Hasler W.L., Amidon G.L., Sun D. Mechanistic Deconvolution of Oral Absorption Model with Dynamic Gastrointestinal Fluid to Predict Regional Rate and Extent of GI Drug Dissolution. The AAPS J. 2019

Hens B, Corsetti M, Bermejo M, Löbenberg R, González PM, Mitra A, Desai D, Chilukuri DM, Aceituno A. "Development of Fixed Dose Combination Products" Workshop Report: Considerations of Gastrointestinal Physiology and Overall Development Strategy. The AAPS Journal

Associated documents

Hens et al. posaconazole-final.pdf

FinalArticleASA.pdf

Coordinated by

Financed by