Physiologically based pharmacokinetic modelling

Commonly used acronym: *PBPK*

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SCOPE OF THE METHOD

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

DESCRIPTION

Method keywords

Pharmacokinetics

Drug metabolism

absorption

Serum protein binding

mathematical modelling

excretion

In vitro-in vivo extrapolation (IVIVE)

drug development

drug-drug-interactions

Scientific area keywords

pharmacology

clinical pharmacology

systems biology

computational modelling

Regulatory Science

Method description

Physiologically based pharmacokinetic (PBPK) modeling is an *in-silico* modelling technique that aims to predict how a drug moves through the body by mathematically representing real anatomical and physiological structures. Overall, PBPK provides a powerful framework for bridging *in vitro* data, experimental studies, and clinical outcomes. It divides the body into compartments such as liver, kidney, lung, or fat, each with known blood flow rates, volumes, and tissue compositions. These compartments are connected to mimic actual circulation and tissue distribution. PBPK models also incorporate drug-specific properties like solubility, permeability (e.g. LogP), and metabolism rates (intrinsic clearance) to simulate absorption, distribution, metabolism, and excretion. Because the parameters are mechanistic and biology-based, the models can be adapted across species, age groups, and clinical scenarios. PBPK helps researchers understand how changes in physiology, disease, or interactions with other drugs affect drug exposure. It is often used to support dose selection, drug-drug interactions, and regulatory submissions.

Lab equipment

Specific PBPK software (e.g. Simcyp, PK-Sim, GastroPlus). When *in-vitro* drug-related parameters are not already available in the literature, they can be generated using various *in-vitro* assays, including plasma protein binding assays, microsomal stability assays, transporter affinity assays, and others.

Method status

Published in peer reviewed journal

PROS, CONS & FUTURE POTENTIAL

Advantages

- PBPK models also allow testing of “what-if” scenarios without exposing humans or animals to risk.

- PBPK models are based on real physiological and biochemical parameters, providing a mechanistic insight into drug absorption, distribution, metabolism, and excretion.

- PBPK models are increasingly accepted by regulatory agencies to support dosing decisions, labeling, and clinical trial design.

Challenges

- Accurate PBPK models require extensive physiological and drug-specific data, which may not always be available.

- PBPK cannot reliably predict outcomes if key biological mechanisms are unknown or poorly characterized.

- Validation of PBPK models requires some preclinical or clinical drug concentration data, although typically less than what is needed for more empirical pharmacokinetic models.

Modifications

PBPK modelling can be improved with better physiological data (more accurate and comprehensive organ-specific parameters) and by developing more robust models for pathological conditions (e.g., liver or kidney impairment, cancer) to predict altered pharmacokinetics.

Future & Other applications

PBPK modeling primarily focuses on therapeutic agents in humans, particularly small molecules and monoclonal antibodies. Future applications may extend PBPK to novel therapeutic modalities, such as siRNA, CAR-T therapies, and other advanced biologics. Additional potential applications, although not yet well established, include veterinary medicine for dose selection across different animal species, cosmetics for estimating systemic exposure to chemical ingredients, and occupational exposure studies, such as modeling the absorption and distribution of inhaled substances.

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

References

1. Yuan Y, He Q, Zhang S, Li M, Tang Z, Zhu X, et al. Application of Physiologically Based Pharmacokinetic Modeling in Preclinical Studies: A Feasible Strategy to Practice the Principles of 3Rs. Front Pharmacol [Internet]. Frontiers; 2022 [cited 2025 Nov 18];13. https://doi.org/10.3389/fphar.2022.895556.

2. Zhang X, Yang Y, Grimstein M, Fan J, Grillo JA, Huang S-M, et al. Application of PBPK Modeling and Simulation for Regulatory Decision Making and Its Impact on US Prescribing Information: An Update on the 2018-2019 Submissions to the US FDA's Office of Clinical Pharmacology. The Journal of Clinical Pharmacology. 2020;60:S160–78. https://doi.org/10.1002/jcph.1767

3. Miller NA, Reddy MB, Heikkinen AT, Lukacova V, Parrott N. Physiologically Based Pharmacokinetic Modelling for First-In-Human Predictions: An Updated Model Building Strategy Illustrated with Challenging Industry Case Studies. Clin Pharmacokinet. 2019;58:727–46. https://doi.org/10.1007/s40262-019-00741-9.

4. De Sutter P-J, Gasthuys E, Vermeulen A. Comparison of monoclonal antibody disposition predictions using different physiologically based pharmacokinetic modelling platforms. J Pharmacokinet Pharmacodyn. 2024;51:639–51. https://doi.org/10.1007/s10928-023-09894-4.

5. De Sutter P-J, Rossignol P, Breëns L, Gasthuys E, Vermeulen A. Predicting Volume of Distribution in Neonates: Performance of Physiologically Based Pharmacokinetic Modelling. Pharmaceutics. Multidisciplinary Digital Publishing Institute; 2023;15:2348.

https://doi.org/10.3390/pharmaceutics15092348.

6. De Sutter P-J, De Cock PD, Johnson TN, Musther H, Gasthuys E, Vermeulen A. Predictive Performance of Physiologically Based Pharmacokinetic Modelling of Beta-Lactam Antibiotic Concentrations in Adipose, Bone, and Muscle Tissues. Drug Metab Dispos. American Society for Pharmacology and Experimental Therapeutics; 2023;51:499–508. https://doi.org/10.1124/dmd.122.001129.

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