frontiers | Frontiers in Drug Discovery

TYPE Editorial
PUBLISHED 10 June 2025
DOI 10.3389/fddsv.2025.1636070

OPEN ACCESS

EDITED AND REVIEWED BY
José L Medina-Franco,
National Autonomous University of Mexico, Mexico

*CORRESPONDENCE
Simone Brogi,
simone.brogi@unipi.it
Patric Schyman,
schymanp@eikontx.com
Vishal B. Siramshetty,
siramshetty.vishal_babu@gene.com

RECEIVED 27 May 2025
ACCEPTED 02 June 2025
PUBLISHED 10 June 2025

CITATION
Brogi S, Schyman P and Siramshetty VB (2025) Editorial: Pharmacokinetics modeling in the Artificial Intelligence Era.
Front. Drug Discov. 5:1636070.
doi: 10.3389/fddsv.2025.1636070

Editorial: Pharmacokinetics modeling in the Artificial Intelligence Era

Simone Brogi[1]*, Patric Schyman[2]* and Vishal B. Siramshetty[3]*

[1]Department of Pharmacy, University of Pisa, Pisa, Italy, [2]Eikon Therapeutics, Millbrae, CA, United States, [3]Translational Safety, Genentech, Inc., South SanFrancisco, CA, United States

KEYWORDS

machine learning, drug discovery, ADME-tox, new compounds discovery, cheminformatics, pharmacokinetics modeling

Editorial on the Research Topic
Pharmacokinetics modeling in the Artificial Intelligence Era

Introduction

To explore and investigate the potential contribution and impact of Artificial Intelligence (AI), Machine Learning (ML), and *in silico* methodologies in a particular field of the drug discovery trajectory, such as the evaluation of Absorption, Distribution, Metabolism, Excretion (ADME) properties and toxicological liabilities (i.e., *h*ERG liability, hepatotoxicity, etc.), in July 2023, we launched a Research Topic entitled "Pharmacokinetics Modeling in the Artificial Intelligence Era" hosted by the journal *Frontiers in Drug Discovery*–section *In silico Methods and Artificial Intelligence for Drug Discovery*. In fact, nowadays, the discovery and development of novel drug candidates are undergoing fundamental transformation with the advancement of AI and ML technology. Our capacity to estimate substance behavior in biological systems has substantially increased, shifting from purely theoretical study to a crucial role in pharmaceutical research and development. Accordingly, the Research Topic aimed to explore the most effective use of ML models in the field of ADME/Toxicology to increase the efficiency of drug development process. The objective is to not only create the most effective ML models for particular applications, including permeability and toxicity, but also to enhance the capability to understand ML predictions, thereby streamlining modifications to molecule design. Our objective is to tackle issues related to the choice of ML models that strike a balance between high predictive precision and real-world usability in drug development, which is vital for reducing risk in the drug development process. In this context, we received several article submissions to consider in the mentioned Research Topic, and finally five articles were published (4 research articles and 1 review article). In this editorial, we delve into a Research Topic of studies that underscore the transformative role of AI and ML in drug discovery, ranging from bibliometric analyses of pharmacokinetic models to innovative applications in predicting drug bioavailability and interactions. These contributions highlight the breadth and depth of current research efforts in harnessing computational methods to advance pharmacokinetics and toxicology modeling, paving the way for enhanced drug development processes.

Bibliometric analysis of population pharmacokinetic models

According to the significant increase in using computational methods in drug discovery and development, the review article authored by Yao and colleagues highlighted, by a bibliometric analysis, the impact of population pharmacokinetic (PPK) model in the current scientific research focused on the drug discovery campaign. The authors, using a systematic approach, collected research and review articles to explore the usage of PKK model in a definite period of time (2000–2024). It is worth mentioning that this is the first comprehensive paper regarding the advancement of developing this type of model. The systematic search was conducted considering the Web of Science (WoS) database, and the collected data were analyzed utilizing different tools (i.e., CiteSpace, Bibliometrix R, Microsoft Excel). In the period considered, the authors indicated that 6,125 papers (128,856 citations) focused on PKK models were published. An in-depth analysis revealed that relevant publications experienced a typical annual growth rate of over 10%, indicating a growing interest in this particular field. Research outputs are predominantly found in North America, Western Europe, and East Asia, with the United States at the forefront with 2,340 publications and boasting the highest H-index of 93 and total citations of 54,965, whereas the subject categories for most publications are Pharmacology and Pharmacy. Interestingly, authors found that ML, voriconazole, tacrolimus, critically ill patients, dose optimization, external evaluation, polymyxin b, model-informed precision dosing, and extracorporeal membrane oxygenation are current research hotspots and future research trends (Yao et al.).

AI-driven pharmacokinetic/pharmacodynamic thresholds for antibiotics

Wu and coworkers, in a research article, reported the use of AI to establish the pharmacokinetic/pharmacodynamic (PK/PD) threshold values for sitafloxacin (STX) effectiveness against targeted pathogens to inform the development of clinical breakpoints for antimicrobial susceptibility testing. This issue is pivotal in clinical settings to provide effective therapeutic interventions. In particular, a PPK model was developed, considering 342 individuals, to calculate the dosing-regimen-dependent PK factors of STX-infected patients, which were combined with *in vitro* PD data and PK/PD target data. The cumulative fraction of response (CFR) and probabilities of attainment (PTAs) values for different STX dosing regimens against *S. pneumoniae, S. aureus, E. coli, K. pneumoniae*, and *P. aeruginosa* were determined using the Monte Carlo method. Results indicated that STX can be used against the mentioned bacterial species/strains at different doses (50 mg/q12 h, 100 mg/q24 h, and 100 mg/q12 h) with effective outcomes against *S. pneumoniae*-related infections, whereas the efficacy against *P. aeruginosa*-related infections should be further confirmed (Wu et al.).

Multimodal approaches to drug-drug interaction detection

Another significant issue in the drug discovery field is related to potential drug–drug interaction. In this context, Yu and coworkers developed a multimodal feature fusion model using bi-directional gated recurrent units (BiGRU) and Transformer (BiGGT) to retrieve relevant drug-drug interactions in clinical practice. This model was conceived taking into account the drug molecule topology structure, graph information, and medical corpus (Word2vec, Mol2vec, and GCN methods were used, respectively). Notably, the BiGGT-based model is a superior approach in extracting information related to drug-drug interactions compared with the current approaches. The model showed a precision of 78.22%, indicating the feasibility of applying the multimodal deep learning (DL) approach in BiGGT model for improving the performance of extracting drug-drug interactions data (Yu et al.).

Predicting brain bioavailability using machine learning

Morales and colleagues, by developing a ML-based model, demonstrated the possibility of effectively determining unbound drug bioavailability in the brain. The determination of brain bioavailability is crucial for developing drug candidates to treat diseases affecting the central nervous system (CNS). To this end, the authors used a lot of PK parameters to determine the brain bioavailability of drugs. These data were included in a manually curated dataset comprising 157 different molecules collected from the literature. The obtained dataset was divided into training and test subsets through the use of a clustering method. A refined dataset was used to train additional models after known substrates of P-gp and/or Breast Cancer Resistance Protein (BCRP) had been removed from the original dataset. A variety of supervised ML algorithms have been evaluated, including Gradient Boosting Machine (GBM), Support Vector Machine (SVM), Linear Discriminant Analysis (LDA), Extreme Gradient Boosting (EGB), k-nearest neighbors (kNN), DL, Random Forest (RF), and classificatory Partial Least Squares (cPLS). The development of the models adhered to proper procedures for developing predictive quantitative structure-activity relationships (QSAR). The results indicated that the model developed using the EGB method was the best performing tool in the study, with an accuracy of 85.1% for the test set. Similar results were achieved conducting a prospective validation approach in which a subset was used to compare the estimated drug brain bioavailability with experimental findings. The proposed computational approach demonstrated applicability in real-world settings, and the dataset utilized along with the molecular descriptors and code are publicly available within the article to be used by the scientific community to expand and improve the performance of the model, aiding the drug discovery pipeline (Morales et al.).

Deep learning for rapid toxidrome prediction

The last published article authored by Liu and collaborators described the application of computer-based methods to develop a tool able to identify chemical agents that could cause toxidromes (undesired features provoked by toxicological issues emerging from medical treatments), allowing a fast evaluation of potential toxicity risks of drug treatments. The authors used a DL-based approach for mapping chemicals with their possible toxidromes based on communicative message passing neural network (CMPNN) algorithms. In this way, it is possible to consider several different small datasets for model training with respect to classical deep neural networks. CMPNN-based ensemble learning demonstrated the best performance in predicting toxidrome-related chemicals with respect to a single CMPNN model. Considering toxidromes for which there is not sufficient experimental data or established molecular mechanism for the model training step, the authors used a similarity-based ensemble strategy to improve the information to generate AI-based models. Finally, a web-based interface was generated to access the data and toolset of this study (https://toxidrome.bhsai.org/) (Liu et al.).

We would like to thank the Frontiers editorial staff, authors, co-authors, and reviewers for their valuable contributions to this Research Topic. Their efforts made it successful. This topic is a valuable resource for researchers and students, and we anticipate that it will promote the development and application of AI-based tools and *in silico* models for drug discovery regarding PK issues. The Research Topic is freely consultable at the following link https://www.frontiersin.org/research-topics/56980/pharmacokinetics-modeling-in-the-artificial-intelligence-era/articles.

Author contributions

SB: Conceptualization, Supervision, Data curation, Writing – review and editing, Writing – original draft. PS: Conceptualization, Writing – review and editing, Writing – original draft, Data curation. VS: Writing – original draft, Conceptualization, Data curation, Writing – review and editing.

Funding

The author(s) declare that no financial support was received for the research and/or publication of this article.

Acknowledgments

The authors thank all the contributors of the Research Topic, reviewers and the Editorial Office of Frontiers in Drug Discovery for useful advice during the management of the submitted manuscripts.

Conflict of interest

Author VS was employed by Genentech, Inc. Author PS was employed by Eikon Therapeutics.

The remaining author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The author(s) declared that they were an editorial board member of Frontiers, at the time of submission. This had no impact on the peer review process and the final decision.

Generative AI statement

The author(s) declare that no Generative AI was used in the creation of this manuscript.

Publisher's note