Intelligent Pharmacy xxx (xxxx) xxx

Contents lists available at ScienceDirect

Intelligent Pharmacy

journal homepage: www.keaipublishing.com/en/journals/intelligent-pharmacy

The importance of in-silico studies in drug discovery

ARTICLE INFO

Keywords
In-silico
Drug discovery
Computer-aided drug design

ABSTRACT

The use of in-silico research in drug development is growing. Aspects of drug discovery and development, such as virtual ligand screening and profiling, target and lead finding, and compound library creation, are simulated by computational approaches. Databases, pharmacophores, homology models, quantitative structure–activity connections, machine learning, data mining, network analysis tools, and computer-based data analysis tools are examples of in-silico techniques. These techniques are mostly applied in conjunction with the production of in vitro data to build models that facilitate the identification and refinement of new compounds by providing insight into their features related to absorption, distribution, metabolism, and excretion.

To the Editor,

The term "in-silico drug discovery" describes the process of identifying and designing possible drug candidates using computer techniques. This strategy makes use of additional molecular modelling tools as well as computer-aided drug design (CADD) methods such virtual ligand screening and profiling, in silico structure prediction, refinement, and optimisation. Because it cuts down on the time and resources needed to find and improve therapeutic candidates, in-silico drug discovery has grown to be an essential component of contemporary drug research.[1] In order to maximise the likelihood of discovering viable drug candidates, in-silico approaches are frequently combined with physical screening techniques.[2]

Drug development benefits greatly from in-silico research for a number of reasons. They facilitate the process of identifying prospective drug candidates by facilitating the screening, design, and therapeutic potential prediction of new medications.[3] Furthermore, in-silico methods aid in toxicity prediction, enabling research groups to recognise potentially harmful effects early in the development process, thereby saving time and money. By predicting the binding modes of possible drug candidates and examining their interaction patterns, computational techniques like virtual ligand screening, molecular modelling, and docking-based virtual screening help find novel and promising compounds.[1,4] Additionally, in-silico research makes early drug development more flexible and morally sound by utilising knowledge already in existence to guide future procedures. All things considered, the advantages of in-silico drug discovery have resulted in the establishment of a $8.3 billion yearly industry in 2022, and this trend is anticipated to continue.

Many promising therapeutic candidates have been found thanks to in-silico drug discovery. For instance, in-silico techniques were utilised to find the HIV treatment medication raltegravir.[1] Another such is the melanoma medication vemurafenib, which was found by virtual screening.[5] Furthermore, prospective COVID-19 treatment candidates, such as the medication molnupiravir, have been found using in-silico techniques.[2] These illustrations show how effective medication candidates may be found using in-silico drug discovery.

For a number of reasons, in-silico research is essential to the drug development process. Virtual ligand screening, molecular modelling, and docking-based virtual screening are a few examples of computational techniques that may be used to find new drug candidates, anticipate how possible drug candidates would bind, and examine how they interact. By utilising these techniques in conjunction with conventional in vitro and in vivo investigations, the drug development process may be completed faster and with less resources. In the early phases of drug development, in-silico approaches also help with toxicity prediction, process optimisation, and the discovery of potential compounds, eventually saving time and money. Although important, in-silico techniques cannot completely replace necessary in vitro and in vivo procedures. To maximise the effectiveness of the drug discovery process, they are therefore utilised in combination with conventional experimental methodologies.[1,4]

Some specific in-silico methods used in drug discovery include.

1. **Virtual Ligand Screening and Profiling**: To screen and profile possible drug candidates, this entails using databases, homology models, pharmacophores, quantitative structure–activity correlations, and other molecular modelling techniques.
2. **Structure-Based Drug Design**: involves creating possible treatment options by using the biological target's three-dimensional structure.
3. **Machine Learning and Data Mining**: In-silico drug development is using these methods more frequently to evaluate huge datasets and forecast possible therapeutic possibilities.
4. **Virtual Screening**: Using a virtual library of molecules as a docking partner, this approach predicts the 'binding score' of each molecule to help find possible medication candidates.

These investigations make use of computer-based data analysis tools, databases, homology models, pharmacophores, quantitative structure–activity connections, machine learning, data mining, and molecular modelling techniques.[4] Some of the key benefits of in-silico studies in drug discovery include.

1. **Reduced time and resources**: Because in-silico methods make it possible for researchers to screen a large number of compounds

https://doi.org/10.1016/j.ipha.2024.01.010
Received 24 January 2024; Accepted 26 January 2024
Available online xxxx

rapidly and efficiently, they can aid in the drug development process by saving money and time.
2. **Predictive capabilities**: By predicting toxicity, carcinogenicity, and other possible problems, in-silico investigations enable researchers to find interesting chemicals and streamline their workflows.
3. **Integration with other techniques**: To maximise the likelihood of finding effective medications, in-silico investigations can be combined with computational and physical screening methods.
4. **Leveraging existing knowledge**: In-silico methods make early drug development more flexible and morally sound by utilising knowledge already in existence to guide future procedures.
5. **Cost-effective**: Medicinal chemists and pharmacologists can be supported economically throughout the drug development process with the use of in-silico investigations.

Some challenges in implementing in-silico studies in drug development include.

1. **Validation and Accuracy**: One major problem is ensuring the precision and dependability of in-silico forecasts. To determine a computational model's predictive capacity and applicability, experimental data must be used for validation.
2. **Complexity of Biological Systems**: Because biological systems are so intricate, it can be difficult to precisely simulate their behaviour in silico. One major obstacle is the requirement to portray the subtleties of biological processes and interactions.
3. **Regulatory Acceptance**: It is difficult to get regulatory acceptance for using in-silico data for drug development decision-making. Although in-silico techniques are useful, regulatory agencies need solid proof of their applicability and dependability.
4. **Data Availability and Quality**: The quality and accessibility of data are critical to the success of in-silico research. It might be difficult to obtain complete, high-quality data, which is essential for model building and validation.
5. **Interdisciplinary Expertise**: Proficiency in several domains, including computational biology, chemistry, and pharmacology, is necessary for conducting in-silico experiments. It might be difficult to integrate these many fields of knowledge in order to create and use in-silico procedures efficiently.

To sum up, in-silico studies are crucial to the drug discovery process because they offer a potent tool for predicting the therapeutic potential of new drugs, cutting down on the time and resources needed for the process, and combining with other methods to increase the likelihood of finding effective drugs.

Financial Support

No financial support was provided relevant to this research.

CRediT authorship contribution statement

Miah Roney: Data curation, Formal analysis, Methodology, Validation, Writing – original draft. **Mohd Fadhlizil Fasihi Mohd Aluwi:** Conceptualization, Investigation, Supervision, Validation, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

The authors would like to thanks to the Universiti Malaysia Pahang Al–Sultan Abdullah, Lebuhraya Tun Razak, 26300 Gambang, Kuantan, Pahang Darul Makmur, Malaysia.

References

1. Chang Y, Hawkins BA, Du JJ, Groundwater PW, Hibbs DE, Lai F. A guide to in silico drug design. *Pharmaceutics*. 2023;15(1):49.
2. Sadybekov AV, Katritch V. Computational approaches streamlining drug discovery. *Nature*. 2023;616(7958):673–685.
3. Nimgampalle M, Devanathan V, Saxena A. Importance of in silico studies on the design of novel drugs from medicinal plants against 21st-century pandemics: past, present, and future. In: *Pandemic Outbreaks in the 21st Century*. 2021:211–223.
4. Ekins S, Mestres J, Testa B. In silico pharmacology for drug discovery: methods for virtual ligand screening and profiling. *Br J Pharmacol*. 2007;152(1):9–20.
5. Shaker B, Ahmad S, Lee J, Jung C, Na D. In silico methods and tools for drug discovery. *Comput Biol Med*. 2021;137:104851.

Miah Roney
Faculty of Industrial Sciences and Technology, Universiti Malaysia Pahang Al-Sultan Abdullah, Lebuhraya Tun Razak, 26300, Gambang, Kuantan, Pahang Darul Makmur, Malaysia
Centre for Bio-aromatic Research, Universiti Malaysia Pahang Al-Sultan Abdullah, Lebuhraya Tun Razak, 26300, Gambang, Kuantan, Pahang Darul Makmur, Malaysia

Mohd Fadhlizil Fasihi Mohd Aluwi*
Faculty of Industrial Sciences and Technology, Universiti Malaysia Pahang Al-Sultan Abdullah, Lebuhraya Tun Razak, 26300, Gambang, Kuantan, Pahang Darul Makmur, Malaysia
Centre for Bio-aromatic Research, Universiti Malaysia Pahang Al-Sultan Abdullah, Lebuhraya Tun Razak, 26300, Gambang, Kuantan, Pahang Darul Makmur, Malaysia

* Corresponding author.
E-mail address: fasihi@umpsa.edu.my (M.F.F. Mohd Aluwi).