Bulletin of Pharmaceutical Research 2024;14(1):182

An Official Publication of Association of Pharmacy Professionals

ISSN: 2249-6041 (Print); ISSN: 2249-9245 (Online)

DOI: 10.21276/bpr.2024.14.1.2

REVIEW ARTICLE

ACCELERATING DRUG DISCOVERY: THE ROLE OF NEW MOLECULES AND SOFTWARE TOOLS

Basanta Kumar Behera[1,2]*, Amiya Kanta Mishra[1], Satyasnata Sahoo[1] and Sunit Kumar Sahoo[2]

[1]*Department of Pharmaceutics, College of Pharmaceutical Sciences, Puri-752002, Odisha, India*
[2]*University Department of Pharmaceutical Sciences, Utkal University, Vani Vihar, Bhubaneswar-751004, Odisha, India*

**E-mail*: basanta77behera@gmail.com
Tel.: +91 8917603282.

Received: Dec 13, 2023 / Revised: Mar 10, 2024 / Accepted: Mar 16, 2024

New drug molecules are needed for several reasons, including targeting mutated proteins in diseases, reducing side effects, and treating currently untreatable diseases like Alzheimer's. Desirable properties for new drug molecules include high selectivity, affinity, low toxicity, good pharmacokinetic properties, manufacturability, and intellectual property protection. Key guidelines from the ICH and FDA govern the development, manufacturing, and safety of new drug molecules. Plant-based medicines offer promising therapeutic compounds, such as artemisinin for malaria and taxol for cancer. Synthesis sources have produced drugs like ruxolitinib, ibrutinib, nivolumab, pembrolizumab, and ocrelizumab for various diseases. Software tools like molecular modeling, computational chemistry, cheminformatics, virtual screening, and machine learning aid in drug discovery and development by improving efficiency, accuracy, collaboration, creativity, and cost-effectiveness. Advantages of using software tools in drug discovery include increased efficiency, improved accuracy, facilitated collaboration, enhanced creativity, reduced costs, and increased safety. However, there are some potential disadvantages, such as limitations in accuracy, dependence on data quality, high software costs, complexity, lack of transparency, and ethical concerns. Overall, new drug molecules are essential for addressing various diseases, and software tools play a crucial role in accelerating the drug discovery process by providing predictive capabilities and aiding in decision-making.

Key words: Drug discovery, Mutated proteins, Side effects, Machine learning, Collaboration, Creativity.

INTRODUCTION

"Novel" drugs are new drugs never before approved or marketed. Innovative drugs often mean new treatment options for patients and advances in health care. In the fields of medicine, biotechnology and pharmacology, drug discovery is the process by which new candidate medications are discovered. A new molecule is developed by the innovator company/ organization in the early drug discovery stage, which after undergoing clinical trials could translate into a drug that could be a treatment for some disease. Synthesis of a new chemical entity is the first step in the process of drug development [1].

The need for new drug molecules

There are a number of reasons why new drug molecules are required. First, many diseases, such as cancer, are caused by mutations in proteins that are essential for cell function. These mutations can make the proteins more active or less active, which can lead to disease.

New drug molecules can be designed to target these mutated proteins and inhibit their activity, which can help to treat the disease [2-5].
Second, many drugs are effective in treating diseases, but they can also have side effects. These side effects can range from mild to severe, and they can include nausea, vomiting, diarrhoea, headaches, and fatigue. New drug molecules can be designed to have fewer side effects, which can improve the quality of life for patients [6-9].
Finally, new drug molecules can be designed to treat diseases that are currently untreatable. For example, there are currently no drugs that can effectively treat Alzheimer's disease. New drug molecules could be designed to target the proteins that are involved in Alzheimer's disease, which could help to slow down or stop the progression of the disease [10-13].
This study aims to provide an overview of the need for new drug molecules, their desirable properties, key guidelines for their development, and the contributions of plant-based medicines, synthesis sources, and software tools in drug discovery. The objective is to highlight the importance of new drug molecules and the role of software tools in accelerating the drug discovery process.

The ideal properties of new drug molecules
There are a number of properties that are desirable in new drug molecules. These include:

High selectivity
The drug should bind to its target protein with high selectivity. This means that it should not bind to other proteins in the body, which could lead to side effects.

High affinity
The drug should bind to its target protein with high affinity. This means that it should have a strong binding interaction with the protein, which will help to ensure that it is effective in treating the disease.

Low toxicity
The drug should have low toxicity. This means that it should not cause any harmful side effects in patients.

Good pharmacokinetic properties
The drug should have good pharmacokinetic properties. This means that it should be able to be absorbed into the body, distributed to the target tissue, and metabolized and eliminated in a way that is safe and effective.

Good manufacturability
The drug should be easy to manufacture in a cost-effective way.

Good intellectual property protection
The drug should have good intellectual property protection. This means that it should be difficult for other companies to copy the drug, which will help to ensure that the company that develops the drug can make a profit from it [14-19].

Key ICH guidelines for new drug molecules
The International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) has developed a number of guidelines for the development of new drug molecules. These guidelines are designed to ensure that new drugs are safe and effective. Some of the key ICH guidelines for new drug molecules include:

ICH Q1A(R2)
Good Manufacturing Practice for Active Pharmaceutical Ingredients This guideline provides guidance on the manufacturing of active pharmaceutical ingredients (APIs). It covers a wide range of topics, including the quality control of APIs, the validation of manufacturing processes, and the handling of APIs.

ICH Q1B(R2)
Good Manufacturing Practice for Finished Pharmaceutical Products This guideline provides guidance on the manufacturing of finished pharmaceutical products. It covers a wide range of topics, including the quality control of finished products, the validation of manufacturing processes, and the handling of finished products.

ICH Q2A(R1)
Validation of Analytical Procedures This guideline provides guidance on the validation of analytical procedures. It covers a wide range of topics, including the selection of analytical procedures, the design of validation studies, and the interpretation of validation results.

ICH Q3A(R2)
Stability Testing of New Drug Substances and Products This guideline provides guidance on the stability testing of new drug substances and

products. It covers a wide range of topics, including the selection of stability tests, the design of stability studies, and the interpretation of stability data.

ICH Q4B(R2)
Pharmacovigilance Plan for Drug Registration Applications This guideline provides guidance on the development of pharmacovigilance plans for drug registration applications. It covers a wide range of topics, including the identification of potential risks, the design of pharmacovigilance studies, and the monitoring of drug safety after marketing [20-27].

Key FDA guidelines for new drug molecules
In addition to the ICH guidelines, the US Food and Drug Administration (FDA) has also developed a number of guidelines for the development of new drug molecules. These guidelines are designed to ensure that new drugs are safe and effective for use in the United States. Some of the key FDA guidelines for new drug molecules include:

21 CFR 314.125
Investigational New Drug Application (IND) This regulation provides guidance on the submission of an IND to the FDA. An IND is required for any new drug that is being studied in humans. The IND must include a detailed description of the drug, the proposed clinical studies, and the safety data that have been generated in animals.

21 CFR 312.21
IND Safety Reports This regulation requires sponsors of INDs to submit safety reports to the FDA on a regular basis. These reports must include any new information about the safety of the drug, including adverse events, drug interactions, and serious safety concerns.

21 CFR 314.50
New Drug Application (NDA) This regulation provides guidance on the submission of an NDA to the FDA. An NDA is required for any new drug that is being marketed in the United States. The NDA must include a detailed description of the drug, the clinical studies that have been conducted, and the safety and efficacy data that have been generated.

21 CFR 314.101
Approval of New Drugs This regulation sets forth the criteria that the FDA uses to approve new drugs. These criteria include safety, efficacy, and manufacturing quality [28-32].

New drugs of plant origin
New drugs from plant origin are a growing area of research (**Figure 1**). This is due to the fact that plants contain a wide variety of compounds that can have therapeutic properties. Some of the most promising new drugs from plant origin include:

Artemisinin
Artemisinin is a compound that is extracted from the plant *Artemisia annua*. It is a powerful antimalarial drug that is effective against both Plasmodium falciparum and Plasmodium vivax.

Taxol
Taxol is a compound that is extracted from the bark of the Pacific yew tree (*Taxus brevifolia*). It is a powerful anticancer drug that is used to treat a variety of cancers, including breast cancer, ovarian cancer, and lung cancer.

Echinacea
Echinacea is a plant that is native to North America. It is a popular herbal remedy that is used to treat a variety of conditions, including the common cold, flu, and allergies.

Ginkgo biloba
Ginkgo biloba is a tree that is native to China. It is a popular herbal remedy that is used to improve cognitive function and memory.

St. John's wort
St. John's wort is a plant that is native to Europe and Asia. It is a popular herbal remedy that is used to treat depression.

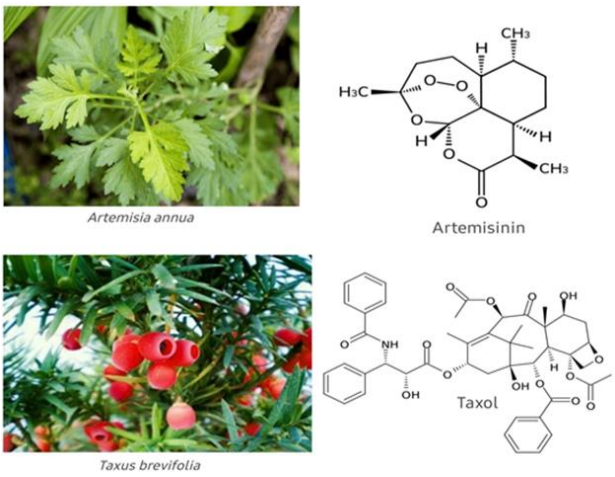

Fig. 1. Some new drugs from plant resources

These are just a few examples of the many new drugs that are being developed from plants. The potential of plant-based medicines is vast, and it is likely that we will see many more new drugs from plant origin in the years to come [33-37].

New drugs from synthesis sources

Some of the most promising new drugs from synthesis sources, as shown in **Figure 2**, include:

Ruxolitinib

Ruxolitinib is a small molecule drug that is used to treat myelofibrosis. It is a JAK inhibitor, which means that it blocks the activity of the JAK enzymes. These enzymes are involved in the regulation of cell growth and differentiation.

Ibrutinib

Ibrutinib is a small molecule drug that is used to treat chronic lymphocytic leukemia. It is a BTK inhibitor, which means that it blocks the activity of the BTK enzyme. This enzyme is involved in the regulation of B cell activation and proliferation.

Nivolumab

Nivolumab is a monoclonal antibody drug that is used to treat a variety of cancers, including melanoma, lung cancer, and kidney cancer. It is a checkpoint inhibitor, which means that it blocks the activity of the PD-1 receptor. This receptor is involved in the inhibition of T cell activation.

Pembrolizumab

Pembrolizumab is a monoclonal antibody drug that is used to treat a variety of cancers, including melanoma, lung cancer, and kidney cancer. It is a checkpoint inhibitor, which means that it blocks the activity of the PD-1 receptor. This receptor is involved in the inhibition of T cell activation.

Ocrelizumab

Ocrelizumab is a monoclonal antibody drug that is used to treat multiple sclerosis. It is a B cell depletion drug, which means that it destroys B cells. B cells are involved in the production of antibodies, which are proteins that help to fight infection [38-43].

Software tools for developing new drug molecules

There are several software tools that are commonly used for developing the new drug molecules. Some of the widely used software

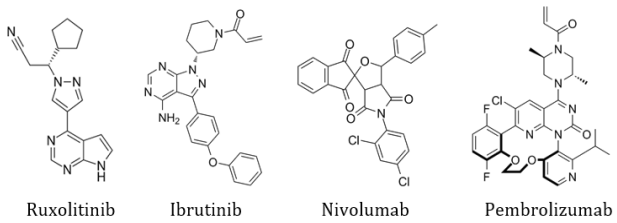

Fig. 2. Some new drugs from synthetic sources

tools include:

Molecular modeling software

This software is used to simulate the interactions of molecules and predict their behavior. It can be used to design new molecules and optimize their properties. Examples of molecular modeling software include Schrödinger, MOE, and Discovery Studio.

Computational chemistry software

This software is used to perform quantum mechanical calculations and simulations to study the chemical properties of molecules. It can be used to predict the behavior of molecules in different environments and to optimize their structures. Examples of computational chemistry software include Gaussian, NWChem, and GAMESS.

Cheminformatics software

This software is used to manage and analyze large databases of chemical information. It can be used to search for molecules with specific properties and to design new molecules based on existing data. Examples of cheminformatics software include ChemDraw, ChemAxon, and Pipeline Pilot.

Virtual screening software

This software is used to screen large databases of molecules to identify potential drug candidates. It can be used to predict the binding affinity of molecules to specific targets and to select the most promising candidates for further study. Examples of virtual screening software include Autodock, Glide, and GOLD.

Machine learning software

This software is used to develop predictive models based on large datasets of chemical information. It can be used to predict the properties of new molecules based on their structures and to identify patterns in large datasets. Examples of machine learning software include TensorFlow, Scikit-learn, and Keras.

These software tools are often used in combination to facilitate drug discovery and development [44-47].

Advantages of software tools

There are several advantages of using software tools in new drug discovery, including:

Increased efficiency

Software tools can simulate and predict the behavior of molecules, reducing the need for time-consuming and expensive experimental testing. This can save time and resources in the drug discovery process.

Improved accuracy

Software tools can provide accurate predictions of molecular behavior, allowing researchers to identify potential drug candidates with a higher likelihood of success. This can reduce the risk of failed clinical trials and improve the overall success rate of drug discovery.

Facilitated collaboration

Software tools can be used to share data and collaborate with other researchers, allowing for more efficient communication and faster progress in drug discovery.

Enhanced creativity

Software tools can provide researchers with new insights and ideas for drug development, allowing them to explore novel avenues and potential drug targets.

Reduced costs

By reducing the need for experimental testing, software tools can help to reduce the overall cost of drug discovery.

Increased safety

Software tools can be used to predict the safety of potential drug candidates, allowing researchers to identify and avoid potentially harmful compounds before they enter clinical trials.

Overall, software tools play an essential role in modern drug discovery, allowing researchers to identify and develop new drug candidates more efficiently, accurately, and safely [48-52].

Disadvantages of software tools

While software tools have many advantages in the new drug discovery, there are also some potential disadvantages to consider, including:

Limitations in accuracy

While software tools can provide accurate predictions of molecular behavior, they are not perfect and can sometimes produce results that are not entirely accurate. This can lead to false positives or false negatives in drug discovery, which can be costly and time-consuming to correct.

Dependence on data quality

Software tools rely on high-quality data to make accurate predictions, and poor data quality can lead to inaccurate results. This can be especially problematic when working with large datasets or when data is incomplete or inconsistent.

High cost of software

Some software tools used in drug discovery can be expensive to purchase and maintain, especially for smaller companies or academic institutions with limited budgets.

Complexity of software

Some software tools can be complex and require a high level of technical expertise to use effectively. This can be a barrier to entry for some researchers or companies that lack the necessary resources or expertise.

Lack of transparency

Some software tools may use proprietary algorithms or data, making it difficult for researchers to understand how the software works or to replicate results. This can limit the ability of researchers to validate or build on existing research.

Ethical concerns

The use of software tools in drug discovery can raise ethical concerns around the use of artificial intelligence (AI) and machine learning (ML) in decision-making processes, especially when it comes to issues of bias, accountability, and transparency [53, 54].

CONCLUSION

In conclusion, the development of new drug molecules is crucial for addressing various diseases by targeting mutated proteins, reducing side effects, and treating currently untreatable conditions. The ideal properties of new drug molecules include high selectivity, affinity, low toxicity, good pharmacokinetic properties, manufacturability, and intellectual property

protection. Key guidelines from organizations like ICH and FDA govern the development, manufacturing, and safety of the new drug molecules.

Plant-based medicines and synthesis sources have yielded promising therapeutic compounds, expanding treatment options. Software tools such as molecular modeling, computational chemistry, cheminformatics, virtual screening, and machine learning, enhance efficiency, accuracy, collaboration, creativity, and cost-effectiveness in drug discovery. While software tools offer advantages, limitations in accuracy, dependence on data quality, high costs, complexity, lack of transparency, and ethical concerns should be considered. Overall, new drug molecules and software tools play vital roles in advancing healthcare by providing effective treatments and accelerating the drug discovery process.

REFERENCES

1. Hughes JP, Rees S, Kalindjian SB, Philpott KL. Principles of early drug discovery. *Br J Pharmacol*. 2011;162(6):1239-49. doi:10.1111/j.1476-5381.2010.01127
2. Housman G, Byler S, Heerboth S, Lapinska K, Longacre M, Snyder N, et al. Drug resistance in cancer: An overview. *Cancers (Basel)*. 2014;6(3):1769-92. doi:10.3390/cancers6031769
3. Bhullar KS, Lagarón NO, McGowan EM, Parmar I, Jha A, Hubbard BP, et al. Kinase-targeted cancer therapies: Progress, challenges and future directions. *Mol Cancer*. 2018;17:48. doi:10.1186/s12943-018-0815-2
4. Cooper GM. The cell: A molecular approach. 2nd edition. Sunderland, MA, USA: Sinauer Associates Inc, 2000.
5. Rao KV, Faso A. Chemotherapy-induced nausea and vomiting: optimizing prevention and management. *Am Health Drug Benefits*. 2012;5(4):232-40. doi:10.1177/1934578X12444243
6. Ong JJY, De Felice M. Migraine treatment: Current acute medications and their potential mechanisms of action. *Neurotherapeutics*. 2018;15(2):274-90. doi:10.1007/s13311-018-0611-9
7. Stroup TS, Gray N. Management of common adverse effects of antipsychotic medications. *World Psychiatry*. 2018;17(3):341-56. doi:10.1002/wps.20519
8. Zhang P, Wang F, Hu J, Sorrentino R. Exploring the relationship between drug side-effects and therapeutic indications. *AMIA Annu Symp Proc*. 2013;2013:1568-77. doi:10.3389/conf.fninf.2013.2287322
9. Arrué L, Cigna-Méndez AC. New drug design avenues targeting Alzheimer's disease by pharmacoinformatics-aided tools. *Pharmaceutics*. 2022;14(9):1914. doi:10.3390/pharmaceutics14091914
10. Huang LK, Chao SP, Hu CJ. Clinical trials of new drugs for Alzheimer disease. *J Biomed Sci*. 2020;27(1):18. doi:10.1186/s12929-020-0624-1
11. Breijyeh Z, Karaman R. Comprehensive review on Alzheimer's disease: Causes and treatment. *Molecules*. 2020;25(24):5789. doi:10.3390/molecules25245789
12. Singh S, Malik BK, Sharma DK. Molecular drug targets and structure based drug design: A holistic approach. *Bioinformation*. 2006;1(8):314-20. doi:10.1016/S0973-2063(07)82280-7
13. Sun D, Gao W, Hu H, Zhou S. Why 90% of clinical drug development fails and how to improve it? *Acta Pharm Sin B*. 2022;12(7):3049-62. doi:10.1016/j.apsb.2022.04.007
14. Wang L, Wang N, Zhang W, Cheng X, Yan Z, Shao G, et al. Therapeutic peptides: Current applications and future directions. *Sig Transduct Target Therap*. 2022;7:48. doi:10.1038/s41392-022-01041-4
15. Palleria C, Di Paolo A, Giofrè C, Caglioti C, Leuzzi G, Siniscalchi A, et al. Pharmacokinetic drug-drug interaction and their implication in clinical management. *J Res Med Sci*. 2013;18(7):601-10.
16. Gupta H, Kumar S, Roy SK, Gaud RS. Patent protection strategies. *J Pharm Bioallied Sci*. 2010;2(1):2-7. doi:10.4103/0975-7406.62694
17. Mondal SS, Pingali V. Competition and intellectual property policies in the Indian pharmaceutical sector. *Vikalpa*. 2017;42(2):61-79. doi:10.1177/0256090917704561
18. Jamrógiewicz M. Consequences of new approach to chemical stability tests to active pharmaceutical ingredients. *Front Pharmacol*. 2016;7:17. doi:10.3389/fphar.2016.00017
19. Baek IH, Kim JS, Ha ES, Choo GH, Cho W, Hwang SJ, et al. Dissolution and oral absorption of pranlukast nanosuspensions stabilized by hydroxypropylmethyl cellulose. *Int J Biol Macromol*. 2014;67:53-7. doi:10.1016/j.ijbiomac.2014.03.006
20. Giordani A, Kobel W, Gally HU. Overall impact of the regulatory requirements for genotoxic impurities on the drug development process. *Eur J Pharm Sci*. 2011;43(1-2):1-15. doi:10.1016/j.ejps.2011.03.004
21. Behera BK, Sahoo SK. Biodegradable and bioinspired polymers for pharmaceutical formulations and drug delivery: A brief review. *World J Pharm Res*. 2012;1(3):591-625.
22. ICH Harmonized Tripartite Guideline Q2 (R1): Validation of analytical procedures: text and methodology. International Council for Harmonization; 2005. https://database.ich.org/sites/default/files/Q2%28R1%29%20Guideline.pdf.
23. ICH Guideline Q2 (R1), Validation of analytical procedures: text and methodology. European Medicines Agency; 2019. https://www.ema.europa.eu/en/documents/scientific-guideline/ich-q-2-r1-validation-analytical-procedures-text-methodology-step-5_en.pdf
24. ICH Q2 (R1), Validation of analytical procedures: text and methodology. GMP-Compliance.org; 2019. https://www.gmp-compliance.org/guidelines/gmp-guideline/ich-q2r1-validation-of-analytical-procedures-text-and-methodology
25. ICH Q2 (R1), Validation of analytical procedures: text and methodology. U.S. Food and Drug Administration; 2019. https://www.fda.gov/media/152208/download
26. Blair Holbein ME. Understanding FDA regulatory requirements for investigational new drug applications for sponsor-investigators. *J Investig Med*. 2009;57(6):688-94.
27. Leffel EK, LeClaire RD. Chapter 5 - Regulatory process in the United States of America, Europe, China, and Japan. In: Translational Medicines Tools and Techniques. Shahzad A (ed). Academic Press, Elsevier Inc: 2016; 109-33. doi:10.1016/B978-0-12-803460-6.00005-2

28. Chiodin D, Cox EM, Edmund AV, Kratz E, Lockwood SH. Regulatory Affairs 101: Introduction to investigational new drug applications and clinical trial applications. *Clin Transl Sci*. 2019;12(4):334-42. doi:10.1111/cts.12635
29. Kepplinger EE. FDA's Expedited approval mechanisms for new drug products. *Biotechnol Law Rep*. 2015; 34(1):15-37. doi:10.1089/blr.2015.9999
30. U.S. Food and Drug Administration. Regulations: Good Clinical Practice and Clinical Trials. https://www.fda.gov/science-research/clinical-trials-and-human-subject-protection/regulations-good-clinical-practice-and-clinical-trials
31. Krishna S, Bustamante L, Haynes RK, Staines HM. Artemisinins: Their growing importance in medicine. *Trends Pharmacol Sci*. 2008;29(10):520-7. doi:10.1016/j.tips.2008.07.004
32. Khanal P. Antimalarial and anticancer properties of artesunate and other artemisinins: Current development. *Monatsh Chem*. 2021;152(4):387-400. doi:10.1007/s00706-021-02759-x
33. Badshah SL, Ullah A. Increasing the strength and production of artemisinin and its derivatives. *Molecules*. 2018;23(1):100. doi:10.3390/molecules23010100
34. Mannan A. Survey of artemisinin production by diverse Artemisia species in northern Pakistan. *Malar J*. 2010;9(1):310. doi:10.1186/1475-2875-9-310
35. Manayi A, Vazirian M. Echinacea purpurea: Pharmacology, phytochemistry and analysis methods. *Pharmacogn Rev*. 2015;9(17):63-72. doi:10.4103/0973-7847.156449
36. Schwartz DM, Kanno Y. JAK inhibition as a therapeutic strategy for immune and inflammatory diseases. *Nat Rev Drug Discov*. 2017;17(1):78.
37. Ayala-Aguilera CC, Valero T. Small molecule kinase inhibitor drugs (1995–2021): Medical indication, pharmacology, and synthesis. *J Med Chem*. 2022;65: 1047-1131. doi:10.1021/acs.jmedchem.2c00236
38. Castelo-Soccio L, Kim H. Protein kinases: drug targets for immunological disorders. *Nature Rev Immunol*. 2023;15:1-23. doi:10.1038/s41577-023-00772-0
39. Zhong L, Li Y, Xiong L, Wang W, Wu M, Yuan T, et al. Small molecules in targeted cancer therapy: Advances, challenges, and future perspectives. *Sig Transduct Target Ther*. 2021;6(1):201. doi:10.1038/s41392-021-00787-2-w
40. Davids MS, Brown JR. Ibrutinib: A first in class covalent inhibitor of Bruton's tyrosine kinase. *Future Oncol*. 2014;10(6):957-67. doi:10.2217/fon.14.51
41. Szklener K, Michalski A. Ibrutinib in the treatment of solid tumors: Current state of knowledge and future directions. *Cells*. 2022;11(8):1338. doi:10.3390/cells11081338
42. Yu W, MacKerell AD Jr. Computer-aided drug design methods. *Methods Mol Biol*. 2017;1520:85-106. doi:10.1007/978-1-4939-6761-0_5
43. Koehler Leman J, Weitzner BD. Macromolecular modeling and design in Rosetta: Recent methods and frameworks. *Nat Methods*. 2020;17(7):665-80. doi:10.1038/s41592-020-0871-7
44. Temml V, Kutil Z. Structure-based molecular modeling in SAR analysis and lead optimization. *Comput Struct Biotechnol J*. 2021;19:1431-44. doi:10.1016/j.csbj.2021.05.048
45. Sharma V, Wakode SR, Lather V, Mathur R, Fernandes MX. Structure based rational drug design of selective phosphodiesterase-4 ligands as anti-inflammatory molecules. *Bull Pharm Res*. 2011;1(2):33-40.
46. Kumar V. Topological models for the prediction of tyrosine kinase inhibitory activity of 4-anilino quinazolines. *Bull Pharm Res*. 2011;1(2):53-9.
47. Batool M, Ahmad B, Choi S. A structure-based drug discovery paradigm. *Int J Mol Sci*. 2019;20(11):2783. doi:10.3390/ijms20112783
48. Carracedo-Reboredo P, Liñares-Blanco J. A review on machine learning approaches and trends in drug discovery. *Comput Struct Biotechnol J*. 2021;19:4538-58. doi:10.1016/j.csbj.2021.08.039
49. Dulsat J, López-Nieto B, Estrada-Tejedor R, Borrell JI. Evaluation of free online ADMET tools for academic or small biotech environments. *Molecules*. 2023;28(2):776. doi:10.3390/molecules28040776
50. Maxim LD, Niebo R, Utell MJ. Screening tests: A review with examples. *Inhal Toxicol*. 2014;26(13):811-28. doi:10.3109/08958378.2014.969201
51. Torres PHM, Sodero ACR. Key topics in molecular docking for drug design. *Int J Mol Sci*. 2019;20(18):4574. doi:10.3390/ijms20184574
52. Paul D, Sanap G, Shenoy S, Kalyane D. Artificial intelligence in drug discovery and development. *Drug Discov Today*. 2021;26(1):80-93. doi:10.1016/j.drudis.2020.08.007
53. https://www.genengnews.com/insights/virtual-drug-design-promises-real-benefits
54. https://www.cancer.org/cancer/types/breast-cancer/treatment/targeted-therapy-for-breast-cancer.html

*****