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# The Process Of Drug Designing In Modern Times: An Analytical Study

**AHMED NAWAZ KHAN**

Department of Pharmacy, Graphic Era Hill University, Dehradun, Uttarakhand, India 248002

**Abstract**

Any chemical substance that enters your body and causes a physiological effect is known as a drug. These may be administered orally or via injection. The pharmaceutical industry revolves around finding novel strategies for drug designing and development, and much has changed since the inception of this field. Today, drug designing is mostly based on computational methods such as computer aided drug designing and molecular docking. These computational methods have revolutionised the drug development process by making it less time-consuming and expensive conventional drug discovery methods. They also allow for a far more targeted methodology to drug design, increasing the probability of success in clinical trials. Additionally, the application of artificial intelligence (AI) in the hunt for novel medicines is rapidly making inroads. An enormous amount of information can be quickly sorted through by machine learning algorithms to find potential leads and create innovative molecules with desirable properties. One cannot imagine a world without drugs; therefore, it is imperative to keep enhancing the process to reach new zeniths of development. This paper aims to discuss and analyse the current process of drug designing.

**Keywords-** Molecular Docking, Drug Designing, Drug Discovery, Computer Aided Drug Designing, Machine Learning

## Introduction

Over the past decade, naturally produced product-based drug discovery has been a popular approach among scientists. Hundreds of products are in clinical trials, primarily as agents that show effects against cancer and infection. These have been sourced from fungi, bacteria, plants, animals, or semi-synthetic origin. An increased understanding of molecular biology has helped identify naturally produced products as targets or leads, and combinational chemistry approaches that utilise organic product scaffolds are being used to create screening libraries that are very similar to drug-like compounds. Interestingly, these products can be used in treatment therapies for a range of diseases and disorders like cardiovascular issues, inflammation, metabolic imbalances, and skin infections and are of a hormonal, neuropharmacological, or immunosuppressive nature (Harvey, 2008). One of the most significant benefits of natural products is that they have evolved over millions of years, resulting in diverse ecosystems of chemical structures with discrete biological activities. These molecular and biochemical structures are utilised as origin points for the development of new drugs. For instance, chemists at the 'Eisai Research Institute' synthesised halichondrin B to create E7389, a innovative tubulin inhibitor in clinical trials against breast cancer. The novel drug has a different scaffold structure from its parent molecule (Newman, 2008). It is quite exhilarating to see the transformation of the folklore of the use of medicinal plants as therapies into scientifically backed research. This has been

brought about by fields like systems biology, which combines analytical chemistry, biochemistry, and bioinformatics to analyse thousands of small compounds or molecules (metabolites, proteins, genes, or even larger molecules like glycans and lipids) in biological systems. Such initiatives led to the creation of large mass spectral or NMR spectral libraries that provide complete characterization of naturally bioactive molecules, thereby aiding in their use in drug discovery (Dias, Urban, & Roessner, 2012).

Another such field is bioinformatics, which has opened new avenues for drug discovery and provided an abundance of tools and databases to make the process much faster and easier. ChEMBL is a large-scale bioactivity database that contains detailed intelligence on the physiological activities of small molecules, primarily those tested for their ability to interact with proteins and other targets. The ChEMBL database contains over 2 million bioactivity measurements for over 1 million compounds, making it one of the most extensive and comprehensive databases of its kind. Its user-friendly interface and advanced search capabilities make it a popular choice among researchers (Gaulton et al., 2011). The Schrödinger computational suite is a popular software package for analysing protein-peptide interactions. It provides an array of software tools for molecular modelling and simulation, such as Glide and Piper, as well as “molecular docking, molecular dynamics simulation, and quantum mechanics”-based methodologies. It, like ChEMBL, has an easy-to-use interface and powerful analytical capabilities, making it an excellent tool for new therapeutic research. The accuracy of the simulations, however, is determined by the quality of the input structures and force fields used in the simulation studies (Bhachoo & Beuming, 2017). These methods and tools have been discussed further.

**Literature Review**

In 2007, fragment-based drug designing completed almost a decade's worth of research and advances. As the name suggests, this method deals with working with smaller parts of the drug, or ‘fragments,' to better simplify the computational process of ligand and receptor studies. These ligands and receptors are usually drug targets. Eventually, all the information from different fragments is put together for complete characterization. Researchers Hajduk & Greer (2007) have talked about Abott Laboratories as a storehouse of fragment-based drug designs. They have developed several drugs with anti-tumour effects (in animal models), such as ABT-518 and ABT-737, that target enzyme matrix metalloproteinase (MMP), and BCL-2 (B-cell Chronic Lymphocytic Leukemia-2), and BCL-2-like 1 (BCL-XL) proteins, respectively. Fragment-based drug design has been successful to a certain extent but is limited by the need for large amounts of purified proteins. Future growth depends on the ability to express refractory proteins heterologously and on new processes for fragment screening. Advances in the computational scrutiny of fragment binding could reduce dependence on experimental screening.

Imagine being able to make a drug from scratch; this extremely time consuming and attention requiring process has been made simpler with the help of computers. De novo drug design involves target identification, compound selection and optimisation, and validation of the final drug candidate. Virtual screening is used to identify potential lead compounds, which are optimised using computational methods. This process is known as CADD, or computer-aided drug designing. There are two approaches to this process: atom-based and fragment-based. The latter is a shortcut and has been discussed earlier on, while the former has benefits such as the ability to fine-tune molecules and the ability to create a library or chemical world, but this makes it more difficult to find useful compounds (Hartenfeller & Schneider, 2010). These library compounds are then subjected to the “SMILES” (“Simplified Molecular Input Line System”) method, which is a clear and repeatable way to represent molecules in a linear stretch of insignia that computers could read and store quickly. “SMARTS”

("SMILES ARbitrary Target Specification") is an expansion of SMILES that offers substructure search functionality and allows for variation in represented molecular structures. For flexibility in chemical names, SMARTS includes unique atomic and bond icons as well as logical operators like "AND," "OR," and "NOT." For instance, the symbol ";" in SMARTS notation corresponds to any type of bond, and the atom [C,N] i.e., an atom that can be either an aliphatic carbon or an aliphatic nitrogen (Sliwoski, Kothiwale, Meiler, & Lowe, 2013).

Computer-aided designing can be further broken down into two foremost fields: “structure-based drug design (SBDD)” and “Ligand-based drug design (LBDD)”. Both of these have been described below, according to Macalino, Gosu, Hong, & Choi (2015) -:

1. SBDD- A 3D polymeric structure is used as the basis for the design and evaluation of ligands in the SBDD process. De novo and in-silico are two categories into which it can be divided. Virtual screening makes use of small molecule libraries to find compounds with bioactivity, while de novo involves finding tiny fragments that match the binding domain. Molecular docking and scoring is the most popular methods of SBDD and is described in further analysis. CASTp, ConCavity, and eFindSite are commonly sed for binding site prediction.

2. LBDD- To pinpoint the structural and physicochemical characteristics causing the observed biological activity, ligand-based design methods are used. “Quantitative structure-activity relationships” (QSARs) based and approaches based on pharmacophore models are typical ligand-based design strategies. The foundation such QSAR studies is the idea that adjustments in bioactivity are connected to structural and molecular changes in a collection of compounds. Enough bioactivity data, the right choice of compounds, the absence of autocorrelation, and verification using internal and/or external validation are all requirements for producing a trustworthy QSAR model. MOLFEAT, E-Dragon, and Open3DQSAR can be used for QSAR model analysis,

Molecular docking is a widely used computational tool for predicting the connecting interactions between a ligand and a protein. The preparation of these protein and ligand structures, creation of a grid-based depiction of the protein active site, location, and optimisation of the ligand in the active site and scoring of the ligand-protein complex are all steps in the molecular docking process. In the first step, water molecules are taken out of the protein and ligand structures, hydrogen atoms are added, and the structures are then optimised using energy minimization methods. The ligand is then inserted into the protein's active site using a search algorithm in the second step after a grid-based representation of the protein's active site is created to look for potential binding sites. In the final step, the ligand-protein complex is scored using a scoring function that evaluates the fitness of the ligand at the active site. The results of molecular docking can provide valuable insights into the contact interfaces between a ligand and a protein, which can be potentially utilised to guide the design of new and more effective inhibitors (Ferreira, dos Santos, Oliva, & Andricopulo, 2015).

There are two approaches to molecular docking programmes. These include the simulation approach and the shape complementarity approach. The simulation approach involves physical separation of the ligand and target molecules, followed by allowing them to bind post a “definite time of moves” in the structural space of the target molecule. This strategy is better than the shape complementarity one because it can accept ligand flexibility into molecular modelling tool more readily. The shape complementarity approach uses the surface topographical characteristics of the ligand and target to

help with molecular docking. Accomplishment of molecular docking, the target's surface is defined in terms of its hydrophilic surface area, whereas the surface of the ligand is explained in terms of the equivalent surface illustration. On the other hand, the shape complementarity approach is prompt and strong, and involves the quick inspecting of thousands of different ligands in a jiffy to find out the possible binding properties of the ligand on the target molecular surface. (Agarwal & Mehrotra, 2016).

The main technique for figuring out the 3-D structures of nucleic acids, proteins, and viral capsids has been macromolecular X-ray crystallography. It does have some elementary flaws, though, that could be fixed or supplemented by new techniques and technologies used in other branches of structural biology. As many drug candidates are attached to the cell membrane are hydrophobic, solubility is a big hindrance in macromolecular X-ray crystallography for drug identification. The solution to this may be provided by other techniques like NMR and EPR. While NMR offers details about the dynamics of the molecules under investigation, EPR adds more details about various protein conformation states. The third restriction on X-ray crystallography is the detection and characterization of protein modifications such as ubiquitination, phosphorylation, methylation, glycosylation, and acetylation, as these require a relatively homogenous fraction of macromolecules to obtain diffraction quality. In any scientific field, the validation of results is extremely important. Mass spectrometry is an outstanding technique to confirm or deny testable hypotheses on structures determined by X-ray crystallography. “Chemical cross-linking with subsequent mass spectrometry (CXMS)” provides experimental restraints for other techniques, providing proof about the relative assemblies between two domains or two subunits. CXMS complements X-ray crystallography by providing information on interactions within protein centres or between many different proteins (Zheng et al., 2015).

As with any other field in science, AI technology has been employed in drug designing as well. The newest edge in computer based drug discovery is machine learning, that uses human generated data and knowledge to teach and modify itself which compounds can bind to which targets. Multiple firms have come up to create drug-finding algorithms that can be tested in collaboration with large pharmaceutical companies. In 2015, “Exscientia” trained their Artificial Intelligence based tools to find small compounds and molecules that modify two G-Protein Coupled Receptors simultaneously and revealed that they only needed to synthesize less than 400 molecules to identify a potential target. The drug thus found is now moving towards clinical trials for psychiatric illness (Mullard, 2017). Thus, AI and machine learning algorithms have the power to change the entire playing field of drug discovery.

**Objectives of the study**

To measure the process of drug designing in modern times

**Research Methodology**

This study is empirical in nature. In this study 203 respondents were contacted to review the benefits of supply chain digitalisation in manufacturing industry. The data analysis was done with the help of the frequency distribution.

**Data Analysis and Interpretation:**

**Table 1 Modern drug designing focuses on identifying specific molecular targets within the body that are involved in the disease process**

| Particulars | Agree | Disagree | Can't Say | Total |
|---|---|---|---|---|
| **Respondents** | 157 | 27 | 19 | 203 |
| **% Age** | 77.34 | 13.30 | 9.36 | 100 |

Table 1 presents that with the statement modern drug designing focuses on identifying specific molecular targets within the body that are involved in the disease process, it is found that 77.34% of the respondents agree with this statement.

**Table 2 Advances in computational power and algorithms have revolutionized the drug design process**

| Particulars | Agree | Disagree | Can't Say | Total |
|---|---|---|---|---|
| **Respondents** | 153 | 29 | 21 | 203 |
| **% Age** | 75.37 | 14.29 | 10.34 | 100 |

Table 2 presents that with the statement advances in computational power and algorithms have revolutionized the drug design process, it is found that 75.37% of the respondents agree with this statement.

**Table 3 Modern drug discovery often involves screening large libraries of molecules to identify compounds that show activity against the target of interest**

| Particulars | Agree | Disagree | Can't Say | Total |
|---|---|---|---|---|
| **Respondents** | 151 | 30 | 22 | 203 |
| **% Age** | 74.38 | 14.78 | 10.84 | 100 |

Table 3 presents that with the statement modern drug discovery often involves screening large libraries of molecules to identify compounds that show activity against the target of interest, it is found that 74.38% of the respondents agree with this statement.

**Table 4 Advances in genomics and other "omics" technologies have enabled the development of personalized medicine**

| Particulars | Agree | Disagree | Can't Say | Total |
|---|---|---|---|---|
| **Respondents** | 149 | 31 | 23 | 203 |
| **% Age** | 73.40 | 15.27 | 11.33 | 100 |

Table 4 presents that with the statement advances in genomics and other "omics" technologies have enabled the development of personalized medicine, it is found that 73.40% of the respondents agree with this statement

## Conclusion

The discovery and development of drugs have significantly improved as a result of developments in both experimental and computational techniques. Some of the most important technologies being used right now to speed up the drug discovery process include molecular docking, cryo-electron

microscopy, NMR, EPR, MS, and AI-based methods. These technologies have enabled scientists to better understand the molecular mechanisms of diseases and to design more effective drugs with fewer side effects. The secret to effective drug discovery lies in combining various techniques to obtain a comprehensive understanding of the target and ligand interactions. Each method comes with its benefits and disadvantages. The future of drug development appears bright, with the potential to completely change how new drugs are found and developed, improving patient care outcomes. In conclusion, the process of discovering new drugs is difficult and complex, necessitating a multidisciplinary approach.

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