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Advances in Drug Design: Techniques and Strategies

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Abstract

Drug design is an ancient and intricate pharmaceutical discipline. Since Emil Fisher proposed at the end of the 19th century that the interaction between a medication and its receptor is similar to that between a key and a lock, many advancements have been achieved in the area of drug design. Drug design has steadily evolved into a logical, well-structured discipline with a strong theoretical foundation and real-world applications. Examine the many studies conducted by researchers on drug creation approaches and tactics in this page. According to the review, a number of methods, including metabolomics, genomics, and proteomics, complement other approaches well. Additionally, the most recent drug design techniques can be used to find drug molecules with higher target specificity, accuracy, and safety at a lower cost and in a shorter amount of time. Furthermore, recent drug development efforts across a variety of disorders heavily rely on "Computer-Aided Drug Design (CADD)" methodologies. Computer approaches have significantly accelerated the development and optimisation of potential therapeutic medications.

Keywords: Drug design, Computer-Aided Drug Design (CADD) techniques, Structure-Based Drug Design, Ligand Based Drug Design, Artificial intelligence (AI), drug discovery, etc.

1 Introduction

Medication is a synthetic drug that alters biological functions in order to treat, diagnose, or prevent illness. Drugs may be made synthetically or come from natural sources. In addition to being safe and non-toxic, a drug should have a specific action, minimal side effects, chemical and metabolic stability,

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synthetic feasibility, solubility in water at therapeutic concentrations to avoid bloodstream precipitation, solubility in lipids to facilitate distribution during the body and the ability to cross lipid membranes, and uniqueness [1], [2]. Drugs interact with certain bodily targets to produce their effects. Because of these interactions, two types of impacts are produced: the effects of the drug on the body and the effects of the drug on the body. Pharmacodynamics takes these effects into account, whereas pharmacokinetics does the same [3], [4]. Pharmacodynamics is the study of how drugs work, how concentration and effect are related, and how side effects occur. The study of pharmacokinetics examines the drug's absorption, distribution, metabolism, and excretion over time; these are referred to as ADME processes or ADME characteristics [5], [6].

A. Drug design

The terms "drug design" and "ligand design," which refer to the creation of molecules that will attach firmly to their target, are comparable. Even if design techniques for predicting binding affinity are relatively successful, a number of additional features, such as "bioavailability, metabolic half-life, and side effects", needs to be adjusted before a ligand may become a safe and effective drug [7]. It is often challenging to forecast these additional features using logical design methods. "Drug design," "rational drug design," or simply "rational design" refers to the innovative process of creating new medications by a knowledge of a biological target. In order to provide the patient with a therapeutic advantage, the medication is often a small, organic molecule that stimulates or prevents the function of a biomolecule, such as a protein [8], [9]. In its most basic form, drug design is the process of creating compounds that will attach to a biomolecular target because they are complimentary in shape and charge. Although not always, computer modelling techniques are often utilised in medication design [10]. This kind of modelling is also known as computer-aided drug design. Finally, a technique for developing novel pharmaceuticals, structure-based drug design relies on elucidating the biomolecular target's three-dimensional structure [11]. The class of drugs known as biopharmaceuticals, which includes therapeutic antibodies and peptides in particular, is growing in importance alongside small molecules. Computational techniques have also been developed to increase the stability, selectivity, and affinity of these protein-based treatments [12], [13].

B. Prodrugs and analogues

Analogues and prodrugs are two different kinds of molecules that may be created in drug design to alter the drug molecule.

1. Prodrug

In order to become more active and have effects, prodrugs—inactive or low-activity drug forms—go through chemical or enzymatic transformation in vivo. The prodrug conversion to active is intended to occur at the target location, midway during the absorption phase, or pre-post, depending on the needs. Prodrugs are divided into two categories: bioprecursor prodrugs and carrier-linked prodrugs. During an enzymatic or chemical process, the carrier-linked prodrugs (promoeity) temporarily bind to the active moiety that separates within the body [14]. The bioprecursors are the result of molecular conversion of

an inactivated moiety and do not exhibit promoeity, while these prodrugs primarily consist of ester and amid, phosphate, carbamates, and oximes, among others. Within the organism, metabolic conversion transforms the bio-precursors into the active moiety. Prodrugs enhance medication delivery to the brain and allow the active component to be metabolised naturally. Parkinson's disease is treated with L-dopa, a traditional example of a prodrug. Dopamine is very hydrophilic and vulnerable to enzymes in the brain's epithelial cells, which limits its absorption [9].

2. Analogue design

Creating a new molecule that is physiologically comparable to the original therapeutic molecule is known as analogue design. Analogue molecules have better qualities than native ones. In the field of drug development, this method is useful, straightforward, and widely used. Sixty-six percent of small molecules are made using this technique, and several analogue-based compounds, including as steroids, prostaglandins, anticancer medications, and antibiotics, have been commercially accessible for the last fifty years. Before the project is started, the pharmacokinetic and hazardous aspects are taken into account. Actually, drug-structure repositioning creates new drugs in new fabrics, while analogue design creates new chemical entities [9], [15].

2 Literature Review

(Niazi & Mariam, 2024) [16] Computer-Aided Drug Design (CADD), which bridges the fields of biology and technology, is a revolutionary force in the ever-changing field of drug development. This paper covers the history of CADD, how it was classified in structure-based and ligand-based approaches, and how important it is for expediting and simplifying drug discovery. As CADD develops, protecting data privacy and integrating a variety of biological data become critical. There are still issues that need strong ethical frameworks and algorithm optimisation. In order to create a healthier, more promising future for drug development, this paper's conclusion emphasises the need of taking proactive steps in traversing the ethical, technical, and pedagogical boundaries of CADD.

(Ouma et al., 2024) [17] provides information on computational resources for ab initio and silico approaches and methods, such as AI uses for drug discovery and drug metabolism estimates for drug design. MD, molecular docking, QM, QM/MM, and DFT are computational techniques for drug design and development. Thus, the developing approach of synergistically combining various techniques affects traditional treatments for complicated disorders. We address ligand- and structure-based drug discovery, MD simulation force field models, docking techniques, and subtractive and additive QM/MM coupling. Docking and virtual screening, scoring functions, hit optimisation, and ADMET property assessment will be the focus as computer-aided drug (CADD) approaches improve. Based on recent results, computational tools will help find new molecules with good therapeutic effectiveness.

(Gupta et al., 2024) [18] highlights the many computational methods used in the process of in silico aided drug discovery. “Quantitative Structure-Activity Relationship (QSAR) models”, molecular docking, molecular dynamics simulations, and artificial intelligence-based techniques are all essential

for accelerating drug discovery and optimisation. With a focus on their advantages, disadvantages, and possible future paths, this study critically assesses the status of computational approaches in silico aided drug creation. The field of pharmaceutical research has seen a substantial transformation as a result of the use of computational methods into drug discovery. For the quick and efficient discovery of new therapeutic medicines, the combination of in vitro and in silico techniques offers great potential as these techniques advance, closing the gap between computational predictions and experimental validations.

(Naithani & Guleria, 2024) [19] examines the diverse range of integrated computational approaches used in the assessment and discovery of lead compounds. "Molecular modelling, drug-target interaction analysis, cheminformatics, structure-based drug design (SBDD), molecular dynamics simulations, high-throughput screening, and ADMET (absorption, distribution, metabolism, excretion, and toxicity)" computation are some of the techniques that fall under this category. In order to create new therapeutic agents to address a variety of medical problems, this review reveals the vital role of integrative computational methods and highlights how they can transform drug discovery into a more efficient, cost-effective, and target-oriented endeavour.

(Elizabeth & Amalia, 2022) [20] "Structure-Based Drug Design and Ligand Based Drug Design" are two computational drug discovery techniques that have been shown to speed up and improve the likelihood of discovering novel medications. The purpose of this article is to provide a summary of several methods for developing new drugs, with a focus on the advantages of computational methods. The two computational approaches are discussed in this paper, with a focus on their application, which should help the drug research and development industry become more cost- and time-efficient. The drug discovery stage may be shortened to 9–13 years by using computational approaches, while the usual method to new drug development takes around 11–16 years.

(Dheeraj Bisht et al., 2020) [9] Researchers are working on structure-guided drug design utilising a three-dimensional target structure. The drug molecule found by target-based drug design has a lot of promise to prevent different illnesses, but it also has a lot of negative effects. In order to develop a promising therapeutic candidate, this paper delves deeply into the ways in which a multidisciplinary approach to "combinatorial chemistry, gene expression research, structure-based drug design, and artificial intelligence-based drug design" may be used. In the future, creating new medication candidates would need increasingly advanced computer-based techniques.

(Ferreira et al., 2015) [21] Combining experimental and computational methods has proven very beneficial in the discovery and creation of new, promising molecules. In contemporary drug design, molecular docking techniques are widely used to investigate the ligand conformations that are incorporated into the binding sites of macromolecular targets. The ligand-receptor binding free energy is also estimated using this method by assessing important events related to the intermolecular recognition process. These days, there are many different docking algorithms accessible, so knowing the benefits and drawbacks of each approach is crucial for creating strategies that work and producing results that are pertinent. This review's objective is to analyse current molecular docking techniques used in

medicinal chemistry and drug development, examining the field's advancements and the function of combining structure- and ligand-based approaches.

3 Conclusion

The advancements in drug design have revolutionized pharmaceutical research, enabling the discovery of more precise, safe, and cost-effective therapeutic agents. Techniques such as genome expression profiling, metabolomics, genomics, and proteomics, coupled with high-throughput screening, have enhanced target specificity and reduced drug discovery timelines. Structure-based drug design has significantly improved ligand efficiency, while computational methods, including Computer-Aided Drug Design (CADD), have accelerated drug optimization. By accurately forecasting medication interactions and processes, the combination of deep learning and artificial intelligence (AI) has further revolutionised drug research. Even more computational power might be available with quantum computing, which could improve drug design techniques. These advancements have strengthened the pharmaceutical industry's ability to develop treatments for complex diseases with unprecedented efficiency. The synergistic application of computational tools and AI not only enhances drug development but also aligns with the United Nations' Sustainable Development Goal 3, promoting global health and well-being. As drug design continues to evolve, these cutting-edge approaches will drive the development of novel therapeutics, ultimately improving patient outcomes and advancing medical science.

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