**A comprehensive analysis of pharmaceutical compound utilization in the context of molecular docking

1.Mr.Pramod B Chikkodi**

**2.Miss.Rutuja Dashrath Chougule**

**1.HOD -Department of pharmacy ( Nootan college of pharmacy)**

**2.B. Pharmacy student -Nootan college of pharmacy ,sangali**

**Email – rutujachougule4548@gmail.com**

**Abstract -**

Drug design is a longstanding and complex medical science. There have been many successes in drug development since the late 19th century, when Emil Fisher suggested that the interaction between drugs was similar to a key and a lock. Drug development has increasingly evolved into qualitative research integrated with theoretical and practical methods. Drug development is no w the best path to drug discovery. It uses the latest advances in science andtechnology and incorporates them into its extensive arsenal of methods and tools to achieve its main goal: to discover effective, unique, nontoxic, safe and effective medicine

**Keywords**: Drug design, drug discovery and development, QSAR, molecular docking, molecular dynamics, virtual analysis

 **Introduction-**
A drug is a foreign molecule that affects biological processes and is used to prevent, diagnose or treat diseases [1]. Medicines can be natural or synthetic.The ideal drug should have specific effects, be safe, nontoxic, as little or as nontoxic as possible, be chemically and metabolically stable, be able to be synthesized, be soluble in purification water to prevent precipitation in the blood, and be soluble in lipids. It spreads through te  lipid membrane and distributes throughout the body, eventually becoming a molecule

The drug discovery and development process has three main phases: drug discovery, preclinical development, and clinical trials. Drug discovery begins with the discovery of a hit molecule. Hit is a molecule that reveals activity in a test [5,6].

The molecular structure is subsequently fine-tuned to enhance affinity and selectivity, diminish toxicity, boost water and lipid solubility, generally improve ADME properties, and transform molecules identified as hits into lead molecules. Further optimization of lead molecules could produce competitive drugs. Preclinical investigations primarily aim to uncover the drug's mechanism of action, its pharmacokinetics in animals, including aspects like bioavailability, the presence of toxic metabolites (if any), release route, its effectiveness in animals, drug development, and the assessment of safety models. Clinical trials, the most prolonged and costly phase, are comprised of three stages. The initial phase involves the participation of up to 100 healthcare professionals. The primary objectives of this stage are to assess the drug's safety in humans, its pharmacokinetics in humans, and the presence of any immediate side effects.

**Medicines are  high value added products -**

The pharmaceutical industry ranks among the top-performing businesses worldwide. It is not affected by economic or political crises because the number of patients is always there and unfortunately, when there is a crisis, the number of patients also increases. If we look at the financial statements of 5 of the 10 largest pharmaceutical companies (Pfizer, GlaxoSmithKline, Roche, Sanofi and Novartis) for the last 10 years, we can see several interesting facts (Figure 1) [7]. On average, the cost of sales accounts for only 23% of the company's total revenue. Almost half (43%) of revenue is spent on sales, general and administrative expenses. Overall, 16% of all revenue is reinvested in research and development; This is more than the average of 7% of other businesses. Medicines appear to be value-added. Net profit is 18%. This positions the pharmaceutical industry as one of the top three most lucrative sectors globally.

The cost of drug production is increasing exponentially; doubling every ten years. The average cost of a new drug is estimated to be approximately $2.6 billion (2013) [8]. The cost of biological products is particularly high; proteins, monoclonal antibodies, diagnostic products and vaccines [9].

**Drug Discovery -**

There are numerous approaches to uncovering drugs. One of the oldest methods is through serendipity, which involves stumbling upon discoveries by chance or through trial and error. There are many examples of the invisibility of medicine in the history of pharmacy [14]; we start with the most popular of these: the story of penicillin, which saved millions of lives during World War II, for which Fleming, Flory, and Qian won the Nobel Prize. In 1945. This medicine is still used today.

The first benzodiazepine, chlordiazepoxide, was also discovered unintentionally. In the 1920s and 1930s, Leo Sternbach at the University of Kraków developed various heptodiazines for producing synthetic dyes.

Another approach to drug discovery is chemical modification of known drugs or natural products [2,16]. Aspirin was discovered through chemical modification [17]. The natural product salicylic acid is acetylated to ensure stability and reduce allergic reactions in the gastric mucosa. Small drug modifications can improve the treatment of several generations of drugs. For example, ranitidine is a chemical modification of cimetidine with a more potent and longer half-life [18] and pindolol is derived from propranolol but avoids the initial effect in the liver and exhibits high levels of bioavailability [19].

Virtual database searching or scanning databases via high-throughput (HTS) analysis is another method for discovering new drugs [20,21,22]. The first sulfa drug, Perondol, was discovered by random in vitro screening of various dyes for their antibacterial properties [2,23]. Paclitaxel is a new anti-cancer drug also discovered by HTS [24].

**Drug Development – History**

The science of drug development has achieved many achievements, making it the primary method of drug research now and in the future [2] . The first of these is understanding drug receptor identification.

In the initial years of the 1890s, Emil Fisher likened the interaction between drugs and receptors to that of a key fitting into a lock. It is believed that both drugs and receptors interact as waste without altering their metabolism. Recently, Daniel Koshland said that when two molecules interact, they undergo a dynamic change and adopt the best conformation to bind to each other. This theory has been proven time and time again by X-ray models and computer experiments, and we now know that ligands change their relationships during interactions and adopt the perfect fit for contact with space.

**Current Drug Development Method -**

Currently, artificial intelligence (AI) has entered all aspects of the drug discovery process [40, 41, 42]

In the field of drug development, artificial intelligence is applied to anticipate the three-dimensional structure of proteins, interactions between drugs and proteins, and the creation of drug molecules from the ground up. Proficiency in pharmacology is employed to tailor specific molecules and various drugs. In chemical applications, intelligence can design synthesis methods, predict reaction yields, and explain reaction mechanisms. AI is very good at repurposing old drugs for new therapeutic purposes. In drug analysis, toxicity, biological activity, ADME products, physical and chemical properties, etc. There is undoubtedly an indispensable role that artificial intelligence plays in predictive analysis.

Discussion

The utilization of artificial intelligence (AI) in drug design has proven transformative, enabling the tailored design of specific molecules and a wide array of drugs. In the realm of chemical applications, AIdemonstrates its prowess by designing synthesis methods, predicting reaction yields, and elucidating reaction mechanisms. One notable strength lies in AI's adeptness at repurposing existing drugs for novel therapeutic purposes. In drug analysis, AI plays an indispensable role in forecasting various aspects such as toxicity, biological activity, ADME (absorption, distribution, metabolism, and excretion) properties, and physical and chemical attributes.

In the future, trends in drug design are expected to be significantly shaped by progress in science and technology. The current COVID-19 pandemic has emphasized the necessity of accelerating research and development for drugs and vaccines. Investing in drug development is crucial as a well-developed drug candidate during early testing stages significantly reduces the likelihood of failure in subsequent, more costly clinical trials. AI emerges as a promising solution in this context, offering new, efficient, and cost-effective methods for drug discovery.

The pandemic has prompted a reevaluation of strategies to accelerate drug development, and AI stands at the forefront of this revolution. Its capacity to rapidly collect and analyze vast amounts of data allows for the swift identification of suitable targets and ligands, facilitating the design and execution of tests. Looking forward, a central goal in drug development is the ability to design and manufacture unique, non-toxic, and patient-specific drugs within a remarkably short timeframe—potentially within hours. Although this goal might appear ambitious at present, it is entirely achievable in the future.

In essence, AI holds the key to overcoming challenges in drug discovery by streamlining processes, reducing costs, and enhancing efficiency. The marriage of AI with drug development not only addresses the immediate needs posed by the pandemic but also charts a course towards a future where personalized medicine becomes a reality. As technology continues to evolve, the symbiotic relationship between AI and drug design is likely to reshape the landscape of pharmaceutical research and development, ushering in an era of more precise, effective, and patient-centric therapeutics.

**Future Trends in Drug Design-**

All advances in science and technology will have immediate applications in medicine, pharmacy, drug discovery and development. Investing in drug development is necessary because the better a drug candidate is developed during testing, the less likely it is that the drug will fail at the next stage when testing is expensive, again especially in clinical trials. The COVID-19 pandemic is compelling us to reconsider strategies for expediting the research and development of drugs and vaccines. Drug discovery requires new, efficient and lowcost methods, and artificial intelligence can provide them. Artificial Intelligence (AI) has the capability to rapidly gather and analyze extensive data within a brief timeframe, choose suitable targets and additional ligands, and formulate and conduct tests.. The key goal of future drug development is to create the ability to design and manufacture unique, nontoxiceffective, patientspecific drugs within hours. Although this goal seems promising now, it is completely achievable in the future.

**Types of drug design**

**1.Ligand-based therapy**

Drug design based on ligands (or indirect drug design) depends on understanding other molecules that interact with the specific biological target. These other molecules can be used as a pharmacophore model, which defines the minimum required structure that a molecule must bind to its target. [36] Models of biological targets can be created from their binding information, and these models can be used to design new molecular products that interact with the target. Structure-activity relationships (QSARs) can also be provided, where the calculated relationship between molecular substances and their biomarkers can be provided. These relationships in Quantitative Structure-Activity Relationships (QSAR) can be employed to forecast the activity of novel analogs.

**2.Structure-based**

Structure-based drug design (or direct drug design) is based on knowledge of the three-dimensional structure of the biological target obtained by methods such as X-ray crystallography or NMR spectroscopy. [38] If the experimental structure of the target cannot be obtained, the homology structure of the target can be created based on the experimental structure of the relevant protein. Using the biological target model, interactive imagery, and the doctor’s perspective, drug candidates predicted to bind to the target through social and emotional selection can be created. Additionally, many automated calculations can be used to introduce new drug users.

**Conclusion**

In conclusion, the efficacy of drug design hinges on the successful binding of a drug to its target. The creation of models for biological targets based on binding information is pivotal, serving as a foundation for the development of innovative molecular products designed to interact with these targets. The incorporation of Structure-Activity Relationships (QSARs) is essential, offering a calculated understanding of the relationship between molecular substances and their respective biomarkers. These QSAR relationships play a crucial role in predicting the activity of novel analogues. Moreover, Structure-Based Drug Design, also referred to as direct drug design, depends on a thorough understanding of the three-dimensional structure of the biological target. Methods such as X-ray crystallography or NMR spectroscopy are utilized to acquire this structural data. If obtaining the experimental structure of the target proves challenging, generating a homology structure based on the experimental structure of a closely related protein becomes a feasible alternative.

The utilization of the biological target model, interactive imagery, and the expert perspective of healthcare professionals facilitates the creation of drug candidates. These candidates are predicted to bind to the target through a thoughtful integration of social and emotional considerations. Additionally, the introduction of new drug candidates is streamlined through the incorporation of automated calculations, enhancing the efficiency and precision of the drug design process. In essence, a comprehensive and interdisciplinary approach, combining molecular insights, structural knowledge, and computational tools, underscores the advancement of drug design methodologies.

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