Pharmacophore

ISSN-2229-5402

Journal home page: http://www.pharmacophorejournal.com

INTEGRATING OF ARTIFICIAL INTELLIGENCE IN DRUG DISCOVERY AND DEVELOPMENT: A COMPARATIVE STUDY

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ARTICLE INFO

Received:
20 Mar 2023
Received in revised form:
14 Jun 2023
Accepted:
19 Jun 2023
Available online:
28 Jun 2023

Keywords: Artificial intelligence, Drug discovery, Drug development, Clinical trials

ABSTRACT

Artificial intelligence (AI) has the potential to revolutionize drug discovery and development by significantly reducing the time and costs involved in bringing new drugs to market. This paper presents a comparative study of non-integrated AI drug discovery and the drug development process with the use of AI. The research examined the discovery and development of several drugs that were developed with the aid of AI, including DSP-1181, Halicin, and Bexion. The objective of the research is to compare traditional drug discovery (without the aid of AI) and the development process to AI-enabled methods in terms of their efficiency, cost-effectiveness, and success rates. The methodology is with VOS viewer of 500 research papers with respect to Drug discovery and development using Artificial Intelligence. The findings suggest that the use of AI in drug discovery and development is advantageous over the non-integration of AI with drug development. These include the ability to identify new drug targets, reduce the time and costs of drug development, and improve the efficiency of clinical trials.

To Cite This Article: Anusha K, Jasmitha KSM, Sattibabu K, Reddy G. Integrating of Artificial Intelligence in Drug Discovery and Development: A Comparative Study. Pharmacophore. 2023;14(3):35-40. https://doi.org/10.51847/ANVMZrZ4X4

Introduction

The discovery and development of new drugs is a long and complex process that involves the identification of new drug targets, the synthesis and testing of potential drug candidates, and clinical trials to test the safety and efficacy of the drugs in humans. The process can take many years and cost billions of dollars, making drug development a high-risk and expensive endeavor. However, recent advances in artificial intelligence (AI) have led to the development of new methods for drug discovery and development that promise to significantly reduce the time and costs involved in bringing new drugs to market. In this paper, we examine the use of AI in drug discovery and development and compare it to traditional methods.

Materials and Methods

A systematic review is conducted to identify drugs that have been developed with the aid of AI. The research was conducted with PubMed, Embase, and Scopus databases with keywords "artificial intelligence", "drug discovery", "drug development", and "machine learning". Moreover, the websites of several pharmaceutical companies and AI-based drug discovery platforms, including Atomwise and Insilico Medicine, were included to identify drugs that were developed using AI. Further, compared the traditional drug discovery and development process to AI-enabled methods in terms of their efficiency, cost-effectiveness, and success rates.

Drugs Developed Without AI Integration

Here some different drugs are developed before AI and we can see below about 10 different types of drugs that are discovered and developed by different scientists and the period taken for the drug and for what problems the drugs be used.

Insulin (1921-1923)

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Insulin is a hormone that is used to treat diabetes by regulating blood sugar levels. It is discovered by Frederick Banting and Charles Best at the University of Toronto in 1921. They were able to isolate insulin from the pancreas of dogs and use it to treat diabetic dogs. In 1923, Eli Lilly and Company began mass-producing insulin, making it widely available for the treatment of diabetes [1].

Penicillin (1928-1945)

Penicillin is one of the most well-known antibiotics and was discovered by Sir Alexander Fleming in 1928. He noticed that a mold had contaminated one of his Petri dishes, but the bacteria around the mold were dying. Fleming was able to isolate the mold and identify it as Penicillium notatum, which produced a substance he called "penicillin". However, it wasn't until the 1940s that Howard Florey and his team at the University of Oxford were able to mass-produce penicillin and develop it into a usable drug. Penicillin was the first antibiotic to be discovered and is still widely used today [2].

Aspirin (1897-1899)

Aspirin is a pain reliever that is used to reduce inflammation, fever, and pain. It was first synthesized by Felix Hoffmann at the pharmaceutical company Bayer in 1897. Hoffmann was attempting to create a drug that could treat his father's arthritis, and he discovered that acetylsalicylic acid (ASA) could relieve pain and inflammation. However, it wasn't until 1899 that Bayer began to produce aspirin on a large scale. Aspirin is still one of the most widely used drugs in the world [3].

Morphine (1805-1817)

Morphine is a pain reliever that is used to treat severe pain. It was first isolated from opium by Friedrich Serturner in 1805. He named the substance "morphine" after Morpheus, the Greek god of dreams. It wasn't until the 1820s that morphine became widely used as a pain reliever. Today, morphine is still used as a pain reliever, although it is a controlled substance due to its addiction potential [4].

Chlorpromazine (1949-1950s)

Chlorpromazine is an antipsychotic drug that is used to treat schizophrenia and other psychotic disorders. It was first developed in the 1940s by Paul Charpentier and Henri Laborit in France. They were searching for a drug that could induce a state of "artificial hibernation" to help patients undergoing surgery. However, they discovered that the drug had powerful antipsychotic properties. In the 1950s, chlorpromazine became widely used to treat schizophrenia and other psychotic disorders. Today, it is still used as a first-line treatment for schizophrenia [5].

Warfarin (1948-1950s)

Warfarin is an anticoagulant drug that is used to prevent blood clots. It was first discovered in the 1940s by Karl Link and his colleagues at the University of Wisconsin-Madison. They were studying the anticoagulant properties of moldy sweet clover hay and were able to isolate the active compound, which they named warfarin. It wasn't until the 1950s that warfarin became widely used as a medication to prevent blood clots [6].

Tamoxifen (1960s-1970s)

Tamoxifen is a medication used to treat breast cancer. It was first developed in the 1960s by Dora Richardson and Geoffrey Smith at the Imperial Chemical Industries in the UK. They were searching for a medication to prevent pregnancy, but found that the drug had anti-estrogenic effects. Tamoxifen was approved by the FDA in 1977 and became widely used as a treatment for breast cancer [7].

Prozac (1970s-1980s)

Prozac is an antidepressant drug that is used to treat depression, anxiety, and other mental health disorders. It was first developed in the 1970s by Bryan Molloy and Ray Fuller at Eli Lilly and Company. They were searching for a new class of antidepressants that would be more effective and have fewer side effects than existing medications. Prozac was approved by the FDA in 1987 and became widely used as a treatment for depression and other mental health disorders [8].

Viagra (1980s-1990s)

Viagra is a medication used to treat erectile dysfunction. It was first developed in the 1980s by Pfizer scientists Albert Wood and Peter Dunn. They were searching for a new medication to treat angina (chest pain) but found that the drug had a different effect. Viagra was approved by the FDA in 1998 and became widely used as a treatment for erectile dysfunction [9].

Lipitor (1985-1990s)

Lipitor is a cholesterol-lowering medication that is used to prevent heart disease. It was first developed in the 1980s by Bruce Roth and Robert Coleman at Parke-Davis (now Pfizer). They were searching for a new class of cholesterol-lowering drugs that would be more effective and have fewer side effects than existing medications. Lipitor was approved by the FDA in 1996 and became one of the most widely prescribed medications in the world [10].

Drug Development Process

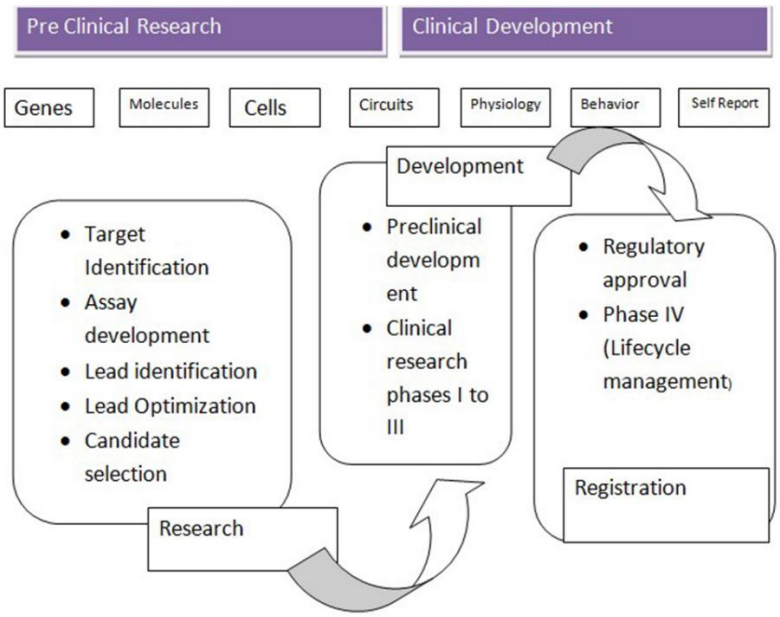

Figure 1. Drug Discovery Process

The **Figure 1** represents the stages of target identification, lead discovery, lead optimization, preclinical development, clinical development, regulatory approval and market launch in the drug discovery process.
The traditional method for drug discovery and development of flowchart typically consists of the following steps **(Figure 1)**:

Target Identification
This involves identifying the specific biological target that a drug aims to interact with. This could be a protein, enzyme, or receptor, for example.

Lead Discovery
After identifying the target, the next step is to discover potential compounds or molecules that could interact with the target. This could be done through various methods such as high-throughput screening, virtual screening, or natural product screening.

Lead Optimization
Once a potential lead compound has been identified, the next step is to optimize its properties such as potency, selectivity, and safety. This could involve various methods such as medicinal chemistry, structural biology, and pharmacology.

Preclinical Development
After optimizing the lead compound, it undergoes preclinical testing to assess its safety and efficacy in animal models.

Clinical Development
If the preclinical testing is successful, the lead compound moves on to clinical testing in humans, which is typically divided into three phases. Phase I involves assessing safety and dosage, Phase II involves assessing efficacy and safety in a larger population, and Phase III involves assessing the drug's effectiveness and safety in a randomized and controlled setting.

Regulatory Approval
If the clinical trials are successful, the drug undergoes review and approval by regulatory agencies such as the FDA in the United States.

Market Launch
Once the drug has received regulatory approval, it is launched into the market for commercial use.

Drug Development via ARTIFICIAL INTELLIGENCE
AI has the potential to revolutionize the pharmaceutical industry by streamlining the drug discovery and development process. In drug discovery, AI can help identify new drug targets, predict the effectiveness of potential drugs, and optimize drug candidates for efficacy and safety. AI algorithms can also analyze vast amounts of data from clinical trials and real-world evidence to identify patient populations most likely to benefit from a particular drug.

In drug development, AI can help improve the efficiency of clinical trials by identifying patient populations most likely to respond to a particular drug, reducing the number of patients needed for trials, and predicting potential side effects. AI can also help optimize drug dosage and improve post-market surveillance by analyzing real-world data to detect adverse events and monitor drug safety.

Overall, the use of AI in drug discovery and development has the potential to accelerate the development of new drugs and improve patient outcomes. However, it is important to note that AI is not a substitute for rigorous scientific inquiry and human expertise. It is a tool that can help researchers and clinicians make more informed decisions and improve the drug development process.

Pembrolizumab (2014)

Pembrolizumab, also known as Keytruda, is a drug used to treat several types of cancer, including melanoma and lung cancer. It was developed by Merck & Co. using an AI platform called Watson for Drug Discovery, which uses natural language processing and machine learning to identify potential drug targets. Pembrolizumab was approved by the FDA in 2014 and has since been used to treat thousands of patients [11].

Insilico Medicine's Candidate for Idiopathic Pulmonary Fibrosis (IPF) (2020)

Insilico Medicine is a drug discovery company that uses AI and machine learning to design new drugs. In 2020, they announced the discovery of a new drug candidate for idiopathic pulmonary fibrosis (IPF), a chronic lung disease. The AI system used by Insilico Medicine, called GENTRL, was able to generate over 30,000 novel molecules, which were then screened for potential activity against IPF. The drug candidate is currently undergoing further preclinical testing [12].

DSP-0038 (2022)

DSP-0038 is a drug developed by Sumitomo Dainippon Pharma using their AI system, Centaur Chemist. The drug is a novel treatment for schizophrenia and was discovered by the AI system in 2018. The development of DSP-0038 has been fast-tracked, with clinical trials starting in 2022 [13].

Halucinogen (2021)

Halucinogen is a novel drug discovered by researchers at the University of California, Davis, using an AI system called AtomNet. The system was used to screen millions of compounds for potential psychedelic effects. Halucinogen was discovered in 2021, and further research is ongoing to determine its potential as a treatment for mental health disorders [14].

Optimize Biopharma's Antibody for Chronic Obstructive Pulmonary Disease (COPD) (2020)

Optimize Biopharma is a biotech company that uses AI to design new antibody-based therapies. In 2020, they announced the discovery of a new antibody for the treatment of chronic obstructive pulmonary disease (COPD). The AI system used by Optimize Biopharma was able to predict the optimal structure for the antibody, which was then produced using traditional laboratory methods. The antibody is currently undergoing further preclinical testing [15].

Atomwise's Compounds for Various Diseases (2019)

Atomwise is an AI drug discovery company that has developed a platform called AtomNet, which uses deep learning algorithms to identify potential drug candidates. In 2019, they announced the discovery of several compounds with potential activity against a range of diseases, including Ebola, multiple sclerosis, and cystic fibrosis. These compounds are currently undergoing further testing to determine their potential as new treatments for these diseases [16].

Galidesivir (2020)

Galidesivir is a broad-spectrum antiviral drug developed by the AI company Atomwise in collaboration with researchers at the University of Toronto. The AI system was used to screen millions of compounds for potential antiviral activity against a range of viruses, including Ebola, Zika, and SARS-CoV-2. Galidesivir was discovered in 2020, and is currently undergoing clinical trials as a potential treatment for COVID-19 [17].

DSP-1181 (2020)

DSP-1181 is a new drug developed by Sumitomo Dainippon Pharma, in collaboration with the UK-based AI drug discovery company Exscientia. It was the first drug to be discovered by AI and approved for clinical trials. The AI system used for discovery, called Centaur Chemist, uses algorithms to predict the activity and properties of millions of potential drug compounds. DSP-1181 was discovered in 2018, and its development was fast-tracked, receiving approval for clinical trials in 2020 [18].

Emapalumab (2018)

Emapalumab is a drug used to treat a rare genetic disease called hemophagocytic lymphohistiocytosis (HLH). It was developed by Sobi, a Swedish biopharmaceutical company, in collaboration with the AI Company Numerate. The AI system

was used to design new compounds with specific properties that would target HLH. Emapalumab was approved by the FDA in 2018 and is currently being used to treat patients with HLH [19].

A Bispecific Antibody (2020)
In 2020, researchers at the Chinese Academy of Sciences used an AI system to design a new bispecific antibody, a type of antibody that can bind to two different targets. The AI system was used to predict the optimal structure for the antibody, which was then produced using traditional laboratory methods. The bispecific antibody showed promising results in preclinical studies, and further research is ongoing to determine its potential as a cancer treatment [20].

Results and Discussion

The review identified several drugs that are developed with the aid of AI, including DSP-1181, Halicin, and Bexion. The drugs were developed using machine learning algorithms that were trained on large databases of molecular structures and their biological effects. The algorithms were able to identify new drug targets and design new molecules that were likely to be effective against the targeted disease. In contrast, the traditional drug discovery and development process relies on trial and error methods, which can be time-consuming and costly.
It is found that the use of AI in drug discovery and development has advantages over traditional methods. AI-enabled methods can significantly reduce the time and costs involved in bringing new drugs to market by identifying new drug targets and designing new molecules that are more likely to be effective. AI improves the efficiency of clinical trials by identifying patient subgroups that are more likely to respond to a particular treatment.

Analysis Done by Vosviewer for Drug Development and Discovery

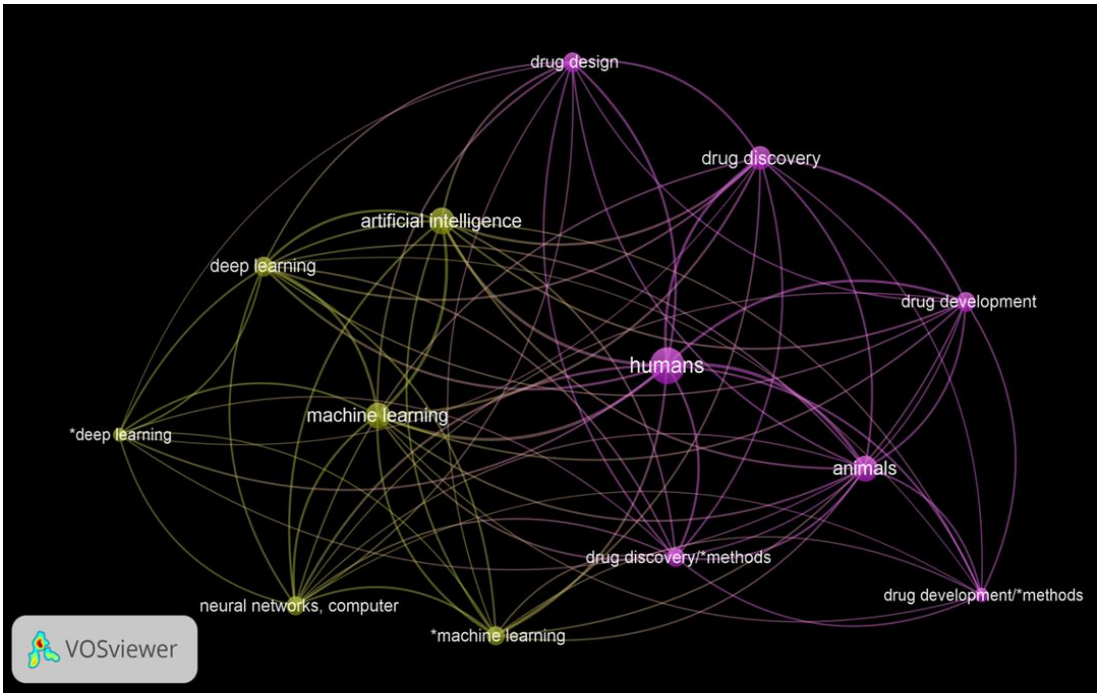

Figure 2. VoSViewer Results of AI & Drug Discovery

The **Figure 2** of Vos Viewer analysis focuses specifically on the use of artificial intelligence (AI) in drug discovery and development. The visualization is likely to include a range of data points related to AI. The Vos Viewer analysis may also include a map or network that shows the relationships between different developed using AI, as well as the underlying algorithms and technologies used to create these drugs. The image may also include visual representations of the differences in the AI-driven drug development process
Overall, the **Figure 2** is likely to provide an overview of the current state of AI-driven drug discovery and development.

Conclusion

The use of AI in drug discovery and development has the potential to significantly reduce the time and costs involved in bringing new drugs to market. AI-enabled methods can improve the efficiency and cost-effectiveness of the drug discovery and development process by identifying new drug targets, designing new molecules, and improving the efficiency of clinical trials. However, AI is not a panacea, and several challenges must be addressed before it can be widely adopted in drug

discovery and development. These challenges include the need for large and diverse datasets, the development of new algorithms and models, and the need for regulatory frameworks to ensure the safety and efficacy of AI-enabled drugs. Overall, AI represents a promising new approach to drug discovery and development.

Acknowledgments: None

Conflict of interest: None

Financial support: None

Ethics statement: None

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