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Advancements in Drug Discovery and Design Emphasizing the Role of Artificial Intelligence

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INTRODUCTION

Any foreign molecule that affects biological processes and that is used to diagnose, treat, or prevent a disease is considered a drug. Drugs are of natural origin or can be produced synthetically. The ideal drug should be safe, have specific action, be non-toxic, have no effects, be chemically and metabolically stable, be synthetically feasible, be soluble in water in order to avoid precipitation in the bloodstream, be soluble in lipids, and distribute around the body.

Artificial intelligence (AI) is the intelligence of software or machines that is opposed to the intelligence of humans or animals. Artificial Intelligence (AI) is involved in various sectors of society including many industries with the pharmaceutical industry as a front-runner beneficiary.

Presently AI is used in diverse areas of the pharmaceutical sectors like drug discovery and development, improving pharmaceutical productivity, drug repurposing, clinical trials, etc. This leads to reducing the human workload and achieving targets in a short period. This review includes the tools and techniques utilized in enforcing AI, the challenges faced, and ways to overcome the challenges in pharmaceuticals. The future of AI in pharmaceuticals is also discussed here.

Drugs interact with specific targets in the human body, and as a result, two types of effects are produced: Pharmacodynamics i.e., the effects of the

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drug on the human body, and Pharmacokinetics i.e., the effects of the human body on the drug.

Pharmacodynamics tells how the drug acts, the relationships between drug concentration and effect, and the adverse reactions by the drug. Pharmacokinetics tells about the ADME properties and processes of drugs i.e., absorption, distribution, metabolism, and excretion of the drug over time.
Three main processes are included in drug discovery and development that are: drug discovery, preclinical development, and clinical trials.

Starting of Discovery of Drug

The finding of a hit molecule that elicits a desired activity in a screening assay leads to the discovery of a drug (Sinha et al., 2018). After the finding of a hit molecule, it is optimized in terms of reducing toxicity, improving affinity and selectivity, improving ADME properties in general, and improving water and lipid solubility thus converting the hit molecule into a lead molecule. The further optimization of the lead molecule provides the drug candidate.

The preclinical studies focus on the action of the drug candidate, and its pharmacokinetics. Pharmacokinetics includes bioavailability, toxic metabolites if any, efficacy on animals, routes of excretion, drug formulation, and stability tests of this formulation. The clinical trials for drug discovery are time-consuming and the most expensive stage of the process, including three phases. The first phase aims to evaluate the safety of the drug on humans and involves 100 healthy volunteers, its pharmacokinetics in the human body, and immediate side effects if there are any. The second phase includes several hundred patients suffering from the target disease and the drug is administered to them. The efficacy of the drug and its short-term safety are tested in this phase.

The third phase involves several thousand patients from several clinical centers around the world. Sufficient data is collected from this study for the efficacy and safety of the drug. Successful passing of this phase, the drug is ready for registration and marketing.

The involvement of AI in the development of a pharmaceutical product assists in decision-making; determining the right therapy for a patient, and managing the clinical data generated and using it for future drug development (Blasiak, 2020).

 E-ISBN: 978-93-6252-893-3

Current Methods for Drug Design

Currently, artificial intelligence (AI) has provided a new tool in drug discovery in all aspects [Paul *et al*., 2021]. AI is used to predict drug–protein interactions, the 3D structure of proteins, and drug activity, and constructs molecules de novo in drug design. In pharmacology, AI is used to design specific molecules and multi target drugs. In chemical synthesis, AI can design synthetic routes to clarify reaction mechanisms and predict reaction yield.

Undoubtedly, AI is irreplaceable in screening drugs for predicting bioactivity, toxicity, ADME properties, physicochemical properties, etc.

The ***Swiss Drug Design*** system is the most popular AI platform used in drug design, developed by the Swiss Institute of Bioinformatics (Duvaud *et al*., 2021).

AI in Drug Discovery

The major achievement in modern drug design is the development of technologies, applied for virtual screening, energy calculations, compound design, SAR and QSAR analysis, modelling of drug–target interactions, and ADME modelling (David *et al*., 2020).

AI can easily recognize, hit, and lead compounds, and can provide a quicker validation of the drug target and optimization of the drug structure and design (Mak and Pichika, 2019).

Many biopharmaceutical companies, such as Roche, Bayer, and Pfizer, have teamed up with IT companies to develop therapies in areas such as cardiovascular diseases and immuno-oncology.

AI can be used for Prediction of the physicochemical properties of the drug. Different AI-based tools can be used to predict the physicochemical properties of drugs such as Machine Learning etc. AI can be used for the prediction of the bioactivity of drugs. Many web applications, like the similarity ensemble approach (SEA) and ChemMapper are available for predicting drug–target interactions (Lounkine 2012). AI-based tools, such as FAME, XenoSite, and SMARTCyp, are involved in determining the sites of metabolism of the drug. The prediction of the toxicity of any drug molecule is important to avoid toxic effects and AI is well-proven in this too. Web-based tools, such as admetSAR, LimTox, pkCSM, and Toxtree, are available to help reduce the cost (Yang, 2019).

AI can easily replace the older trial and error method. Various computational tools can resolve problems encountered in the formulation of porosity, stability issues, dissolution, and so on, with the help of QSPR (Mehta et al., 2019).

Various mathematical tools, such as discrete element modeling (DEM), computational fluid dynamics (CFD), and the Finite Element Method have been used to examine the influence of the flow property of the powder on the die-filling and process of tablet compression (Rantanen and Khinast, 2019).

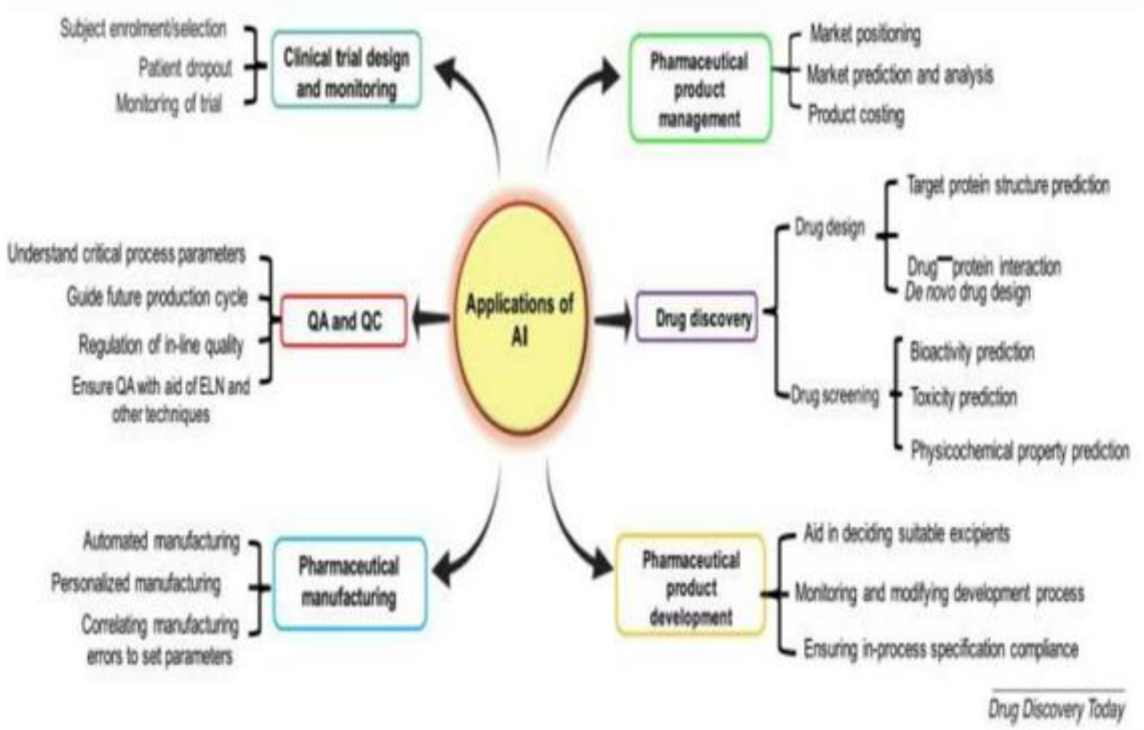

Figure 1: Artificial Intelligence (AI) in different subfields of the pharmaceutical industry, from drug discovery to pharmaceutical product management.

Future Prospects and Emerging Technologies

As the integration of Artificial Intelligence (AI) continues to evolve in drug discovery, several promising future prospects and emerging technologies are poised to further revolutionize the field. These advancements hold the potential to enhance the efficiency, accuracy, and innovation of drug development processes.

1. **Personalized Medicine and AI:** The convergence of AI and personalized medicine is a frontier with immense potential. AI algorithms can analyze individual patient data, including genetic information, biomarkers, and clinical history, to tailor treatments based on a person's unique biological profile. This personalized approach aims to optimize therapeutic outcomes

while minimizing adverse effects, representing a paradigm shift from the one-size-fits-all model of drug development.

2. **Integration of Omics Data:** The increasing availability of diverse 'omics' data, including genomics, proteomics, and metabolomics, presents a rich source of information for AI applications. Integrating and analyzing these multi-dimensional datasets can provide a comprehensive understanding of disease mechanisms and aid in the identification of novel drug targets. AI-driven analyses of omics data are expected to play a pivotal role in uncovering complex relationships and guiding more targeted drug discovery efforts.

3. **AI for Rare Disease Drug Discovery:** AI holds great promise in addressing the challenges of drug discovery for rare diseases. The scarcity of data for these conditions makes traditional approaches difficult, but AI algorithms can analyze limited datasets and identify potential drug candidates. By leveraging AI's ability to find patterns in sparse data, researchers can expedite the identification and development of therapies for rare and orphan diseases.

4. **Generative Models and De Novo Drug Design:** The evolution of generative models in AI, such as Generative Adversarial Networks (GANs) and variational autoencoders, enables de novo drug design. These models can generate entirely new molecular structures with desired properties, allowing for the creation of novel drug candidates. The application of generative models has the potential to significantly expand the chemical space explored in drug discovery, leading to the identification of previously unexplored therapeutic avenues.

5. **Quantum Computing Accelerating Drug Discovery:** Quantum computing, with its unparalleled processing capabilities, has the potential to revolutionize drug discovery by solving complex computational problems at speeds unattainable by classical computers. In drug discovery, quantum computing can simulate molecular interactions, predict protein structures, and optimize drug candidates with remarkable efficiency. As quantum computing technology matures, it is expected to become an indispensable tool for computational chemistry and drug design.

6. **Explainable AI and Ethical Considerations:** The future of AI in drug discovery also involves addressing challenges related to interpretability and ethical considerations. Developments in explainable AI aim to demystify the decision-making processes of complex algorithms, providing transparency and building trust among researchers, clinicians, and regulatory bodies.

Ethical considerations, including data privacy, consent, and bias mitigation, will remain at the forefront to ensure responsible and equitable use of AI in drug development.

In conclusion, the future of AI in drug discovery holds tremendous promise, with advancements in personalized medicine, omics integration, rare disease research, generative models, quantum computing, and ethical considerations shaping the trajectory of the field. These emerging technologies collectively signal a transformative era where AI becomes an indispensable partner in the pursuit of innovative and effective pharmaceutical solutions. As these technologies mature, their integration is poised to unlock new frontiers in the quest for novel therapeutics and improved healthcare outcomes.

Conclusion

The marriage of biology and artificial intelligence is transforming the landscape of drug discovery. The ability of AI to analyze vast datasets, predict molecular interactions, and streamline the drug development process has the potential to revolutionize healthcare. As we navigate the ethical considerations and address the challenges associated with AI in drug discovery, the future holds promise for more efficient, cost-effective, and personalized approaches to developing life-saving therapeutics. The synergy between human expertise and AI capabilities is propelling us towards a new era of medical innovation, where the once-daunting challenges of drug discovery may be overcome with unprecedented efficiency and success.

Investments in drug design are worthwhile because as better is designed a given drug during the experimental stage, as less likely is for the drug to fail in the late stages where the tests are more expensive, especially in the clinical trials.

The pandemic such as COVID forced us to rethink how to accelerate the timelines of discovery and development of drugs and vaccines in such a scenario. AI has the potential to provide effective, and less costly methods for drug discovery.

The ultimate goal of the future drug design is to be able to design and develop a non-toxic, specific, patient-tailored, and effective drug over a period of several hours. Although this goal seems unrealistic at the moment, it is completely achievable in the coming future.

 E-ISBN: 978-93-6252-893-3

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 E-ISBN: 978-93-6252-893-3