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Application of Artificial Intelligence in COVID-19 drug repurposing

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Background and aim: COVID-19 outbreak has created havoc and a quick cure for the disease will be a therapeutic medicine that has usage history in patients to resolve the current pandemic. With technological advancements in Artificial Intelligence (AI) coupled with increased computational power, the AI-empowered drug repurposing can prove beneficial in the COVID-19 scenario.

Methods: The recent literature is studied and analyzed from various sources such as Scopus, Google Scholar, PubMed, and IEEE Xplore databases. The search terms used are ‘COVID-19’, ‘AI’, and ‘Drug Repurposing’.

Results: AI is implemented in the field design through the generation of the learning-prediction model and performs a quick virtual screening to accurately display the output. With a drug-repositioning strategy, AI can quickly detect drugs that can fight against emerging diseases such as COVID-19. This technology has the potential to improve the drug discovery, planning, treatment, and reported outcomes of the COVID-19 patient, being an evidence-based medical tool.

Conclusions: Thus, there are chances that the application of the AI approach in drug discovery is feasible. With prior usage experiences in patients, few of the old drugs, if shown active against SARS-CoV-2, can be readily applied to treat the COVID-19 patients. With the collaboration of AI with pharmacology, the efficiency of drug repurposing can improve significantly.

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1. Introduction

Novel coronavirus disease 2019 (COVID-19), caused by the Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2), continues to spread aggressively. With a mortality rate of about 7%, 213 countries and territories around the world have reported a total of 7,817,195 confirmed cases with a death toll of about 430,397. It started with patients reporting pneumonia-like symptoms of unknown etiology, in the Wuhan district of China (Hubei Province), and was declared a pandemic by the World Health Organization (WHO) on March 11, 2020 [1,2]. SARS-CoV-2 is a class of enveloped viruses with a positive-sense RNA genome. They come under the Betacoronavirus group, having the same phylogenetic similarity with the previous severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) [1,3]. Thus it is the 3rd coronavirus epidemic, and as a result of evolution of the virus, the spread of COVID-19 is more severe than that of the previous SARS-CoV and the MERS-CoV [2]. The SARS-CoV-2 pandemic has forced researchers to invent new strategies for rapid antiviral treatment. Host-based antiviral agents target host cellular machinery essential for viral infections or innate immune responses to interfere with viral pathogenesis [4]. It can be augmented by employing well-validated drug discovery approaches. There are two basic strategies in drug discovery, conventional drug development and drug repositioning [5]. Besides the success rate being very low, the conventional way typically takes 10–15 years, is very expensive and needs high investments. Drug repositioning, instead reuses old drugs for exploring new therapeutics, making it more efficient, economical, and riskless [6]. More than 80 pioneering clinical trials have been instigated at
present to test coronavirus treatment, including potential old drugs and investigational new drugs [7]. Recycling and reusing old drugs, recovering shelved drugs and increasing patients’ lives makes drug repositioning an appealing system of drug discovery. It requires a thorough in-depth knowledge of present practices acquired by assessing both biological and pharmaceutical learning and interpreted mechanism-of-action of drugs.

In this regard, the pharmaceutical industry is also looking for novel leading-edge technologies to track, monitor and restrict the dissemination of COVID-19 disease [2,8]. AI is one such parallel novel leading-edge technologies to track, monitor and restrict the preclinical testing and clinical trials omitting the initial steps, thus narrowing down the risks and lowering the costs. Fundamental principle in drug repurposing is that a common molecular pathway is associated and accountable for numerable diseases and a multitude of explicit information that is accessible on the formulation, dose, toxicity, pharmacology and clinical trial data of the authorized, approved, shelved or discontinued drugs [11].

3. Drug repurposing for COVID-19

Drug “repurposing” in this article refers to the use of existing approved drugs for the treatment of a never-considered therapeutic indication - in this case, COVID-19. The discovery and development of new molecular entities being lengthy, time-killing and high-priced for clinical trials to earn regulatory authorizations or sanctions, the momentary passage thus to potential treatments is the repurposing (repositioning) of prevailing approved drugs for the treatment of COVID-19. In this context, Chloroquine (CQ) and it’s Hydroxyl analogue Hydroxychloroquine (HCQ) have been reported in the treatment of viral infection. These drugs have anti-malarial activity and also showed in vitro treatment against COVID-19 [12]. Similarly, an antiviral drug Remdesivir primarily used in the treatment of Ebola virus clinical studies exposed new successful effects against COVID-19 in vitro. It is an adenosine analogue, basically integrates into nascent viral RNA chains and shows in early termination [13]. Lopinavir and Ritonavir were used in the ministration of COVID-19 patients. These two antiviral agents mainly affect proteolysis in coronavirus replication cycle [14]. Ribavirin is an analogue of ribonucleic and inhibitor of RNA polymerization. This drug has shown in vitro activity against SARS-CoV-2 in preclinical studies [1].

Furthermore, Tocilizumab, an immunosuppressive drug, was also used in the treatment of COVID-19 patients in vivo in China. This is chiefly employed to aid rheumatoid arthritis tested in COVID-19 patients. The drug successfully mitigates the clinical symptoms of viral infection, but the numbers of patients investigated in the study were very few [15]. The Anti-flu drug of Japan is revealed significant results in clinical trials over 340 patients [16]. In China, this drug is accepted for the treatment of Influenza and also shown to be efficient against a different type of viruses including SARS-CoV-2. Similarly, Ascorbic acid (Vitamin C) combination with other antiviral drug has shown to be supportive in the treatment of COVID-19 patients. In this context, more studies are suggested for a future drug against COVID-19 [17].

**Fig. 1.** Different steps followed to discover new drugs against drug repurposing.
4. Proposed AI techniques for drug repurposing

The main hindrance in drug repositioning is diagnosing and identifying the unique drug-disease relationship. To address this issue, a variety of approaches have been developed including computational approaches (such as AI), biological experimental approaches, and mixed approaches. Thus there are chances that the application of the AI approach in drug discovery is feasible [18]. Researchers have found many similarities between the COVID-19 virus and the 2003 SARS Virus and based on the existing data that caused SARS, AI learning models can be created to predict drug structures that could potentially treat COVID-19 [19]. Notwithstanding effectively affirmed repurposed drugs, there is a requirement for recognizing more repurposed drugs [19]. AI and machine learning (ML) can support this procedure by rapidly recognizing drugs having adequacy against COVID-19 and thus overcome any barrier between a large number of repurposed drugs, laboratory/clinical testing, and final drug authorization. A good amount of information, discharged by different health agencies and organizations, is accessible on open stages [20]. AI likewise contains the ability to learn with or without being modiﬁed by an external user. Machine learning is divided into supervised, unsupervised, and reinforcement learning [21]. Supervised learning contains characterization and relapse strategies where the present model is created dependent on the information from information and yield sources i.e., output. Unsupervised learning includes bunching strategies by gathering and deciphering information dependent on input information only. Another ﬁeld of ML is deep learning. It uses AI neural network with multiple hidden layers apart from the input and output layer. Deep learning permits machines to take care of complex issues in any event, when utilizing an informational index that is exceptionally differing and unstructured. The more Deep learning calculations learn, the better they perform. The development of DL was seen with the expanding measure of information and the nonstop development of computer power. The striking distinction that DL makes is the adaptability in the design of neural systems such as repetitive neural networks (RNN), convolutional neural networks (CNN), deep belief networks (DBN), and completely associated feed-forward systems. The whole explanation will be better understood by Fig. 2. It presents the AI-empowered drug repurposing strategy. We need a Repurposed Drug Database, Open Chemical/Drug Database as an input to the model. Then different algorithms could be applied to the input and the required drug could be obtained [22].

The best and the truly necessary technique during circumstances is to order this unique medication information with the goal that AI scientists can apply their calculations to determine noteworthy bits of knowledge. For this, the world offices and policymakers need to step up to push huge Pharma organizations and exploration labs to unite with littler examination associations and pool information sources. To foresee increasingly exact outcomes, specialists need arrangements of good information which is as of now not accessible and are therefore constrained by lack of data or too much noisy data. Associations over the globe are taking vital activities to utilize AI for testing which is empowering, be that as it may, there is a requirement for progressively symptomatic testing [8].

A few associations have begun to use these advancements to quicken COVID-19 medication disclosure and better fathom how the resistant framework battles the infection. Toward the beginning of April, pharmaceutical organizations GlaxoSmithKline (GSK) and Vir Biotechnology joined forces to progress coronavirus treatment advancement utilizing computerized reasoning and CRISPR. Furthermore, in the scholarly area, the Harvard T. Chan School of Public Health as of late united with the Human Vaccines Project to dispatch the Human Immunomics Initiative, which uses man-made reasoning models to quicken antibodies for a scope of infections, including COVID-19 [23]. A group from Southern Illinois University (SIU) as of late built up an information representation device that uses GPS data to show users the locations of known COVID-19 cases. Google and Apple have likewise collaborated to build up a contact following application powered by Bluetooth innovation. These methods may prove effective in the data collection in a great and accurate amount [23]. Organizations are running experimentation explores different avenues regarding effectively approved drugs, having built up wellbeing proﬁles in people, based on fundamental comprehension of the infection. With regards to COVID-19, hydroxychloroquine (endorsed to treat Malaria) and remdesivir (for Ebola) are the two most popular instances of this up until now [24]. So, the data set of the effectiveness of these medicines may be a good input for an AI model. The organizations which are utilizing AI for repurposing existing medications for COVID-19 are listed in Table 1.

5. Conclusion

This article explores the recent advances of AI-empowered drug repurposing for COVID-19. In the age of big data, drug repurposing can be done efﬁciently by using deep learning methods. The AI-based drug repurposing is a cheaper, faster, and effective approach and can minimize the failures in clinical trials. The repurposed drug can directly enter the advanced phase for trial without the initial trials and toxicity tests. Though presently the AI-empowered drug repurposing is in its nascent stage, this approach is a promising solution for the development of potential drugs for the cure of COVID-19. The computational intelligence aided drug molecule design and re-positioning of drug molecules can help in the prediction of excellent anti-viral therapeutics. However, the prediction efficiency can increase with a systematic training database and development of relevant learning algorithms. With technological advancements in AI coupled with increased computational power, the AI-empowered drug repurposing can prove beneﬁcial in the COVID-19 scenario.
Declaration of competing interest

All authors have participated in (a) conception and design, or analysis and interpretation of the data; (b) drafting the article or revising it critically for important intellectual content; and (c) approval of the final version.

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