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MINI REVIEW

Therapeutic Repurposing of Antiviral Drugs Available for COVID-19 Therapy: A Mini Review

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The impact of repurposing drugs that now *in vitro* inhibit significant chronic respiratory illness corona virus type 2 was indeed underestimated or ignored during the early phases of the COVID-19 virus. Recent clinical data, however, suggest that remdesivir and favipiravir may hasten to heal, but lopinavir/ritonavir had minimal impact on very ill patients. The interferon appears to be the primary impact of triple therapy with ribavirin, lopinavir and interferon-1b. The role of hydroxychloroquine, marketed as Plaquenil® or chloroquine, marketed as Aralen®, in the treatment and prevention of COVID-19 is presently unknown due to the small sample size research. Anti-cytokine drugs may not benefit persons with mild disease or severe illness. Traditional Chinese medicine (TCM) is commonly used for COVID-19 patients in China and has antiviral and immunomodulatory effects on SARS-CoV-2. This review outlines existing COVID-19 therapeutic options and advocates for clinical trials for children, persons with mild disease and those in the early stages of COVID-19.

Keywords: Antiviral agents, Covid-19 therapy, Drugs, Corona virus, Covid-19 disease.

INTRODUCTION

New bronchopneumonia created by a pathogen that was unseen bacteria discovered in the city of Wuhan in central China, a city of more than 11 million people in December 2019. The initial instances occurred and were identified because of exposures at the Wuhan food store [1]. The Chinese Government has registered 2835 verified cases on the Chinese mainland as of January 27, 2020, with 81 fatalities. Several cases were reported in Hong Kong, Macau and Taiwan; 39 imported cases were reported in Southeast Asia, Japan, South Korea (including U.S.A), Vietnam (including U.S.A), Singapore (including Nepal), France (including Australia), Canada and the United Kingdom (including the United Kingdom). The disease was swiftly recognized as a novel coronavirus, according to the researchers (2019-nCoV), which is strongly linked with CoV that causes acute respiratory distress disease severe (SARS-CoV). There is yet no effective therapy for the new virus. As a result, finding effective antiviral medications to tackle the illness is critical [2]. A cost-effective strategy for medication development is launched to determine the efficacy of currently available antiviral medicines in treating similar viral infections. SARS-CoV and Middle East respiratory disease CoV are among the betacoronaviruses that include 2019-nCoV (MERS-CoV). Numerous medicines have already been utilized in individuals with SARS or MERS, including ribavirin, interferon, lopinavir-ritonavir and corticosteroids, while the usefulness of these treatments is still debated [3].

SARS and Middle East Respiratory Syndrome (MERS) were coronavirus epidemics in the previous two decades, with outbreaks in 2003 and 2014 [4]. The 2019-nCoV's reproduction number is expected to be between 2 and 3, with a mortality

rate of 0.5 to 1.5%. Fever, dry cough, loss of taste, tiredness and shortness of breath are the most common symptoms among in COVID-19 patients [5,6]. Recently, COVID-19 patients, anosmia is also one of the most concerning signs. This type of COVID-19 is claimed to become more contagious than some other coronaviruses and transmit at a faster pace than that of the closely related SARS-CoV-10 strain, according to the researchers. SARS-CoV-1 and SARS-CoV-2 have several traits in common, including genome length, receptor type and the ability to trigger cytokine storms in the body [7-9].

These viruses are made of ribonucleic acid (RNA) since they have a single-stranded RNA that is positive and that makes them dangerous. This group of viruses is dangerous for humans and many other animals. The word "Corona" means crown in Latin and the reason they were named coronaviruses is that they looked like crowns when they were seen through an electronic microscope [8,9]. During the pandemic, the FDA developed programs that allowed therapists to acquire access to experimental medications. The expanded access (EA) and emergency use authorization (EUA) programs provided for the fast deployment of exploratory and investigational medicines with growing evidence. Rizk *et al.* [10] reviewed the function of each of these measures, as well as their relevance in providing medical countermeasures in the case of infectious illness and other dangers.

The virus quickly turned out to be a new coronavirus (2019-nCoV), which is very similar to the virus that causes severe acute respiratory syndrome (SARS-CoV). There is no specific treatment for the new virus so far. Therefore, finding effective antiviral drugs to fight the disease is very essential. This review describesthe success of the treatment using inhibitors as antiviral medications in the therapy of patients with COVID-19.

Antiviral agents available for the treatment of Covid-19: The development of SARS-CoV-2 *in vitro* was recently found to be inhibited by an antiviral agent, one of which being chloroquine (an antimalarial medicine) [11]. It has been observed that chloroquine and hydroxychloroquine are both effective in the treatment of SARS-CoV-2 and reported to be effective in the treatment of COV-19 in Chinese patients. When hydroxy-chloroquine is administered, the effects on respiratory virus counts were examined. As a method, where the French Patients with confirmed COVID-19 infection were enrolled in a single-arm protocol from early March to March 16th, during which they received 600 mg of hydroxychloroquine daily and their viral load in nasopharyngeal swabs was assessed daily in the hospital environment. Azithromycin was used as part of the treatment in the clinical presentation of the patients. Patients from another facility who were not treated and cases who refused to follow the procedure were used as negative controls [11,12]. The outcomes of this inquiry were based on the treatment of twenty instances and the findings revealed a substantial at D6 since there was a decrease in viral transmission as compared to the trials, after addition. Using azithromycin in conjunction with hydroxychloroquine resulted in a significant improvement in virus elimination. Finally, even with the smaller sample size, individuals with COVID-19 who received hydroxychloroquine medication had a lower viral load/disappearance rate and this effect is strengthened by azithromycin [11,13].

Anticancer drugs were examined as a possible therapy for COVID-19. The discovery of new antiviral agents necessitates extensive clinical studies [14]. The benefit of adapting pharmaceuticals to explain off-label use is tied to the well-established tolerability, which could also change on the ailment and pooled data on pharmacodynamics, pharmacokinetics and efficacy from phase I–IV trials. One noteworthy finding was that some of the cellular targets that interfere with the viral development cycle, such as kinases, are widely shared across multiple viruses and various types ofillnesses [15].

Several inhibitors of COVID-19 protease have been identified as promising drugs, including carfilzomib has been authorized by the FDA as antineoplastic agent for the therapy of individuals with various myeloma [16]. Several clinical trials have looked at it in the context of various cancers, including leukemia and anti-lymphoma, among other types of cancer, such as diffuse large B-cell lymphoma and mantle cell lymphoma. Furthermore, carfilzomib is a second-generation anti-proteasome that inhibits the proteasome at a greater maximal percentage than bortezomib at the highest tolerated dose [17]. By attaching to the protease enzyme region of the center of the proteolytic system, this mechanism causes the 26S enzyme responsible for proteasome, which is required for the development of myeloma, to be irreversibly inhibited [17]. Virtual docking screening is a type of virtual screening, which is based on the structure of the drug approach interaction with certain enzymes at specific binding locations or regions, was recently used to repurpose carfilzomib for COVID-19 [18].

Carfilzomib outperformed numerous other prospective medications, The conformations of many antiviral medications, including 'eravacycline' is fluorocycline antibacterial, 'elbasvir' is a therapy of hepatitis, 'lopinavir' is an HIV-specific protease inhibitor with a high level of specificity and 'valrubicin' a chemotherapy drug, was measured. *In silico*, the data from this research indicated low effectiveness of SARS-CoV-2 [11].

Some drugs, like arbidol, remdesivir and favipiravir, are being tested in China to see if they work and are safe for treating Coronavirus infection in 2019 (COVID-19). There have been some encouraging findings. This review lists the drugs that could help fight SARS-CoV-2 [19]. The Japanese Government in 2014 approved to treatment of new and re-emerging pandemic influenza with favipiravir, which is an oral drug. It is very effective against the corona virus-2 against serious critical respiratory diseases. When the dose is high, the CC_{50}/EC_{50} ratio for the high dose is very large, which shows that it is safe. Moreover, COVID-19 clinical studies have shown that favipiravir has a faster viral clearance rate than lopinavir/ritonavir (LPV/RTV) but is more effective than umifenovir in terms of recovery, which is used to treat HIV. However, favipiravir has shown encouraging outcomes in research trials conducted in China, Russia and Japan and further tests were being conducted in a other countries too, like the United States, the United Kingdom and India, to further validate these findings [20]. According to the World Health Organization, at this time, no specific drug is suggested for the prevention or treatment

of the novel coronavirus (WHO). Clinical trials will be used to examine some specific medicines that are currently under development.

Jin *et al.* [21] tried to find new drugs quickly by integrating structure-based computational modeling and pharmacogenomics, computational drug discovery drug screening and high throughput screening (HTS). This project was about finding drugs that could stop the 3C-like protease of SARS-CoV-2: this M^{pro} is a crucial enzyme in corona viruses. It helps corona viruses grow and reproduce, which makes it a good drug target for SARS-CoV-2.

The epidemic caused by COVID-19, which is caused by SARS-CoV-2, necessitates the use of antivirals. The virus-activating host cell protease TMPRSS2 is congested by the therapeutically verified proteolytic enzyme inhibitor camostat mesylate, which is available only *via* prescription. However, the antiviral efficacy of camostat mesylate metabolites and the possibility for viral resistance have not been examined. Camostat mesylate's antiviral activity in human lung tissue has yet to be validated [22].

Remdesivir is another antiviral drug recently available as a potential antiviral medication against a broad range of viral infections in cultivated cells and using a technique of growing, animals (rats/mice) and nonhuman primate (NHP) models it means the animals most closely related to humans, including SARS/MERS-CoV5 and of Ebola virus infection, it currently in the clinical development phase. It's an adenosine analog that has been absorbed into the nuclei of nascent viral RNA chains, causing the viruses to terminate prematurely [22]. This was demonstrated by their time-of-addition, which is consistent with the anticipated antiviral action of remdesivir's use as a nucleotide analog. Following intravenous injection of a 10 mg/kg dosage of remdesivir, Warren *et al.* [23] demonstrated that the drug produced sustained amounts of its organic metabolite in the blood simultaneously (10 mM). In the NHP model, remdesivir provides 100% prevention to Ebola pathogens [22].

Remdesivir's EC_{90} value in contrast to nCoV-2019 in Vero E6 and has been 1.76 M for the number of cells, indicating that its working concentration is likely to be obtained in NHP, according to this study. It was found that remdesivir effectively reduced viral contamination in a human cell line (Huh-7 cells, which are susceptible to 2019-nCoV) in our early results, which was likewise susceptible to virus infection [23].

Novel chemical drugs, such as prulifloxacin, bictegravir, nelfinavir and tegobuvi, were found to be good candidates for modifying against the 2019-nCoV. Favipiravir and merimepodib are among several antiviral medicines now becoming studied. The combination of lopinavir and ritonavir has been proven to be ineffective in research. Furthermore, recent scientific studies show a tendency. Remdesivir and favipiravir may speed up recovery; lopinavir/ritonavir has little effect on severe individuals. The predominant effect of triple treatment with ribavirin, lopinavir and interferon-1b. The relevance of hydroxychloroquine or chloroquine in the therapy and prevention of COVID-19 remains uncertain in limited sample size studies. According to specialists and limited sample size observational studies, combining TCM with antiviral medicines (ex. interferon, lopinavir or arbidol) can reduce inflammation in extreme COVID-19 patients. Many reported investigations involved COVID-19 extreme or urgent patients [24].

The development of new therapeutics for coronavirus illness in 2019 is critical (Covid-19). In addition to significant worldwide illness and death, the Covid-19 epidemic has caused significant economic damage practically in major countries. This kind of catastrophe may have been avoided if more specific antiviral medicines had been developed that were accessible, orally permeable and fast-acting. In response to this requirement, Molnupiravir, an orally accessible prodrug of N4-hydroxycytidine (NHC), has begun to address it. It's a novel therapeutic oral molecular antiviral that is effective against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Bernal *et al.* [25] have published the findings of phase 2-3 placebo-controlled study of molnupiravir may be the first step toward addressing this global epidemic. The medicine was delivered orally (800 mg [four tablets] twice a day for 5 days) and the results were compared to those of a matched control group.

According to the findings of multiple studies, molnupiravir should be investigated much more as soon as possible to prevent hospitalization and/or death in nonhospitalized individuals having Covid-19. Yoseph *et al.* [26] studied phase 2/3 test of molnupiravir for behaviour of Covid-19 in nonhospitalized adults when observed that many trials' findings encourage continued investigation of molnupiravir as a viable therapy for reducing hospitalizations and/or death in non-hospitalized individuals with Covid-19 in the coming years. Arribas *et al.* [27]. Also studied randomizedexperimental of molnupiravir in patients hospitalized with COVID-19. For the first time, an oral, forceful antiviral has been proven very efficient in depressing nasopharyngeal SARS-CoV-2 communicablegerm and viral RNA, in addition to having an excellent pharmacological also toxicological characteristic.

Although the social and economic costs of CoV infections as well as the potential of future human epidemics of much more severe pathogen CoVs, effective antiviral treatments and prevention techniques are still lacking. In humans, the new virus might develop regularly due to frequent cross-species infections and spillover occurrences. The development of computational approaches for developing anti-CoV chemicals is crucial. The integrated AI-based drug discovery pathway generated new therapeutic molecules against 2019-nCoV in this investigation. The results show that this innovative technique for developing novel anti-CoV therapies is both cost-effective and time efficient.

Conclusion

Apart from antiviral drugs, the COVID-19 vaccine is the most hopefulchoice to halt the current epidemic. The development of severe acute respiratory-specific antiviral medicines should improve treatment outcomes for COVID-19 patients. Successful vaccinations and antiviral medicines necessitate interdisciplinary collaboration. In absence of antiviral medications or viable vaccinations, repurposing pharmaceuticals is still the norm. Antiviral drugs may help people in the initial steps of COVID-19. In addition, antiviral and anti-inflammatory therapies can help COVID-19 individuals with cytokine-release disease.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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