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A Review for Current Treatment Strategies and the Role of Antiviral Medication as Potential Therapeutic Interventions for Coronavirus Disease 2019 (COVID-19) Outbreak

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Abstract

The Coronavirus disease 2019 (COVID-19) is an infection caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) that leads to pneumonia; it was first identified in China in late 2019. This is a new coronaviruses strain that has not been previously identified or studied in humans. The common symptoms are cough and fever, similar to other respiratory tract infection. Early infected patients are difficult to detect, and the disease is rapidly spreading worldwide. Currently, there are no specific therapies or vaccines that are effective in treating or preventing this disease.

Introduction:
This review article summarizes and combines information gathered from international sources, including the United States and China, on the novel coronavirus (CoV), SARS-CoV-2, and examines potential treatments for COVID-19 disease. The COVID-19 infection caused by novel corona virus SARS-CoV-2 has rapidly spread from China to over 110 countries over the last several months (as reported by the World Health Organization [WHO] on March 11, 2020. The first confirmed case was reported in December 2019. More than 110,000 people have been confirmed to be infected by SARS-CoV-2, and more than 4,200 deaths have been reported all over the world as of March 11, 2020. As a result, WHO has declared the outbreak of COVID-19 is the first pandemic cause by coronavirus. Both The Center for Disease Control and Prevention (CDC) and WHO confirmed that COVID-19 infection has the capacity to spread from person to person; this is primarily believed to occur when people are in close contact with one another or when touching a surface that is contaminated by the virus and then touching the mouth, nose, or eyes [1-5]. An epidemiology report from the Chinese Center for Disease Control and Prevention indicates that 86.6% of confirmed patients are between 30 to 79 years old, 80.9% of cases are considered mild cases, and the overall fatality rate is 2.3% [6]. Furthermore, 23.2% of confirmed cases have at least one underlying medical comorbidity, such as hypertension, diabetes, chronic heart disease, chronic obstructive pulmonary disease, or cancer, and these patients accounted for 37.6% of severe cases [6,7]. In addition to patients with underlying medical comorbidities, other high-risk populations include older individuals and immunocompromised patients.

LITERATURE REVIEW

Viral Classification and Drug Targets

The SARS-CoV-2 is a coronavirus which is an enveloped, positive sense, single-stranded RNA virus. Corona viruses are a large family of viruses that can cause infection in both animals and [7-9] humans. Human corona viruses were first identified in the mid1960s. Common human corona viruses, including types (HCoVs) -229E, -NL63, -OC43, and -HKU1, can cause upper and lower respiratory tract infection [10,11]. Two human coronavirus infections, Severe Acute Respiratory [9] Syndrome (SARS) and Middle East

Respiratory Syndrome (MERS), emerged in 2003 and 2012 causing worldwide pandemics that resulted in over one thousand deaths. The Coronavirus Study Group of the International Committee on Taxonomy of Viruses recognized SARS-CoV-2 as a sister to SARS-CoV of the species severe acute respiratory syndrome-related corona virus [10]. Interestingly, bats and rodents are the most common hosts of corona viruses in nature, and when the genome sequences among different coronavirus are compared, SARS-CoV-2 shares 88% identity with two bat-derived SARS-like corona viruses and 96% identity with Bat-CoVRaTG1312-14. The SARS-CoV-2 genome sequences obtained from patients with COVID-19 share 79.6% sequence identity to SARSCoV15. The WH-human genome, a representative of the SARS-CoV-2 found in ORFia and spike gene (S-protein), shared a better sequence homology toward the genomes SARSCoV_Tor216. The S protein of coronaviruses has two function domains. The S1 domain is responsible for receptor binding, and the S2 domain is responsible for cell membrane fusion. Similar to SARS-CoV, SARS-CoV-2 uses the receptor binding domain of the surface S protein to engage angiotensin-converting enzyme 2 (ACE2). Importantly ACE2 plays a critical role in enabling SARS-CoV-2 to fuse with cellular membranes, and, as a result, lung cells with ACE2 expression may act as target cells and are susceptible to SARS-CoV-2 infection. It is postulated that infection with SARS-CoV-2 primarily causes pulmonary, and sometimes gastrointestinal symptoms, because ACE2 predominates in the lungs and the gastrointestinal tract.

Both SARS-CoV and SARS-CoV-2 share key genomic elements which can be used to design the drug targets [19,20]. The SARS-CoV-2 genome encodes for both non-structural proteins (such as 3-chymotrypsin-like protease, papain-like protease, helicase, and RNA-dependent RNA polymerase [RdRp]) (Figure 1), which are involved in viral transcription and replication, and surface structural proteins (such as spike glycoprotein) (Figure 1), which are involved in the viral cell receptor interaction. These structural proteins and non-

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structural proteins are potential drug target for COVID-19 treatments. Another potential drug target is the RNA genome. Short interfering RNA (siRNA) molecules interfere with the specific genes by degrading mRNA after transcription and preventing translation [21]. However, current technology cannot support siRNA medication use in a large infected population [22,23]. Among existing broad-spectrum antiviral, protease inhibitors, nucleoside analogues that target RdRp, and several other small-molecule agents may be considered as potential antiviral options for COVID-1924. Finally, although significant research is underway, there is no vaccine currently available to preventSARS-CoV-2 infection. Consequently, it is essential to examine antivirals that are currently available or already in the research pipeline for the treatment of other viruses as 6 potential therapeutic strategies This article reviews the antiviral medications currently used in the COVID-19 treatments worldwide (especially China and United States) and other potential therapeutic strategies.

CONCLUSION

This review summarizes the current understanding of COVID-19, including the molecular characteristics and potential drug targets for SARS-CoV-2. Evidence-based therapeutic strategies and antiviral medications that could potentially be used in COVID-19 treatment are also described. Three agents, remdesivir, favipiravir, and chloroquine, have some efficacy data against SARS-CoV-2 in vivo or in vitro. However, this evidence is not conclusive enough to support any specific antiviral recommendations and more clinical evidence is needed.

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