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REVIEW ARTICLE

Current pharmacological treatments and vaccines for novel coronavirus disease 2019 (COVID-19)

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ABSTRACT

Coronavirus disease caused by SARS-CoV-2 faces an unparalleled challenge in the pursuit of suitable drugs for prevention and treatment. Given the rapid speed of scientific study and clinical evidence provided by the vast number of people readily infected with SARS-CoV-2, clinicians need evidence of effective medical care for this infection. Although some recent COVID-19 trials have shown clinical progress, several of these trials are ongoing, including pharmacokinetics, the optimum dosage regimen and the therapeutic and treatment period, and even considering randomised controlled experiments. Antimalarial, anti-inflammatory and antibiotics are present clinical proof of their success in treating COVID-19 patients. Vaccination is one of the safest strategies for managing infection. Effective vaccines therefore need to be developed. Recent progress in the manufacture of coronaviras vaccines is outlined and current vaccine adjuvants for efficacy improvements are highlighted.

INTRODUCTION

Coronavirus (CoV) viruses are able to use a variety of host organisms, and as host switches in CoV production are a common function, new CoV can still be added. Seven different coronaviruses are currently known to cause human breathing disorders. The latest SARS-CoV-2 coronavirus outbreak in December 2019 is in the coronavirus 2B type, which is 80% identical to the SARS-CoV genome. In the future too, continuous mutation is likely. A variety of CoV therapies, such as immunomodulations, vaccines, antivirals specific to CoV and host-specific antivirals are being developed. Many people with COVID-19 have severe breathing problems. Senior citizens and people who have prior health problems such as diabetes, cardiovascular disease, heart or kidney disorders, and certain cancers may develop severe disorders [1]. Coronaviruses are a group of enveloped viruses named for their coronary appearance with positive single-stranded RNA genomes. In addition to six well-known strains of human-infectious coronaviruses, two other particularly pathogenic SARS-CoV and MERS-CoV-viruses, SARS-CoV-2 also causes major respiratory failure and death. Furthermore, the population has become vulnerable to highly pathogenic coronaviruses and has grown into events of public health, thereby increasing the need to prepare a possible reappearance or to produce new viruses [2-5]. COVID-19 is hard to foresee before the end of the pandemic; high-death coronavirus. However, latest estimates show that mortality in China is 4.1%, Italy 12.8%, Spain 10.2%, the United States 3.9% and Germany 2.3%. Covid-19 is very similar in symptoms as with other respiratory viral infections. Cases range between mild and extreme, causing severe medical problems or even death. However, it is projected that incubation periods would take 2 or 14 days for the New coronavirus. According to the novel virus it does not develop unique modes of transmission. Originally originating as a different source, it now spreads from one individual to another [6]. The transmission of the virus was suspected whereas the carrier (infected person) did not display symptoms, but it has not been scientifically confirmed. The current symptoms of cough, sudden onset of

fever and respiratory problems are recorded. The complications that may arise from infection include Pneumonia, sepsis, septic shock, and ARDS (acute respiratory distress syndrome). Suspicion may arise with the above symptoms and a recent history of travel to or from countries affected by Covid19 to any foreign country [7]. This strain has now been diagnosed to many citizens in the United States. The CDC has suggested that it should spread to more people. In at least 25 other countries, COVID-19 induced instability. The first COVID-19 individuals had relations with the market of livestock and seafood. This evidence suggests that animals transmitted the virus initially to humans. However, there were no company contacts or exposed individuals with a newer diagnosis, meaning that people would pass the virus on to each other. There are currently few virus data. Climate change formed in the past by close contact with coronaviruses such as SARS and MERS have spread. WHO Director-General issued a 17 February 2020 media conference, which included details on the extent to which 44,000 diagnostic details confirming the COVID-19 symptoms are fatal or severe [8].

Table 1: The Director-General also noted that the risk of serious complications increases with age.

Stage of severity	Rough percentage of people with COVID-19
Mild disease from which a person can recover	More than 80%
Severe disease, causing breathlessness and pneumonia	Around 14%
Critical disease, including septic shock, respiratory failure, and the failure of more than one organ	About 5%
Fatal disease	2%

1. Virus characteristics and clinical manifestations

They have the same spherical form as other coronaviruses, with genetic material inside and the spicy proteins rising out from their top, helping to fuse the human cell and the transition of genes into the host cell. The latest studies show that spikes SARS-CoV-2 bind enzyme 2, an enzyme converting angiotensin, to the receptors of human cell surfaces such as the one causing the outbreak of SARS in 2002. The current virus can cause infections of the respiratory system, including pneumonia and acute ARDS, in patients, from mild to fatal conditions. In most patients, respiratory conditions can be mild to moderate and recover from supportive treatment and no special care/therapy is required. The most common pathology of COVID-19 is that of geriatric patients and patients with combined-morbidities, such as diabetes, hypertension, chronic respiratory disorders, cancer, immunodeficiency patients, and other chronic conditions. Mental and neurological relationship (such as delirium and encephalopathy, hysteria, stroke, meningoencephaly) to symptoms which (based on data of MERS-CoV), include fever, nicotine, shortness of breath, difficulty breathing, recurrent chest pain or tension. Three additional kinds of pulmonary complications, including liver lesions such as other corona (SARS and MERS), and fulminant myocarditis and acute kidney damage, were identified by COVID-19 patients sadly. Host-cell receptors and endosomes are used to enter cells after receptor binding. A serine protease type 2 transmembrane host, TMPRSS2, enables the entry into cells by means of the S enzyme. Viral polyproteins encoding the replicase transcriptase complex have been synthesised within the cell. The virus then synthesis RNA via its RNA based on polymerase, synthesizing structural proteins prior to the assembling and the completion of viral particles. The potential drug treatment goals include these steps towards the viral life cycle. Promising drug targets include non-structural proteins that have a homology with other novel coronaviruses (nCoV) (for example, 3-chymotrypsine-like proteases, papainlike protease, RNA based polymerase RNA). Other drug objectives include viral mechanisms and immune regulation [8-9].

2. Pharmacological Treatment Recommended for SARS and SARS-CoV-2 Management

2.1 Pharmacological Agents

2.1.1 Hydroxychloroquine and Chloroquine

Chloroquine and hydroxychloroquine (HCQ) have been used extensively in malaria over the past century, while new antimalarial drug production has been stimulated by the continuing growth of Plasmodium falciparum drug-resistant strains. However, these compounds, in particular the less toxic HCQ, are currently used as a treatment of autoimmune disorders, such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and anti-phospholipid syndrome (APS), because of their immunomodulatory and anti-thrombotic

properties. In addition, CQ and HCQ have proved to directly inhibit and spread in several models *in-vitro* and *in-vivo* for the treatment of viral infections. The drugs were then offered for the treatment of various human viruses, including SARS-CoV-2 coronaviruses. However, the relevance of this knowledge for infectious human viral diseases is still lacking. A detailed review of findings from randomised controlled research and the retrospective registry of outcomes based on the efficacy, duration, and toxicity of these medicines should be conducted to confirm their real effectiveness. Initially synthesised in 1934, chloroquine has been widely used for the treatment and prevention of malaria and the treatment of autoimmune disorders including rheumatoid arthritis and systemic lupus erythematosus. Later introduced in 1955, hydroxychloroquine was rapidly preferred because of its highest safety profile. These drugs are thought to be partly links to their interplay with DNA and inhibition of hema polymerisation. The mechanism of action of Plasmodium parasites Hydroxychloroquine's immunomodulatory function is related to a large number of immune control networks, which have been extensively investigated in other studies. In addition to rheumatic diseases, two antipallarial agents displayed a wide range of other diseases, including antiphospholipid syndrome, therapeutic or immune modulatory effects. SARS-CoV-2 has yet to be thoroughly elucidated with the hydroxychloroquine action mechanism. In SARS coV, the coronavirus outbreak of SARS occurs in 2002 – 2003 and was initially screened for chloroquine. SARS-CoV is 79% SARS-CoV-2-like in genetic order but is predicted to result in a more extreme 10% versus 3% SARS-CoV-2 fatality risk infection. Studies of the SARS-CoV are based on a preliminary assessment, and the SARS-CoV-2 is estimated to be entering into cells via binding with ACE-2 inhibitor. New research has shown that the binding of SARS-CoV-2 to gangliosides can be prevented further by hydroxychloroquin that may inhibit viral interaction with the ACE-2 receptor. Hydroxychloroquine and chloroquine can also be absorbed into endosomes and lysosomes, which contributes to a pH rise in intracellular cells. These organelles typically need an atmosphere for acidic homeostasis. The effect is a defective protein degradation, endocytosis and exocytosis required for viral infection, replication and spread. Earlier research has also shown that coronaviruses can use proteins for viral entry into host cells on the endosomal and endolysosome surfaces. Entry in the endolysosome may take place in the cytoplasm of infected cells to release the viral genome. However, it remains uncertain how changes in endosomal conditions in particular pH can influence the integrity of the SARS-CoV-2 viral genome. Hydroxychloroquine / chloroquine can typically affect multiple cell pathways and may have multiple mechanisms for SARS-CoV-2 action [10-11].

2.1.2 Remdesivir

COVID-19 therapeutic medicine is successful. It is a C-nucleoside phosphoramidate medicine and a wide-spectrum antiviral agent which Gilead Sciences synthesised and developed to treat Ebola virus infection in 2017. The active form GS-441524 metabolises Remdesivir, which obscures RNA polymers and prevents the proofreading of viral exonuclease, which reduces viral RNA growth. A delayed cessation of nascent viral RNA in the chain is the antiviral mechanism of remdesivir. Animal studies have shown that remdesivir can effectively reduce the viral load of MERS-CoV infected mice in your lung tissue and improve pulmonary function. Wang and al. Remedesivir firmly blocks SARS-CoV-1 infections and has high levels of selectivity (Half Maximum Effective Concentration (EC50), 0.77 μM; Half Cytotoxic Concentration (CC50) = 100 μM; Half Cytotoxic Concentration (SI > 129.87). The treatment of a COVID- 19 patient recovering from pneumonia was successful when the administration of Remdesivir. On February 5, 2020, China initiated a randomised, placebo-controlled, multicenter, Phase III clinical trial to evaluate the efficacy and safety of the medication in COVID-19 patients. In addition to standard therapy, the initial dose of 200 mg remdesivir was taken and 100 mg intravenous infusion was taken in patients from the study group for 9 consecutive days. The same dose of placebo medicine was taken in patients in the control group. The trial is expected for completion by the end of April 2020. There are 308 and 452, respectively, to be registered. The new prescription for Remdesivir requires 10 day remdesivir treatment regimes: 200 mg loading dose on day 1 followed by 100 mg of maintenance once day in both trials 9 days. This therapy is identical to the previous randomised Ebola virus clinical trial. Approximately 70 per cent of oxygen patients receive remdesivire by compassionate use in the US, and many patients that have been artificially ventilated have been extubated. There was no

control group in this study, so extrapolating these results is difficult. Remanufacturers have too early a direct antiviral effect in the increased clearance of viral stress in the respiratory tract to be verified, but the therapeutic effect of remdesivir is positive [12-15].

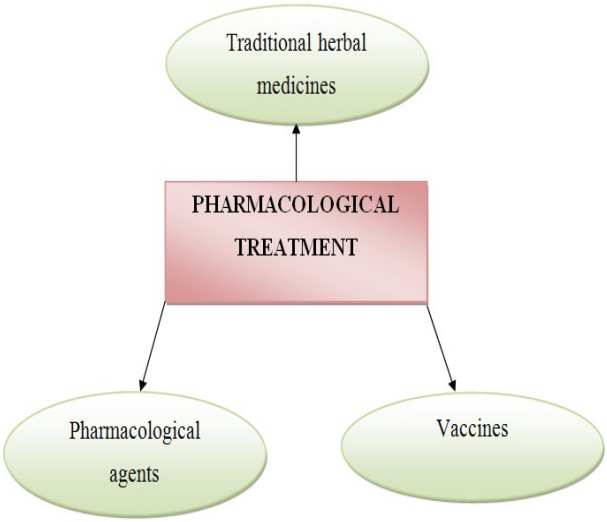

Figure 1: Pharmacological treatment

2.1.3 Umifenovir (Arbidol)

Umifenovir was first developed in Russia in 1988 and has since been approved for the treatment of influenza A and B prophylaxes, infections, and other arboviruses in Russia and China, as a derivative of indole carboxylic acids. Umifenovir subsequently displayed *in vitro* antiviral effectiveness in the widespread spread of strains of the viruses including Ebola, herpesvirus 8 (HHV-8) and hepatitis C (HCV) viruses. Its main mechanism for action is to avoid viral cell membrane fusion and fusion by mixing the cell membranes and interfering with the network of hydrogen phospholipid bindings [16]. With flu virus, hemagglutinin (HA) stabilisation has been demonstrated to interact with virus particles directly, which decreases the likelihood of the lower pH threshold required for conformation to functional fusogenic HA, i*n-vitro* SARS-CoV-1 and SARS-CoV-2 umifenovir operation. The combination of umifenovir and LPV-RTV indicates a greater negative rate of conversion of SARS-CoV-2 relative to the group-only lopinavir-ritonavir (LPV-RTV), as well as an enhanced chest CT scan. However, a further prospective study has shown that umifenovir is less effective in comparison to favipiravir in the rate of clinical recuperation and fever and cough. The efficacy and safety of umifenovir against COVID-19 are being tested in two randomised and open-label trials in China. The effect of umifenovir plus standard treatment vs. LPV-RTV plus standard therapy will be assessed, and the effect of umifenovir plus standard therapy vs. standard therapy in NCT04260594 [17-19].

2.1.4 Oseltamivir (Tamiflu)

Oseltamivir is an influenza A and B approved drug. Oseltamivir prevents the spread of the influenza virus within the human organism in the neuraminidase spread on the influenza virus surface. A research in Wuhan found no promising results after antiviral treatment with oseltamivir. In the treatment of SARS-CoV-2, a number of clinical trials continue to test for the effectiveness of oseltamiveir. In a variety of combinations, Oseltamivir is also added, for example in chloroquine and favipiravir, as support treatment for COVID-19 patients, in the absence of the vaccine or other SARS-CoV-2 antiviral medicines [20]. The following additional treatments are stressed such as azithromycin, ascorbic acid, corticosteroids and anakinra. Some of these drugs are used to try to avoid the cytokine storm, which is typically seen in the progression of the disease. There is still to be decided the desired administration plan. The most mechanistic idea can conceptually appear to inhibit the development of cytokine before this progress to an unreasonable stage. In COVID-19, a high serum IL-6 concentration has been associated with poorer outcomes and a key goal could be to inhibit the active use of directed treatment by this pro-inflammatory mediator. Other supplements identify bacterial , viral or alternative pathways for viral replication [21-22].

2.1.5 Immunomodulatory and Anti-inflammatory Agents

In COVID-19 patients, a variety of immunomodulatory drugs are being investigated currently. These drugs include synthetic drugs and biologic drug modulating specific inflammatory pathways by inhibiting IL-6 human receptor, metabolism, motility and chemical chemotaxis of the polymorphonuclear cells, production of JAK or TNF-α. Tocilizumab was one of the first medications to be used in COVID-19 patients. The ligand binding antibody IL-6R is monoclonal and serves to treat rheumatoid arthritis and systemic idiopathic juvenile arthritis. Research suggests that the IL-6 pathway is an important factor for controlling the inflammatory immune response of the pulmonary alveolate stage in COVID-19 patients. This immune response causes lung parenchyma damage, which substantially reduces breathing

function. The medication was checked for the first time in 20 patients with serious infection with SARS-CoV-2. Therapy included lowering oxygen consumption, addressing CT lesions, normalising the count for lymphocytes, decreasing the C-reactive level of proteins and discharging to hospitalisations for an average period of 13.5 days. Following the clinical performance, it is commonly used at many of the Italian hospitals, such as Cotugno Hospital in Naples. Since tocilizumab seems to be able to avoid inflammatory pathway hyperactivation, it can also be used in patients with COVID-19 that are not critical at an early age. There are currently three clinical trials, one of which is AIFA-approved. Sarilumab is of the same drug class and three studies are currently underway to assess the efficacy and safety of Sarilumab in approximately 1,500 COVID-19 patients, either by themselves or in combination with standard care [23]. Over the course of COVID-19 treatment at Chinese and Italian health centres, two other drugs, chloroquine and hydroxycloroquine, are marked as "miracle" in the USA. These compounds are authorised as anti-malarian medicines and are used to treat autoimmune diseases, including lupus and rheumatoid arthritis. Although both drugs are considered safe for typically mild and transitory adverse effects, both can be associated with cardiovascular disorders, including life-threatening QT prolongation. Long-term retinal toxicity may also occur. In addition, the incidence of liver defects in patients with COVID-19 rises significantly, leading to an increased risk of liver failure may be predicted to induce a deficiency metabolism of the two medicines. Some preclinical studies have shown that chloroquine has human coronavirus SARS antiviral efficacy [24]. OC43 (Teyaerts et al., 2009) and influenza A H5N1 (Gao, Tian & Yang, 2020; Inglot, 1969) suggested the possible role for SARS-Cov-2 infection. Further studies have shown that chloroquine influences terminal glycosylation of the functional enzyme ACE2, which adversely affects the virus-receptor binding. Indeed, clinical studies have shown high efficacy in preventing infection by remdesivir / chloroquine or hydroxychloroquine with SARS-Cov-2. The AIFA, having regard to the particular safety profile of both drugs used in Italy in patients with SARS-Cow-2 diseases, particularly in cases of heart failure, glucose-6-phosphate dehydrogenases, or other con-substances, has been recommended by AIFA healthcare professionals to carry out careful evaluations for these patients. Data from an *in-vitro* replication of SARS coV-2 were found to be effective from a recent systematic analysis of six scientific studies and 23 current clinical trial studies. However, the authors have acknowledged the urgent need to confirm the beneficial effectiveness and safety profile (Cortegiani, Ingoglia, Ippolito, Giarratano and Einav 2020) in high-quality clinical trials for COVID-19 patients for the help of clinical investigation into chloroquine. At present, rheumatoid arthritis is allowed with baricitinib. It is an inhibitor of JAK1 and JAK2 that is selective and reversible [25]. These intracellular signals translate haematopoiesis, inflammation and immunity to cytokines and growth factors. In addition, baricitinib prevents the virus from connecting to the alveolar epithelium by blocking the AP2 associated protein kinase 1 (AAK1) (Mayence & Vanden Eynde, 2019). A study published in The Lancet has indicated that it could be a viable treatment alternative for COVID-19 (Richardson et al., 2020). The efficacy and safety of baricitinib, lopinavir/ritonavir, hydroxychloroquine and sarilumab in 1,000 COVID-19 hospitalised patients was recently evaluated in non-randomised phase II clinical trials. Similarly, sunitinib, fedratinib and ruxolitinib may all have the potential to reduce inflammation and cytokine levels such as IFN-τ, IL-6, and viral endocytesis, with a potential effect against SARS-CoV-2 [26].

2.1.6 Nitazoxanide and Tizoxanide

Nitazoxanide and its metabolite as well as tizoxanide demonstrated an inhibitory effect of MERS-CoV in LLC-MK2 cells. Nitazoxanide has been reported to inhibit other corona viral strains, such as the corona virus murine, the hepatitis A59 (MHV-A59) mouse virus strain, the bovine corona virus strain L9 (BCoV-L9), and human enteric corona virus 4408 (HECoV-4408), as a result of the viral N protein suppression. Nitazoxanide has been utilised for inhibiting pro-inflammatory cytokines in the peripheral mononuclear blood cells (PBMCs) and *in vivo* IL-6. However, the value of this information is currently unknown [27].

2.1.7 Miscellaneous Agents and Therapies

Thiazolidinediones Studies have demonstrated the advantage to the respiratory syncytial virus, or H1N1 infections, of thiazolidinedione and its derivatives, which are treatments for type 2 diabetes mellitus. But their work as a therapeutic drug against coronavirus is not yet under investigation. It is interestingly known that the

receptor ACE-2, which is set as a binding site for SARS-CoV- 2, can be upregulated in host cells. However, the absence of clinical evidence does not explicitly suggest their therapeutic efficacy for coronavirus infections [28].

2.2 Traditional Herbal Medicines

In the conventional herbal remedies, past epidemic outbreaches such as SARS and H1N1 influenza were historically used to control or handle disease outbreaks. To date, China and South Korea have provided guidelines for COVID-19 prevention and care for traditional medicine. More than 85% of SARS-CoV-2 patients in China have been reportedly treated with some form of traditional Chinese medicine (TCM). Similar to SARS-CoV, SARSCoV-2 is using the cellular ACE2 receptor, which seems to be able to target ACE2, and which promises to prevent SARS-CoV-2 infection. In China and Korea, a variety of herbal products have been used in care for patients with SARS-CoV-2 infections due to the high similitude between the SARS-CoV-2 and the SARS-CoV-2 epidemiological, genomic, and pathogenesis [29-30].

2.3 Advances in the Development of SARS-CoV Vaccines and MERS-CoV Vaccines

For CoV vaccines it is important to establish strong humour and cellular immunities. Previous research has shown that the serum-neutralizing antibody level is reversely linked to pulmonary virustiters, effectively increasing host vaccine survival. High title antibodies can prevent replication of MERS-CoV in the lungs of the vaccinated mice to emphasise the importance of antibody neutralisation to combat infection by viruses. In addition, a number of studies have shown the importance of T-cell responses to CoV infection [31]. For instance, before the SARS-CoV challenge cell depletion in mice caused survival rates to drop to 35% and 45 %, respectively. Interestingly, SARS survivors 6 years after the infection were found with viral-specific T-cells but not anticonneutralizing them, which suggested that T-cell memory reactions can give good, long-term protection against SARS-CoV infection [32]. In general, both antibody neutralisation levels and T-cell responses should be included in the current strategies for CoV vaccination. There is currently no human approved CoV vaccine. Many CoV vaccines are currently in the pre-clinical process. In addition to regular inactivated and attenuated live vaccines, additional CoV vaccines are mainly based on the coronavirus S protein. These types of vaccines dependent on S protein include nucleic acid, viral vector, virus particle (VLPs), and subunit vaccines. Since SARS-CoV-2 vaccine research is still in its early stages, the following analysis will address strategies for the development of SARS-CoV and MERS-CoV vaccines in the hope of providing useful guidance for SARS-CoV-2 vaccine development [33-34].

2.4 Viral-vector Vaccines

Viral vectors have a molecular mechanism that helps to enter the target gene and to infect cells, an important vector medium for CoV vaccines. Comprehensive analysis of MERS-CoV and SARS-CoV Protein S viral vector-based vaccines has been performed. Avenovirus (Ad), modified ankara vaccine (MVA), attenuated parainfluenza virus (BHPIV3), and rabies virus (RV) have been used as the currently available vaccine vector [35]. A previous study has indicated that SARS-CoV S-specific neutralizing anticouns and mucosal responses, defending African green monkey against SARS-CoV infection, are elicit in African green monkeys that are vaccinated with BHPIV3 / SARS-S vector vaccines [36]. An additional study revealed the ability of strong SARS-CoV-neutralizing antibody response via a single inoculation that expresses the SARS-CoV S protein with the VRV-based vaccines. MERS-CoV S-specific neutralising antibodies and T-cell responses in antenocyte mice are also caused by vaccines based on human adenovirus or MVA after MERS-CoV vaccination [37-40].

2.4.1 Subunit Vaccines

Subunit vaccines consist of highly purified antigens that involve only a portion of the pathogen in order to induce a protective immune reaction. High safety, controllable efficiency and large-scale easy production characterise subunit vaccines, which increasingly make the number of researchers an aim. Compared to the full-length S protein, RBD contains many important neutralising epitopes and does not contain non-neutralization epitopes which can cause harmful pathological responses [41]. Sub-unit RBD-dependent vaccines can therefore not only induce successfully neutralising the antibody, they can also avoid adverse immune reactions. In terms of protection and efficacy the RBD-based CoV vaccines are more suitable candidates for developing CoV vaccines [42].

2.4.2 Virus-like Particle (VLP) Vaccines

Multi-protein structures, which mimic the organisation and conformation of native viruses,

but lack infectious genetic materials, are viral-like particles (VLPs). VLP is a potential candidate to develop safe and efficient CoV vaccines to efficiently activate innate and adaptive immune response functions. In VLP growth, extensive use has been made in the bacterial, mosquito, yeast, and mammalian cell expression systems. A research has shown that the coexpriming of SARS-CoV S proteins and mouse-hepatitis virus E, M and N proteins contributes to the neutralisation of antibodies in an successful way and thus prevents the replication of SARS-CoV in the lungs. Antibodies will be guided to neutralise and defend mice of death by other chemical VLps that express SARS-CoV S and M1 protein influenza [37]. Similar to vaccines for SARS-CoV VLP that cause broad antibodies to neutralise CoV infection, MERS-CoV VLP vaccines also show cell immune responses to MERS-CoV79 infections with antigen specific. VLP provides defence against emerging pandemic pathogens. VLP vaccine VLPs, however, must also be considered preventive vaccine with some problems. For example, viral mutations may cause antibody-mediated neutralisation to escape the virus [43-44].

2.5 Current Clinical Treatment Experience and Recommendations

The Centers for Disease Control and Prevention for Clinical Patient Care (COVID-19) emphasises that COVID-19 does not provide a particular treatment and stresses the timely implementation of the prescribed infection prevention and control measures and support for complication management. Unless otherwise mentioned, corticosteroids should be prohibited by the Centres for Disease Control and Prevention Recommendations specifically. Study therapies are described as alternatives, in specific solutions, through using compassionate medicine or by continuing clinical trials. In the same way, the World Health Organisation's (WHO) guidance paper states that "no evidence exists to support any particular anti-COVID 19 treatment of patients with confirmed COVID-19. This guidance emphasises the importance of promoting care depending on the seriousness of the condition, ranging from the symptomatic treatment of mild air traffic control associated with ARDS. The WHO recently announced plans for the launch of a global "megatrial' SOLIDARITY with a constructive trial design to randomise evidence, that systemic corticosteroids are not routinely administered outside the clinical trials to treat viral pneumonia and that research-related therapies against COVID-19 should be used only in approved, randomized, controlled trials [45, 46].

CONCLUSION

The pandemic COVID-19 represents the greatest concern of public health in this century and potentially the pandemic influenza outbreak since 1918. In order to test potential treatments, the speed and reach of clinical trials demonstrate both the need and resources to provide high-quality evidence even in the midst of a pandemic. We have identified the information given clinically for several medications, mainly antiviral, immune modulatory and anti-inflammatory agents, and more research is required to demonstrate the effectiveness and safety of Chinese and Western integrated medicines. CovS vaccines based on protein also include vaccines for virus vectors, nucleic acid (DNA andRNA), vaccines for VLPs, and protein vaccines in different classes. The vaccines subunit were the focus of current research because of its various advantages but also required appropriate adjuvants in order to enhance their immunogenicity. In the USA, aluminium, MF59 and CpG are the adjuvants to licenced vaccines. Therefore, development of SARS-CoV-2 vaccines still requires a relentless effort from researchers worldwide. Eight vaccines including three inactivated vaccines from the Wuhan Institute of Biological Products are required.

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CONFLICTS OF INTEREST

There are no conflicts of interest to declare.

REFERENCES

[1] Sohrabi C, Alsafi Z, O'Neill N, Khan M, Kerwan A, Al-Jabir A. World Health Organization declares global emergency: a review of the 2019 novel coronavirus (COVID-19). Int J Surg 2020; 76: 71e6.

[2] Fung T.S, Liu D.X. Human coronavirus: host-pathogen interaction. Annu. Rev. Microbiol. 2019; 73: 529–557.

[3] Toit A. Outbreak of a novel coronavirus. Nat. Rev. Microbiol. 2020; 18 (3): 123-128.

[4] W.G. Carlos. Novel Wuhan (2019-nCoV) coronavirus. Am. J. Respir. Crit. Care Med. 2020; 201(4): P7–P8.
[5] Nkengasong J. China's response to a novel coronavirus stands in stark contrast to the 2002 SARS outbreak response. Nat. Med. 2020; 26 (3): 310–311.
[6] Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) *in vitro*. Cell Res. 2020; 30: 269e71.
[7] Gao J, Tian Z, Yang X. Breakthrough: chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. BioSci Trends. 2020; 14: 72e3.
[8] Puavilai S, Kunavisarut S, Vatanasuk M, Timpatanapong P, Sriwong ST, Janwitayanujit S. Ocular toxicity of chloroquine among Thai patients. Int J Dermatol. 1999; 38: 934e7.
[9] Yan Y, Zou Z, Sun Y, Li X, Xu KF, Wei Y. Anti-malaria drug chloroquine is highly effective in treating avian influenza A H5N1 virus infection in an animal model. Cell Res. 2013; 23: 300e2.
[10] Projean D, Baune B, Farinotti R, Flinois JP, Beaune P, Taburet AM, et al. *In vitro* metabolism of chloroquine: identification of CYP2C8, CYP3A4, and CYP2D6 as the main isoforms catalyzing N-desethylchloroquine formation. Drug Metab Dispos. 2003; 31: 748e54.
[11] Hoffmann M, Kleine-Weber H, Schroeder S, Kru¨ger N, Herrler T, Erichsen S. SARS-CoV-2 cell entry depends on ACE2 andTMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell. 2020; 181: 271e80.
[12] Wang H, Wang Z, Dong Y, Chang R, Xu C, Yu X. Phaseadjusted estimation of the number of coronavirus disease 2019 cases in Wuhan, China. Cell Discov. 2020; 6: 10.
[13] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020; 395: 497e506.
[14] Gordon CJ, Tchesnokov EP, Feng JY, Porter DP, Gotte M. The antiviral compound remdesivir potently inhibits RNA-dependent RNA polymerase from middle-east respiratory syndrome coronavirus. J Biol Chem. 2020; 295: 4773e9.
[15] Guan Y, Zheng BJ, He YQ, Liu XL, Zhuang ZX, Cheung CL. Isolation and characterization of viruses related to the SARS coronavirus from animals in Southern China. Science. 2003; 302: 276e8.
[16] Woo PC, Lau SK, Lam CS, Lau CC, Tsang AK, Lau JH. Discovery of seven novel mammalian and avian coronaviruses in the genus deltacoronavirus supports bat coronaviruses as the gene source of alphacoronavirus and betacoronavirus and avian coronaviruses as the gene source of gammacoronavirus and deltacoronavirus. J Virol. 2012; 86: 3995e4008.
[17] Li F. Structure, function, and evolution of coronavirus spike proteins. Annu Rev Virol 2016; 3: 237e61.
[18] Sun P, Lu X, Xu C, Sun W, Pan B. Understanding of COVID-19 based on current evidence. J Med Virol. 2020; 92: 548e51.
[19] Belouzard S, Millet JK, Licitra BN, Whittaker GR. Mechanisms of coronavirus cell entry mediated by the viral spike protein. Viruses 2012; 4: 1011e33.
[20] Wrapp D, Wang N, Corbett KS, Goldsmith JA, Hsieh CL, Abiona O. Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. Science 2020; 367:1260e3.
[21] Gao J, Tian Z, Yang X. Breakthrough: chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. BioSci Trends. 2020; 14: 72e3.
[22] Bernstein H, Zvaifler N, Rubin M, Mansour AM. The ocular deposition of chloroquine. Invest Ophthalmol. 1963; 2: 384e92.
[23] Haeusler IL, Chan X, Gue´rin PJ, White NJ. The arrhythmogenic cardiotoxicity of the quinoline and structurally related antimalarial drugs: a systematic review. BMC Med. 2018; 16: 200.
[24] Leecharoen S, Wangkaew S, Louthrenoo W. Ocular side effects of chloroquine in patients with rheumatoid arthritis, systemic lupus erythematosus and scleroderma. J Med Assoc Thai. 2007; 90: 52e8.
[25] Puavilai S, Kunavisarut S, Vatanasuk M, Timpatanapong P, Sriwong ST, Janwitayanujit S, et al. Ocular toxicity of chloroquine among Thai patients. Int J Dermatol. 1999; 38: 934e7
[26] Willmann S, Ho¨hn K, Edginton A, Sevestre M, Solodenko J, Weiss W, et al. Development of a physiology-based whole-body population model for assessing the influence of individual variability on the pharmacokinetics of drugs. J

Pharmacokinet Pharmacodyn. 2007; 34: 401e31.

[27] Yan Y, Zou Z, Sun Y, Li X, Xu KF, Wei Y. Anti-malaria drug chloroquine is highly effective in treating avian influenza A H5N1 virus infection in an animal model. Cell Res. 2013; 23: 300e2.

[28] Hamming I, Timens W, Bulthuis ML, Lely AT, Navis G, van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. J Pathol. 2004; 203: 631e7.

[29] Ducharme J, Farinotti R. Clinical pharmacokinetics and metabolism of chloroquine. Focus on recent advancements. Clin Pharmacokinet. 1996; 31: 257e74.

[30] Yadav A, Mohite S. A Review on severe acute respiratory infection (SARI) and its clinical management in suspect/confirmed novel coronavirus (nCoV) cases Res. J. Pharma. Dosage Forms and Tech. 2020; 12(3): 178-180.

[31] Wu YC, Chen CS, Chan YJ. The outbreak of COVID-19: an overview. J Chin Med Assoc 2020; 83: 217e20.

[32] Liang H, Acharya G. Novel corona virus disease (COVID-19) in pregnancy: what clinical recommendations to follow. Acta Obstet Gynecol Scand 2020; 99: 439e42.

[33] Baez-Santos YM, St John SE, Mesecar AD. The SARS-coronavirus papain-like protease: structure, function and inhibition by designed antiviral compounds. Antivir Res. 2015; 115: 21e38.

[34] Lin CW, Tsai FJ, Tsai CH, Lai CC, Wan L, Ho TY, et al. Anti- SARS coronavirus 3C-like protease effects of Isatis indigotica root and plant-derived phenolic compounds. Antivir Res. 2005; 68: 36e42.

[35] Yadav A, Mohite S. A Review on Novel Coronavirus (COVID-19). International Journal of Pharma Sciences and Research. 2020; 11(5): 74-76.

[36] Ganeshpurkar A, Gutti G, Singh SK. RNA-dependent RNA polymerases and their emerging roles in antiviral therapy. In: Gupta Satya, editor. Viral polymerases: structures, functions, and roles as antiviral drug targets. New York: Academic Press. 2019: 1e42.

[37] Jang KJ, Jeong S, Kang DY, Sp N, Yang YM, Kim DE. A high ATP concentration enhances the cooperative translocation of the SARS coronavirus helicase nsP13 in the unwinding of duplex RNA. Sci Rep. 2020; 10: 4481.

[38] Aboagye JO, Yew CW, Ng OW, Monteil VM, Mirazimi A, Tan YJ. Overexpression of the nucleocapsid protein of Middle East respiratory syndrome coronavirus up-regulates CXCL10. Biosci Rep. 2018: BSR20181059.

[39] Wang LL, Shi DL, Gu HY, Zheng MZ, Hu J, Song XH, et al. Resveratrol attenuates inflammatory hyperalgesia by inhibiting glial activation in mice spinal cords. Mol Med Rep. 2016; 13: 4051e7.

[40] Yadav A, Mohite S. A Novel approach for treatment of COVID-19 with Convalescent Plasma. Res. J. Pharma. Dosage Forms and Tech. 2020; 12(3): 227-230.

[41] Kimbrough CW, Lakshmanan J, Matheson PJ, Woeste M, Gentile A, Benns MV, et al. Resveratrol decreases nitric oxide production by hepatocytes during inflammation. Surgery 2015; 158: 1095e101.

[42] Yadav A, Mohite S. A Review on Novel Coronavirus (COVID-19). International Journal of Pharma Sciences and Research. 2020; 11(5): 74-76.

[43] Zulueta A, Caretti A, Signorelli P, Ghidoni R. Resveratrol: a potential challenger against gastric cancer. World J Gastroenterol 2015; 21: 10636e43.

[44] Toth P, Tarantini S, Tucsek Z, Ashpole NM, Sosnowska D, Gautam T. Resveratrol treatment rescues neurovascular coupling in aged mice: role of improved cerebro-microvascular endothelial function and down regulation of NADPH oxidase. Am J Physiol Heart Circ Physiol. 2014; 306: H299e308.

[45] Gliemann L, Nyberg M, Hellsten Y. Effects of exercise training and resveratrol on vascular health in aging. Free Radic Biol Med. 2016; 98: 165e76.

[46] Lau KM, Lee KM, Koon CM, Cheung CS, Lau CP, Ho HM. Immunomodulatory and anti-SARS activities of Houttuynia cordata. J Ethnopharmacol 2008; 118:79e85.