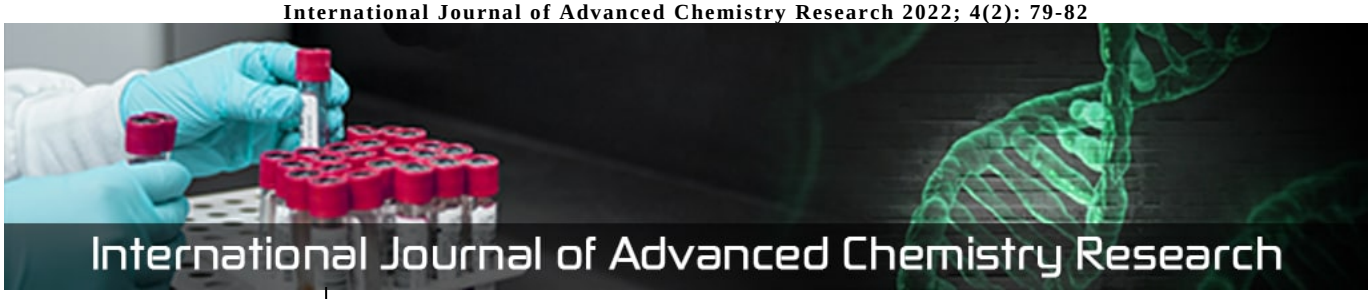

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A concise overview of novel coronavirus 2019 for future reference based on established facts

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Abstract
In December 2019, a highly contagious novel coronavirus disease 2019 (COVID-19) emerged in Wuhan, China, and has since rapidly spread to multiple regions within China and numerous countries worldwide. The World Health Organization (WHO) declared this outbreak the sixth public health emergency of international concern. As of March 26, 2020, at 0:00 am, there have been 416,686 reported cases of COVID-19 across 197 countries, with 18,589 deaths. Ongoing research is dedicated to developing medications against COVID19. In this review, we comprehensively summarize the symptoms, virus transmission routes, diagnosis, and treatment methods based on current published data. The aim of this research paper is to help the public better understand and effectively manage COVID-19 while providing a reference for future studies.

Keywords: Coronavirus disease 2019, Coronavirus, Severe acute respiratory syndrome coronavirus, middle-east respiratory syndrome coronavirus

Introduction
Very recently, a novel unidentified epidemic coronavirus (CoV), specifically known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in the city of Wuhan, China, in December 2019, and rapidly spread throughout the country within one month. However, on February 11, 2019, the WHO announced a new name for it: coronavirus disease 2019 (COVID-19). CoV is a single positive-stranded RNA virus that belongs to the Coronaviridae family and can lead to respiratory and neurological diseases. It is categorized into four types: alpha-CoV, beta-CoV, delta-CoV, and gamma-CoV. Previously, six CoVs had been identified, including HCoV-229E (alpha-CoV), HCoV-OC43 (beta-CoV), SARS-CoV-1 (beta-CoV), HCoV-NL63 (alpha-CoV), HCoV- HKU1 (beta-CoV), and Middle East respiratory syndrome coronavirus (MERS-CoV) (beta-CoV) [1, 2]. The newly discovered seventh HCoV, SARS-CoV-2, is responsible for respiratory infections. SARS-CoV-2 falls under the beta-CoV category (Figure 1) and has various potential natural hosts, intermediate hosts, and final hosts. Compared to other viruses like SARS-CoV and MERSCoV, this virus exhibits high transmissibility and infectivity, despite having a lower mortality rate [3-5].

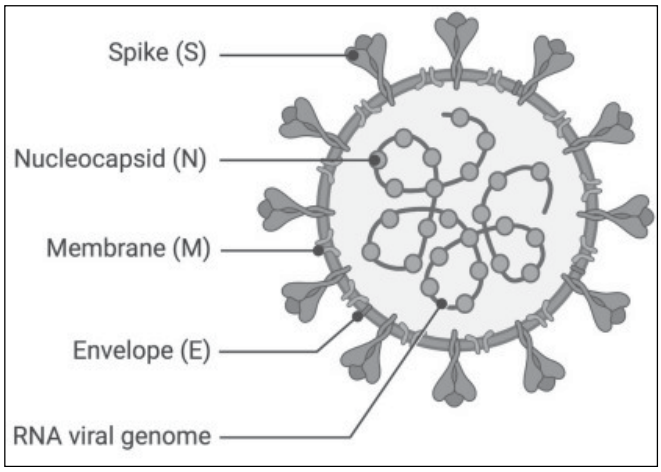
The CoV Situation in India
The inaugural case of the COVID-19 CoV in India surfaced on January 30, 2020, specifically in the state of Kerala. As of April 9, 2020, at 8:00 am, the Indian Council of Medical Research (ICMR) and the Ministry of Health and Family Welfare have documented a cumulative total of 5,095 cases, with 472 recoveries, 1 migration, and 166 fatalities within the country (source: https://www.mohfw.gov.in/).
To combat the spread of the CoV, India's Prime Minister, Narendra Modi, initiated the Janata curfew in response to the 2020 CoV pandemic in India. On March 22, 2020, the Prime Minister advised all Indian citizens to observe a voluntary "curfew" from 7 am to 9 pm Indian Standard Time. This measure aimed to curtail the communal transmission of the CoV disease in India (source: https://en.wikipedia.org/wiki/ Janata_Curfew).

Symptoms
As of February 20, 2020, and based on 55,924 laboratory-confirmed cases, individuals infected with COVID-19 exhibited a spectrum of symptoms, including fever (87.9%), dry

cough (67.7%), fatigue (38.1%), sputum production (33.4%), shortness of breath (18.6%), sore throat (13.9%), headache (13.6%), myalgia or arthralgia (14.8%), chills (11.4%), nausea or vomiting (5.0%), nasal congestion (4.8%), diarrhea (3.7%), hemoptysis (0.9%), and conjunctival congestion (0.8%).

Routes of Virus Transmission

Coronaviruses have the potential to cross species boundaries. Initially, COVID-19-infected patients were suspected to have contracted the virus at the Wuhan wholesale seafood market, suggesting animal-tohuman transmission. However, a substantial number of cases have been reported in individuals with no exposure to markets, indicating that COVID-19 also spreads through person-to-person contact [6, 7]. Previous epidemiological studies have identified three primary factors contributing to virus spread: person-to-person contact, aerosol transmission, and transmission through touch [8, 9]. The virus is primarily believed to transmit from one person to another in close proximity (within approximately 6 feet), primarily through respiratory droplets generated when an infected individual coughs or sneezes. These droplets may land in the mouths or noses of nearby individuals or potentially be inhaled into their lungs. While it is possible to contract COVID19 by touching a surface or object contaminated with the virus and then touching one's own mouth, nose, or eyes, this is not considered the primary mode of transmission. Early and rapid detection of COVID-19 proves highly effective in controlling sources of infection and enables patients to mitigate disease progression, thereby reducing the spread of the coronavirus [10].



Diagnosis of SARS-COV-2

The field of nucleic acid detection has experienced rapid advancements paralleling the progress in molecular biology technology, enabling the identification of viruses with precision.

Nucleic Acid Amplification Test (NAAT)

The Nucleic Acid Amplification Test (NAAT) has emerged as a pivotal technique for discerning specific genetic sequences of the COVID-19 virus. This methodology utilizes reverse transcription polymerase chain reaction (rRT- PCR) for amplification purposes, owing to its merits such as specificity and the facilitation of a straightforward quantitative assay. Furthermore, rRTPCR exhibits an enhanced capability to detect earlystage infections compared to conventional RT-PCR assays [11]. Consequently, real-time RT- PCR remains a prevalent and indispensable tool for detecting various Coronaviruses (CoVs), including the formidable SARSCoV-2 [14].

Serology Test

Serology testing serves as a valuable tool for individuals who may have encountered the virus, enabling the identification of past infections (in terms of antibodies to MERS-CoV). These antibodies, emanating from the body's immune system, play a pivotal role in targeting and neutralizing viruses, bacteria, and other microbial invaders during an infection. The presence of MERS-CoV antibodies signifies a prior encounter with the virus, resulting in the development of an immune response.

Serological surveys prove instrumental in ongoing outbreak investigations and retrospective assessments of attack rates or outbreak severity. In cases where NAAT assays yield negative results, yet there exists a clear epidemiological link to a COVID-19 infection, the deployment of paired serum samples (capturing both the acute and convalescent phases) can facilitate a diagnosis once validated serology tests become accessible. Consequently, it is prudent to preserve serum samples for future analysis, although challenges regarding cross-reactivity with other CoVs persist [15]. Presently, both commercial and non-commercial serological tests are undergoing development, with a handful of studies presenting COVID-19 serological data [16, 17].

Viral Sequencing

Standardized serological tests have been innovated for the detection of anti-MERS CoV antibodies in human sera, subsequently validated to support diagnostic and surveillance endeavors associated with the disease. These assays are founded upon indirect immunofluorescence assay (IFA) and enzyme-linked immunosorbent assay (ELISA) technologies. Collaborative efforts with leading virology institutes in Germany, including the Institute of Virology at the University of Bonn Medical Center and the Robert Koch Institute, have culminated in the development of serological tests for the detection of anti-MERS-CoV antibodies in human sera [15].

Moreover, Professor Zhang F from MIT has pioneered a test paper utilizing SHERLOCK technology for expedited detection of SARS-CoV-2 within a mere hour. While clinical validation remains pending, this breakthrough technology holds promise for swift disease diagnosis [18]. Notably, a research consortium at Peking University, China, has unveiled a novel approach for the rapid construction of transcriptome sequencing libraries, facilitating the expedited sequencing of SARS-CoV-2 [19].

Vaccination for COVID-19 (Underway)

At the Kaiser Permanente Washington Health Research Institute in Seattle, the first clinical trial of a COVID-19 vaccine has commenced in the United States, featuring Moderna's mRNA-1273. This mRNAbased vaccine is engineered to target the encoding of the pre-fusion stabilized form of the spike (S) protein of SARS-CoV-2, a selection made in collaboration with the Vaccine Research Center (VRC). The VRC, a constituent of the National Institutes of Health (NIH) and the National Institute of Allergy and Infectious Diseases, is integral to this pioneering effort (source: https://www.pharmaceuticalbusiness-

review.com/news/ moderna-mrna-1273-coronavirus-trial/).
In the Phase I trial, a cohort of 45 healthy adults aged between 18 and 55 years has been recruited to assess the safety and immunogenicity of mRNA-1273 at three dosage levels: 25 µg, 100 µg, and 250 µg. The vaccine is administered as a two-dose regimen, with the doses spaced 28 days apart. The study also encompasses a 12-month follow-up period after the second vaccination. The primary objective is to evaluate the safety and reactogenicity of the two-dose regimen, while the secondary objective pertains to the immunogenicity of the SARS-CoV-2 S protein (source: https://www.clinicaltrialsarena.com/news/first-uscovid-19-vaccinetrial-moderna/).

Treatment for COVID-19

Convalescent Plasma (CP) Therapy

Over the preceding decades, Convalescent Plasma (CP) therapy has demonstrated remarkable success in treating various viral infections, including MERS [20], SARS [21], H1N1 [22], and H5N1 [23]. Presently, no specific antiviral drugs are available for combatting the novel SARS-CoV-2, with some drugs still undergoing investigation. Consequently, CP therapy emerges as one of the most promising treatments for addressing SARS-CoV-2 infection. CP therapy entails the infusion of antibodies obtained from the blood of individuals who have recovered from the virus, bolstering the recipient's immune system.
A recent article published by a Chinese research team in the Proceedings of the National Academy of Sciences presents a pilot study on CP therapy, revealing a potential therapeutic benefit and low risk in the treatment of severe COVID-19 patients [24]. In a case report documented in the Journal of Korean Medical Science, physicians administered CP therapy to two patients afflicted with SARS-CoV-2. The outcomes demonstrated full recovery from COVID-19 in both cases [25].

Medicinal Plant Extracts

In recent years, Chinese herbal medicinal extracts have been harnessed for the treatment of both SARS and MERS [26-28]. The 3-chymotrypsin-like cysteine protease (3CLpro) plays a pivotal role in the replication of Coronaviruses (CoVs), making it an indispensable target for drug discovery efforts, spanning SARS-CoV, MERS, and SARS-CoV-2. Among the Chinese herbal extracts, the following demonstrated the ability to inhibit the enzymatic activity of SARS 3CLpro: extracts of Chinese Rhubarb, water extracts of Houttuynia cordata, flavonoids extracted from Litchi seeds, and beta-sitosterol derived from the root extract of Isatis indigotica. Additionally, certain herb-derived compounds, including sinigrin, indigo, aloe-emodin, hesperetin, quercetin, epigallocatechin gallate, gallocatechin gallate, herbacetin, rhoifolin, and pectolinarin, displayed the capability to inhibit SARS 3CLpro activity [29].

Remdesivir 20

Remdesivir (development code GS-5734) represents a groundbreaking antiviral medication belonging to the nucleotide analog class, exhibiting a broad-spectrum antiviral effect against numerous RNA viruses. Developed by Gilead, this drug initially found utility in the treatment of Ebola and related viruses, owing to its ability to inhibit the replication enzyme RNA-dependent RNA polymerase, effectively curtailing the replication process. According to a case report in the New England Journal of Medicine (NEJM), a young resident of Snohomish County, Washington, was administered remdesivir when his condition deteriorated, and the following day witnessed a notable improvement.
Professor Jiang Shibo of Fudan University in Shanghai, China, a seasoned researcher in the field of Coronavirus therapy, cautions that individual case data, while valuable, do not singularly establish the safety and reliability of a drug. Nevertheless, among the drugs under evaluation in the SOLIDARITY trial, "remdesivir holds the greatest potential for hospital use."

Chloroquine and Hydroxychloroquine

On February 17, 2020, the Chinese State Council conducted a news conference, revealing the significant efficacy and acceptable safety profile of chloroquine phosphate—an established malaria medication—in the treatment of COVID-19, as indicated by multicenter clinical trials conducted in China. A recent publication by a Chinese research team further highlighted the utilization of chloroquine and hydroxychloroquine in addressing SARS-CoV-2, with hydroxychloroquine (EC50=0.72% µM) exhibiting greater effectiveness compared to chloroquine (EC50=5.47% µM). Notably, reports by Gautret indicated the successful treatment of COVID-19 patients with hydroxychloroquine and azithromycin, effectively curbing virus transmission and global COVID-19 spread.

Ritonavir/Lopinavir

A case report in the NEJM documented a study wherein doctors in Wuhan, China, administered two pills of lopinavir/ritonavir twice daily in conjunction with standard care to 199 patients. However, no discernible benefit was observed with lopinavir–ritonavir treatment beyond that conferred by standard care. The Indian Council of Medical Research (ICMR) has suggested a combination therapy involving lopinavir/ritonavir for treating COVID-19 patients, drawing from observational studies highlighting clinical benefits in individuals with SARS-CoV and MERS-CoV [19-21]. Furthermore, the National Institute of Virology, Pune, conducted docking studies to inform this therapeutic approach.
In a notable case, a British national receiving treatment at Ernakulam Medical College Hospital in Kochi, India, for COVID-19 was administered HIV antiretroviral drugs (ritonavir and lopinavir), resulting in a subsequent negative test for the virus (source: https://www.indiatoday.in/india/story/coronavirus-pandemicforeigner-treated-hiv-drugs-covid-19- tests-negative-1659761-2020-03-26, dated: 26-03-2020).

Conclusion

The emergence of COVID-19, a novel Coronavirus, in Wuhan, China, in December 2019 has given rise to a severe global epidemic. Its symptoms bear striking resemblance to those of SARS, encompassing fever, dry cough, fatigue, sputum production, shortness of breath, sore throat, and headache. This virus poses a substantial threat to global health and safety, compelling us to take swift measures to curb its spread. Presently, effective vaccines and drugs for this virus remain elusive, fueling ongoing research endeavors for their development.
In light of this, it is imperative that we implement measures to halt virus transmission, leverage existing drugs to control the disease's progression, and maintain a minimum distance

of 1 meter between individuals.

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