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Review Article

# Drugs being tested against COVID-19 to slow down its spread and find effective treatment: A systematic review.

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## Abstract

**Background:** The SARS-CoV-2's spread from continent to the continent has resulted in an increased number of mutations in the viral gene encoding proteins. As a result, mutations in target proteins provide a significant challenge in creating antiviral drugs and vaccines. The present review discussed the COVID-19 epidemiology and the effects of drugs being tested against COVID-19/SARS-CoV-2. Dosage of these drugs along with associated challenges was also discussed.

**Methodology:** Systematic review was conducted after a thorough search in the PubMed, NIH, Elsevier, Scopus, Web of Science, Science direct and Google Scholar database. 45 studies on drugs associated with COVID-19 fulfilled the inclusion criteria and were selected for this review.

**Results:** Food and Drug Administration (FDA) only accepted the Remdesivir drug against SARS-CoV-2, as the hospitalized patients recovered very quickly by taking it. Antiviral EIDD-2801 has been found to make the SARS-CoV-2 unable to infect cells by causing genetic modifications in the virus RNA. Similarly, Nitazoxanide appeared beneficial against SARS-CoV-2 in a primary intervention and severe conditions (including pregnancy) without undesirable effects on the newborns. Children with mild cases can be handled solely by proper caring.

**Conclusion:** Although Remdesivir and Dexamethasone are recommended in severe cases, clinical trials are ongoing to investigate other possible therapies like MAb and Convalescent Plasma antibodies for COVID-19. Older drugs (usually used to treat other conditions) are also under-tested by researchers to see if they are effective for COVID-19. Further tests are essential to validate whether any of the mentioned above possible therapies would be helpful for COVID-19 treatment.

## Keywords

Remdesivir, Coronavirus, SARS-CoV-2, COVID-19, Drugs, Treatment, Clinical Science.

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## Introduction

The rise of the newly detected coronavirus from Wuhan (China) as a pandemic made health workers stop its transmission through conventional health measures based on case isolation and touch monitoring. Hellewell et al. projected two assumptions that this technique could help minimize its spread would be unable to stop it[1]. One of the two reasons was that all persons with symptomatic SARS-CoV-2 were checked for long last. Still, physicians can examine patients suspected only if they have been to the affected area under the guideline with low graded transmission second presumption is that case isolation is only effective for the confinement of the spread of the epidemic. However, quarantine of infected individuals at home and their access is complex, and effectiveness varies, so considerable public health resources are required for accurate monitoring.

Implementing the possible solution for protecting individuals at greater risk of infection, including personal contact and health care staff, by studying the increasing rate of secondary infection in households and close contact can help devise a strategy for possible measures. Pre and post-exposure prophylaxis (before possible exposure or following contact) could play an essential role in preventing disease[2]. The use of post-exposure prophylaxis after a potential exposure is highly recommended by the different organizations.

For introducing antiviral therapy, some criteria have to be followed, including proper drug supply, protection of treatment, and low prices. A Chinese finding in its initial analysis of clinical management was shown promising, although not definitive, owing to the limited sample size[3]. The results of random clinical trials were designed to judge the efficiency of antiviral treatment for COVID-19 to avoid secondary infection and decrease its transmission. The design was similar to the one used for the Ebola virus in 2015[4]. An overview of different drug repurposing approaches is provided in table 1.

Because of SARS-CoV-2, 162,628,327 people got infected, and 3,373,813 people died fighting against it[5]. So, there is a need to search for an effective and efficient cure for COVID-19. Scientists globally started to work by leaps and bounds to handle this deadly virus and begin testing the positive patients in labs and hospitals. Hence, this study has been conducted to analyze the drugs being tested on SARS-CoV-2 and whether any drug showed positive results against the COVID-19 by halting its progression and effectively treating it.

**Table 1: Brief overview of different drug repurposing approaches.**

| Approaches | Purpose |
|---|---|
| **Binding assay** | Identify binding interactions of ligands to assay components |
| **Phenotypic screening** | Evaluation of a series of compounds in an array of independent models |
| **Network mapping** | Involves constructing drug or disease networks based on gene expression patterns, disease pathology, and protein interactions |
| **Drug centric** | Examine the effects of a single drug on multiple targets |
| **Target-based** | Identification of new indications based on the drug's protein targets |
| **Knowledge-based** | Consolidates known information about a drug anticipating unexplored biomarkers |
| **Signature-based** | Based on the comparison of the unique characteristics or 'signature' of a drug against that of another drug, disease, or clinical phenotype |

## Methodology

### Research design

This research is exploratory in nature and was aimed to analyze the progress of finding treatment against COVID-19, technologies, and methods used in drug development and to compare the globally approved current drugs against COVID-19.

### Data collection

With the help of Boolean and search terms, a search string was formulated in electronic databases. The keywords include treatment, therapy, medication, drugs, coronavirus disease, SARS-CoV-2, pandemic, digital health, and digital care of COVID-19.

Data from well-recognized research sources and digital repositories were collected because of the excellent and accurate medical sciences, social, and information systems databases. The research databases and digital repositories include PubMed, WHO, NIH, Elsevier, Scopus, Web of Science (Clarivate Analytics), Google Scholar, Science direct, Taylor and Frances, ProQuest, Inderscience, Emerald, Springer, Sage, ACM, Wiley, and IEEE Xplore.

Besides this, specialized search engines were also used to search a specific keyword with type, year, and publication specialization. The search was started from mid-November 2020 to May 2021 for relevant literature.

### Ethical review statement

No data was collected from human subjects directly by the authors; however, the research was conducted according to the Declaration of Helsinki.

### Endpoints

The severe adverse reactions that appeared after enrollment of drugs 5 days later were observed at the endpoint. Time to clinical recovery (TTCR) is the coming back of the body to normal status maintained for 72 hours.

TTCR is characterized as the period from the beginning of research (active or placebo) to fever standardization and oxygen saturation and amelioration of cough, which is maintained approximately for 72 hours, or active hospital incidents. Following are the normalization criteria.

- Body temperature normalized: having 36.6 Co general body temperatures, 37.2 Co under armpits and mouth, or 37.8 Co in the rectum.
- Cough from medical reports: There is no or mild cough in the asymptomatic area. Temperature with a cough was examined twice daily to determine the average dose.
- Chest CT scan results (radiological changes): one day before the medications or drug administration and one day after the examination for assessment. Aspiratory recuperation is respectably improved if under half pneumonia were ingested, and if over half were assimilated, it would be called significantly improved.
- An asymptomatic case: a person who has a positive test verified by a laboratory and has no symptoms for the duration of the infection.

### Inclusion criteria

Literature having the following terms were the inclusion criteria for the current research.

- Drugs that have been tested on COVID-19 patients.
- Time frame from Mid-November 2020 to September 2021.
- Articles available in online databases for data collection.

### Exclusion criteria

Vaccines-related studies are excluded from this review.

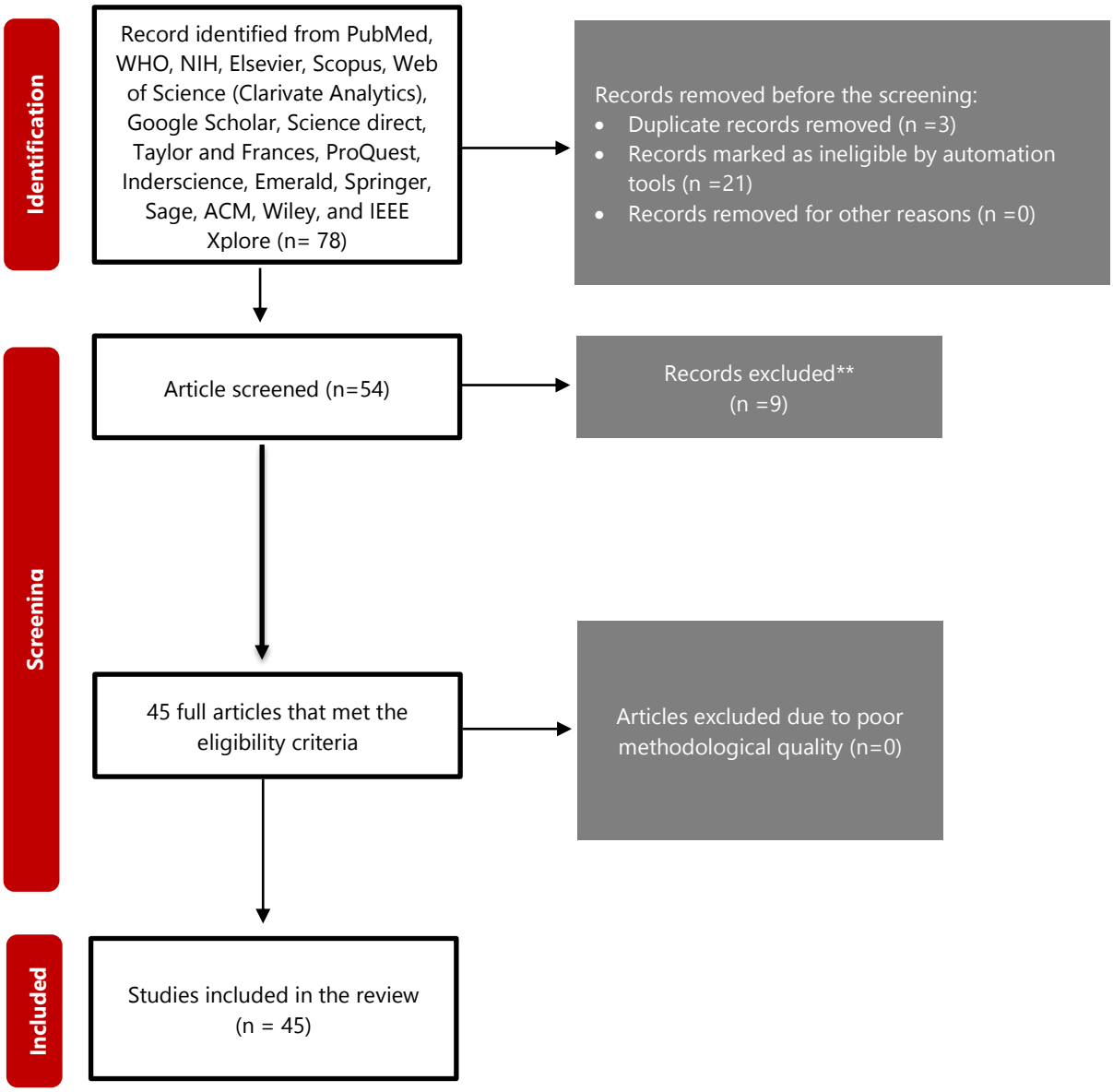



**Figure 1: PRISMA flowchart illustrating the review process for analyzing the drugs being tested against COVID-19 to slow its spread and find effective treatment.**

**Records excluded due to unavailability of sufficient data. Forty-five studies were selected for this review after screening for eligibility (Table 2).

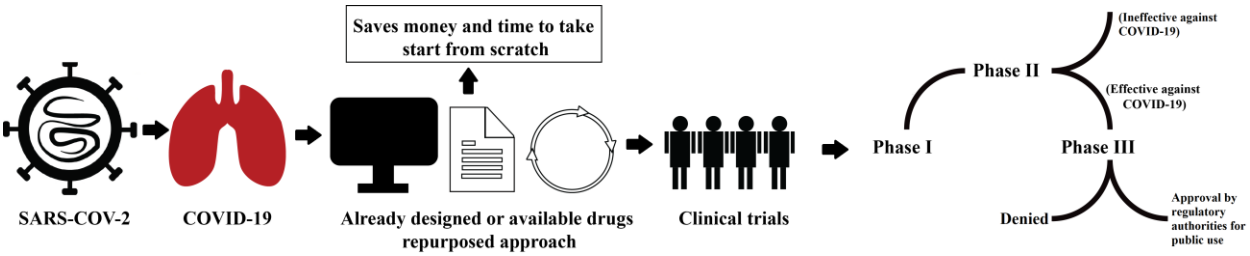



**Figure 2: Graphical representation of the study process for analyzing the drugs tested for COVID-19 treatment.**

## Results

A wide variety of drugs have been tested by researchers that may be used to fight COVID-19[6]. It is hoped that any drug might be discovered as a treatment or cure for COVID-19. Studies found that the following drugs have been experimented with against SARS-CoV-2 (Figure 3, Table 2).

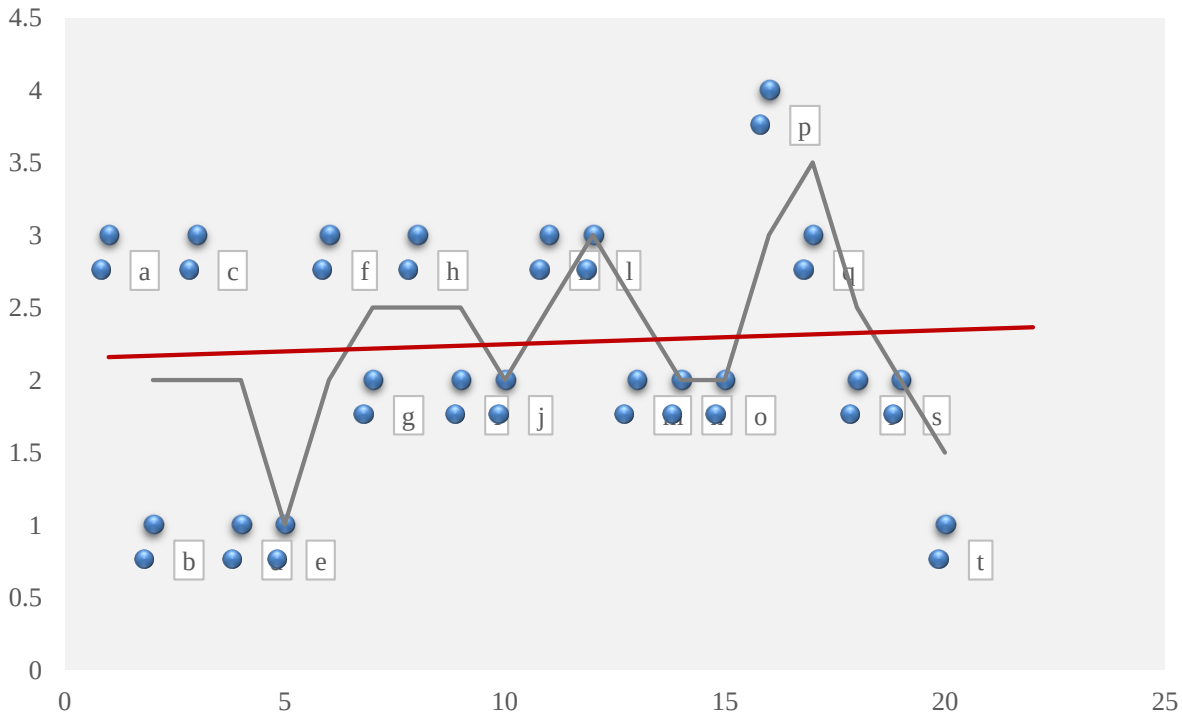
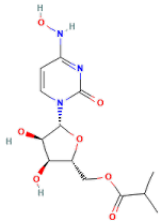
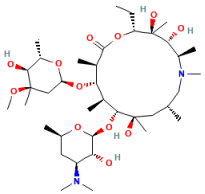
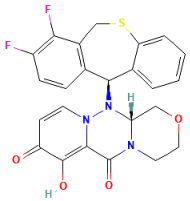
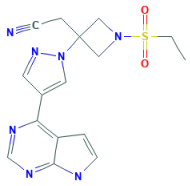
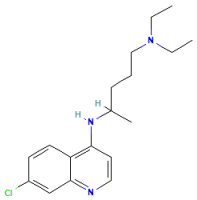
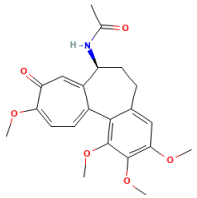
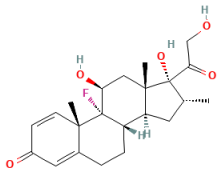
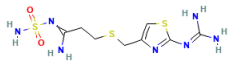


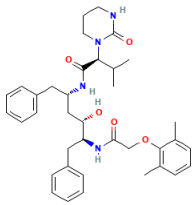
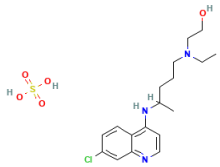
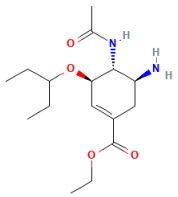
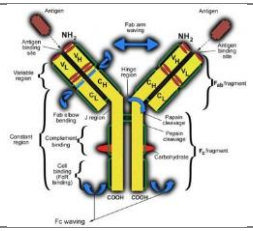
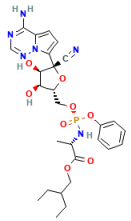

**Figure 3. Funnel plot showing the number of selected studies on different COVID-19 drugs.**

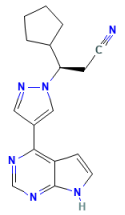
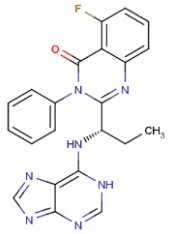
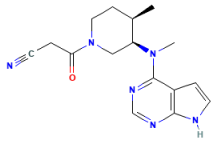
a: Antiviral EIDD-2801, b: Azithromycin, c: Anti-SARS-COV-2 MAb (mAb), d: Baloxavir, e: Baricitinib, f: Chloroquine, g: Colchicine, h: COVID-19 Convalescent Plasma, i: Dexamethasone, j: Famotidine, k: HIV Protease Inhibitors, l: Hydroxychloroquine, m: Neuraminidase inhibitors, n: IVIG, o: Remdesivir, p: Ruxolitinib, q: Sarilumab, r: Siltuximab, s: Tocilizumab and t: Tofacitinib.

**Table 2: Characteristics of the drugs used for the treatment of COVID-19.**

| Drugs/Compounds | Structures**** | Early indications | Dosing for COVID-19* | References |
|---|---|---|---|---|
| **Antiviral EIDD-2801** |  | Broad-spectrum Antiviral | Undertrial | 7,8,9 |
| **Azithromycin** |  | Respiratory tract infections | Day 1=500 mg<br>Days 2-5=250 mg once daily<br>(or 7 days=500 mg once a day in combination with a 5-, 7-, or 10-day Hydroxychloroquine regimen) | 10 |
| **Anti-SARS-COV-2 mAb **** | - | COVID-19 | Depending on the antibodies | 11,12,13 |
| **Baloxavir** |  | Acute uncomplicated influenza | Day 1, 4, and 7=80 mg (not to exceed 3 total doses) | 14 |
| **Baricitinib** |  | Rheumatoid arthritis | 14 days, or until the patient is discharged from the hospital =4 mg orally once daily (Aged ≥9 years) and 2 mg (Aged ≥2 years to <9 years) | 15 |

| | | | | |
|---|---|---|---|---|
| **Chloroquine** |  | Malaria | For 7 days=500 mg twice daily (people aged 18 to 65 weighing more than 50 kg); Day 1, 2=500 mg twice daily and days 3-7=500 mg once daily (adults weighing <50kg) | 16,17,18 |
| **Colchicine** |  | Anti-inflammation | For 3 days=0.5, mg twice daily, then once daily for 27 days | 19,20 |
| **COVID-19 Convalescent Plasma** | - | Did not prevent COVID-19 progression | Approximately 200 mL once *** | 13,21,22 |
| **Dexamethasone** |  | Immunosuppressant | Up to 10 days or until hospital discharge=6 mg orally once daily | 23,24 |
| **Famotidine** |  | Treat and prevent ulcers in the stomach and intestines | Up to 14 days or until hospital discharge=120 mg (proposed total daily dosage of 360 mg) | 25,26 |

| | | | | |
|---|---|---|---|---|
| **HIV Protease Inhibitors (Lopinavir (LPV), Atazanavir (ATV), Darunavir (DRV), Nelfinavir (NFV), Ritonavir (RTV), Saquinavir (SQV), Tipranavir (TPV).** |  | HIV & Influenza | Up to 14 days=LPV, 400 mg/RTV 100 mg twice daily orally (with or without additional antivirals, e.g., interferon, Umifenovir)<br>The dose for other drugs is unknown. | 27,28,29 |
| **Hydroxychloroquine** |  | Malaria | Day 1=800 mg<br>4-7 days=400 mg daily | 2,16,17 |
| **Neuraminidase inhibitors (e.g., oseltamivir, zanamivir and peramivir)** |  | Influenza | 75 mg twice a day or 300 mg (or 4-6 mg/kg) twice a day | 30,31 |
| **Non-SARS-CoV-2-specific (IVIG)** |  | COVID-19 | The dose varies based on indication and formulation. | 32,33 |
| **Remdesivir** |  | Broad-spectrum Antiviral | For 5 or 10 days, take 200 mg on day one and 100 mg once a day on consecutive days | 18, 34 |

| | | | | |
|---|---|---|---|---|
| **Ruxolitinib** |  | Myelofibrosis | For 14 days=5, mg–20 mg orally twice daily for 2 weeks | 32,28,35,36 |
| **Sarilumab** | - | Rheumatoid arthritis | 400 mg (single dose) | 32, 37, 38 |
| **Siltuximab** |  | | Unknown | 39, 40 |
| **Tocilizumab** | - | Cytokine release syndrome | 8 mg/kg (single dose); Dose should not exceed 800 mg. (Administer in combination with dexamethasone) | 41, 42 |
| **Tofacitinib** |  | Acute inflammation | For 14 days=10, mg twice daily | 24 |

*Some of the doses listed here are for approved indications or reported experiences or clinical trials. ** LY-CoV555 (Bamlanivimab, LY-CoV555 (Bamlanivimab) + LY-CoV016 (Etesevimab), REGN-COV2 (REGN10933/Casirivimab + REGN10987/Imdevimab),S309(VIR-7831, Sotrovimab), AZD7442 (COV2-2130/ Cilgavimab + COV2-2196/Tixagevimab), TY027, BRII-196 + BRII-198, CT-P59 (Regdanvimab), BI 767551 (DZIF-10c), SCTA01, ADG20, MAD0004J08, MW33,DXP593,COVI-AMG(STI-2020),LY-CoV1404 + LY-CoV555 (Bamlanivimab) + LY-CoV016 (Etesevimab), XVR011, LY-CoV016
(JS016, Etesevimab), 47D11, ADM03820, DXP604, C144-LS, and C-135-LS (Source: Hwang et al., 2022). ***Additional high-titer COVID-19 convalescent plasma units may be administered based on the prescribing physician's medical judgment and the patient's clinical response.****Source: PubChem

**Antiviral EIDD-2801/MK-4482 (Molnupiravir)**

In vitro studies of the airway and human lung cells showed that an oral drug called EIDD-2801 showed promise[43]. The drug could be even more effective than Remdesivir. According to Scientific American, Remdesivir prevents the SARS-CoV-2 from completely replicating, while EIDD-2801 causes genetic alterations in the virus's RNA. When the RNA replicates, many negative mutations occur, leaving the virus unable to infect cells. The drug was also active against various RNA viruses, and researchers also concluded that it could be a multipurpose antiviral drug. 7.3% of molnupiravir-treated patients were hospitalized or died by day 29, compared to 14.1% of placebo-treated patients who were hospitalized or died[44]. Molnupiravir's safety, tolerability, and pharmacokinetic profile against SARS-COV-2 were recently detailed in a study[7].

**Anti-SARS-COV-2 mAb**

About 10 days following the onset of COVID-19, many people develop neutralizing antibodies to SARS-CoV-2, with antibody levels highest in those who have the disease. The amplitude of antibodies reactive with the N and S proteins of SARS-CoV-2 was linked to the neutralizing activity of COVID-19 patients' plasma. MAb can prevent COVID-19 by targeting S protein and confine the progression to severe disease, especially in patients who have not formed an endogenous response to COVID-19. In severe COVID-19 hospitalized cases, Anti-SARS-CoV-2 mAb has not been detected as helpful[45].

Bamlanivimab (also called LY-COV555 and LY3819253), which targets the RBD of SARS-S CoV-2's protein, is a monoclonal antibody. Etesevimab (also referred to as LY-COV016 and LY3832479) binds to a distinct but overlapping epitope in the SARS-CoV-2 S protein's RBD and is also a neutralizing monoclonal antibody. Imdevimab (REGN10987) and Casirivimab (REGN10933) are recombinant human mAb that attaches to nonoverlapping epitopes of SARS-S CoV-2's protein RBD[11].

FDA approved two combination products, casirivimab plus imdevimab and bamlanivimab plus etesevimab, for Emergency Use Authorizations (EUAs) to treat COVID-19 in nonhospitalized patients at high risk of developing a serious disease or requiring hospitalization. The FDA has stopped the EUA for bamlanivimab and thus will not be supplied in the United States due to the rising number of SARS-CoV-2 mutations, which are resistant to medicine bamlanivimab alone[12,13].

The FDA does not approve Anti-SARS-CoV-2 mAb for patients hospitalized for COVID-19 and requiring oxygen treatment. The mAb is also not approved by the FDA for those on chronic oxygen treatment due to non-COVID-19-related comorbidity and needs an increase in oxygen flow rate from baseline due to COVID-19.

**Azithromycin**

Azithromycin (famous for Z-pak) is a frequently used antibiotic against many diseases, including pneumonia and bronchitis. Studies have shown its antiviral activity against viruses like Zika and influenza A. However, results were negative against MERS-CoV[10]. An examination bunch of COVID-19 patients took azithromycin along with Hydroxychloroquine and declared that about 93% of patients cleared the infection following 8 days. Due to the absence of a benchmark class, it is not confirmed whether the infection was cleared in individuals alone without medicine. There are worries about conceivably actual results when utilizing azithromycin and Hydroxychloroquine[10,16]. However, NIH recommends the use of azithromycin against COVID-19.

**Baloxavir**

Baloxavir is an oral antiviral drug used to inhibit the initiation of viral mRNA, which is an early step in virus replication[46,47]. Baloxavir marboxil is the prodrug, and baloxavir acid is the main metabolite that impedes cap-dependent endonuclease enzyme[48]. Baloxavir is considered an effective drug against SARS-CoV-2 by inhibiting the synthesis of its RNA. In vitro studies showed the antiviral property of baloxavir against SARS-CoV-2[49,14].

**Baricitinib**

Baricitinib, a selective inhibitor of Janus kinase (JAK) 1 and 2, taken orally, was predicted to be a viable therapy against SARS-CoV-2 using artificial intelligence algorithms[50,51]. COVID-19 patients who were taking noninvasive ventilation or high-flow oxygen, baricitinib + remdesivir was beneficial to remdesivir alone in lowering recovery period and speeding the clinical improvement. The combination was also linked to less significant side effects[15].

**BCG vaccine**

Research shows BCG vaccinated people have minor COVID-19 cases per 1 million population. Hegarty et al. observed COVID-19 incidence and mortality rate during 9-24$^{th}$ of March 2020 (15 days) in 178 countries[52]. In nations having BCG programs, the mortality rate was 4.28 per million compared to 40% in those countries that have no such program. The study found that nations with BCG immunization had a COVID-19 incidence of 38.4 per million, compared to 358.4 percent in countries without such a program.

**Chloroquine & Hydroxychloroquine**

Aminoquinolones, Hydroxychloroquine, and Chloroquine (inhibitors of polymerase) are typically known as drugs of choice against malaria. They target heme-polymerase in malaria by accumulating the toxic heme accumulation in the parasites, which results in death. A 2005 study in culture found that applying chloroquine to infected human cells could quell SARS-CoV transmission. Live Science previously reported that chloroquine disrupts the virus invading and division ability in human cells. In vitro studies revealed that chloroquine, hydroxy-chloroquine, and their derivative weaken the replication of SARS-CoV-2[17]. It is believed that for COVID-19, medications help in removing the infection out of host cells by restraining endosomal fermentation and separating the production of proteins (produced by the virus) by hindering glycosylation of host receptors[53]. In the USA alone, the medications are the subject of more than 30 distinctive clinical preliminaries[3].

**Colcrys (Colchicine)**

An anti-inflammatory medication, Colchicine, is used for the treatment of gout. It has some variations in effects, such as interfering with immune cytokines and triggering anti-inflammatory mechanisms. According to researchers, Colchicine may function like Actemra if the immune system becomes excessively stimulated in COVID-19 patients and a cytokine storm happens[54,19]. According to a large clinical trial currently underway, if Colchicine is provided quickly after diagnosis of COVID-19, it appears to lower the death rate and hospitalization. In a survey of 105 patients in Greece, 1 patient in the Colchicine group became severe in the hospital (needing ventilation and may dying) compared to 7 patients in the other non-Colchicine class[20]. To validate the efficacy, further investigation is necessary.

**Convalescent Plasma**

Plasma from COVID-19 survivors may include antibodies against SARS-CoV-2, which could prevent the virus and regulate the inflammatory response[12]. The FDA approved such plasma for COVID-19 treatment under certain hospitalized patients. The FDA updated the convalescent plasma EUA on February 4, 2021, to restrict the authorization to high-titer COVID-19 convalescent plasma and solely for hospitalized patients treated with COVID-19 initial in the illness course or hospitalized with weakened humoral immunity[13]. To give more precise, evidence-related recommendations on the function of convalescent plasma in the treatment of hospitalized COVID-19 patients with no compromised humoral immunity, findings from properly controlled, well-designed, and well-conducted randomized clinical studies are required[21].

**Dexamethasone**

Dexamethasone is a corticosteroid used to treat a large number of illnesses because of its immunosuppressive properties and anti-inflammatory, which help to delay the development of respiratory failure and death. Dexamethasone usage decreased 28-day mortality in COVID-19 patients getting either mechanical ventilation (invasive) or oxygen alone at

randomization and not in those with no respiratory support[55].

**Famotidine**

Famotidine, a counter H2 receptor blocker heartburn prescription, is being studied as a potential cure since Michael Callahan and colleagues in China confirmed that patients taking heartburn drugs in Wuhan were less likely to expire or be ventilated during extreme COVID-19. Intravenous famotidine, combined with Hydroxychloroquine, is currently being studied in New York hospitals, and hundreds of COVID-19 patients are being enlisted for a phase three randomized experiment. The famotidine action-mechanism is unclear, but it is supposed to likely bind a papain-like protease which is encoded by the SARS-CoV-2 genome and necessary for SARS-CoV entrance[25].

**Interleukin-6 Inhibitors (Tocilizumab, Sarilumab, & siltuximab)**

Cytokine-release syndrome is implicated in exacerbating extreme reactions to the virus, resulting in acute respiratory distress syndrome even when the virus burden decreases. Those with severe types of COVID-19 had increased levels of the inflammatory cytokine Interleukin (IL)-6, according to a retrospective analysis of 200 COVID-19 patients. Clinical studies are ongoing on a range of medications that inhibit various cytokines, namely Sarilumab and Tocilizumab, both mAb inhibitors of IL-6 receptors used to treat rheumatoid arthritis. According to NIH, there are two classes of IL-6 inhibitors approved by the FDA i.e. anti-IL-6 mAb (i.e., siltuximab) and anti-IL-6 receptor mAb (e.g., Tocilizumab, Sarilumab)[32,22]. Siltuximab FDA-approved recombinant human-mouse chimeric mAb binds IL-6 and is used in patients with multicentric Castleman disease. Siltuximab prevents IL-6 signaling by inhibiting IL-6 binding to the soluble and membrane-bound IL-6 receptor. Siltuximab is administered as an intravenous infusion[39]. These medications were examined for the cure of COVID-19 patients along with systemic inflammation.

**Kaletra, an HIV drug combination (Lopinavir-Ritonavir)**

Kaletra, an antiviral drug that combines Ritonavir and Lopinavir, sparked an initial interest. Novel data from China found a slight advantage when patients take the medication. About 199 patients with low oxygen levels were consigned randomly to obtain either Kaletra or a placebo[27]. Though Kaletra users died less, the difference was not statistically significant, indicating that it may have been attributed to unplanned. Over time, both classes had equal amounts of virus in the blood. Many trials are being conducted, but there's still a chance that this mixture might be beneficial. If given initially in the disease progression compared with different antivirals, that drug would work better.

Furthermore, the HIV protease inhibitor "Lopinavir-Ritonavir" functions by hindering the 3-chymotrypsin-like protease against coronavirus. The drug's in vitro experiments give active results against MERS-CoV and SARS-CoV. However, no tests have affirmed a similar component of action counter to SARS-CoV-2. In China, the atrial of 200 hospitalized patients showed that the drug combination was not effective as standard care, but additional clinical trials are still waiting[56]. A review concluded that the limited use of drugs might be due to the various side effects, including nausea, increased diarrhea, and risk of liver failure, which all may intensify the COVID-19 indications[57].

**Nafamostat and Camostat**

Both are serine-protease-inhibitors and are approved for pancreatitis treatment in humans in Japan. Both have been known to prevent the entrance of SARS-CoV-2 into cells in vitro. Still, according to a preprint study, nafamostat inhibits viral cell invasion through a 15-fold advanced efficiency compared to camostat[8]. These medications are conducting stage 2 and stage 2/3 clinical studies in the US and Japan to see if they are successful for COVID-19[58].

**2-specific intravenous immunoglobulin**

Excluding a clinical study, the COVID-19 Treatment Guidelines Panel advises using non-SARS-CoV-2 intravenous immunoglobulin (IVIG) against acute COVID-19 treatment. This suggestion may not prohibit the usage of IVIG from treating problems that may emerge during the progress of COVID-19. It is uncertain if products made from plasma donors not been confirmed to have SARS-CoV-2 infection possess a higher titer of SARS-CoV-2 neutralizing immunoglobulin. Additionally, whereas further blood components in IVIG may have extensive immunomodulatory effects, it is not known if those potential benefits would aid COVID-19 patients[22].

**Ruxolitinib**

Ruxolitinib, Janus kinase 1 and 2 inhibitors showed a substantial anti-inflammatory effect by targeting various growth factors and cytokines, with potential ability in cytokine storm seen in COVID-19 patients' severe illness. In recent COVID-19 trials, ruxolitinib medication reduced the time spent on mechanical breathing, hospitalization period, and the requirement for vasopressor care. Furthermore, computed tomography imaging revealed ruxolitinib reduced mortality rates and improved pulmonary congestion. These researches call for further clinical research into Ruxolitinib as a viable therapy option for severe COVID-19[28].

**Remdesivir, a failed Ebola drug**

Remdesivir is being tested to know if it can successfully treat COVID-19, A Gilead Sciences drug tested initially in people infected with Ebola. In vivo research in animal models of EBOV, MERS-CoV, SARS-CoV, and SARS-CoV-2 infection revealed therapeutic and preventive benefits[30]. Use of Remdesivir for the treatment of COVID-19 severe cases has been permitted for treatment presently by FDA[33]. Bruce Aylward from WHO said that "there's only one medicine right now that we think might have possible effectiveness, and that's Remdesivir[59].

**WHO Interim results by Solidarity Trail**

The interim findings were released in the Solidarity Trial on October 15, 2020. In hospitalized patients, all four tested treatments (Lopinavir/Ritonavir, Remdesivir, interferon, and Hydroxychloroquine) were shown to have less or no effect on total mortality, hospital stay period, and ventilation onset. The Solidarity Trial considers assessing other therapies to continue the quest for COVID-19 treatments effectively. Only Corticosteroids against extreme and essential COVID-19 have been found successful. The WHO approved a proposal from the International Steering Committee of the Solidarity Trial Earlier, on July 4, 2020, to discontinue the Lopinavir/Ritonavir and Hydroxychloroquine weapons the trial[35].

**COVID-19 therapy for children**

COVID-19 cases are more severe in adults than in children, and many infected children are asymptomatic. Most youngsters infected with SARS-CoV-2 will not need any treatment. Children with a complex medical history (for example, cardiopulmonary disease, developmental delays, genetic syndromes, immunocompromised individuals, neurologic impairment, and obesity have a risk for serious illness[37].

There is little information on the clinical and pathophysiology range of COVID-19 illness in offspring. Due to the absence of suitable evidence regarding treatment with acute COVID-19, guidelines are mostly based on adult patient results or outcomes and reliable data, and the risk of disease progression in children. Most children with moderate or mild illness may be treated solely with supportive treatment. However, in conjunction with a pediatric infectious disease professional, the following therapy for hospitalized children can be recommended[32,35]. Remdesivir (FDA-approved) is advised for hospitalized children (age 12 years) and older who have any health risks for severe symptoms.

Dexamethasone is approved for treating COVID-19-infected hospitalized individuals who need mechanical ventilation or supplementary oxygen via a high-flow machine[23]. IVIG has been utilized in pediatric patients with multiorgan inflammatory syndrome and COVID-19 in children, mainly those with a Kawasaki disease-like appearance. However,

its efficiency in the administration of MIS-C is currently being researched[33]. All these studies suggest significant progress has been made since the world was faced with a wholly unprepared SARS outbreak seventeen years ago[60].

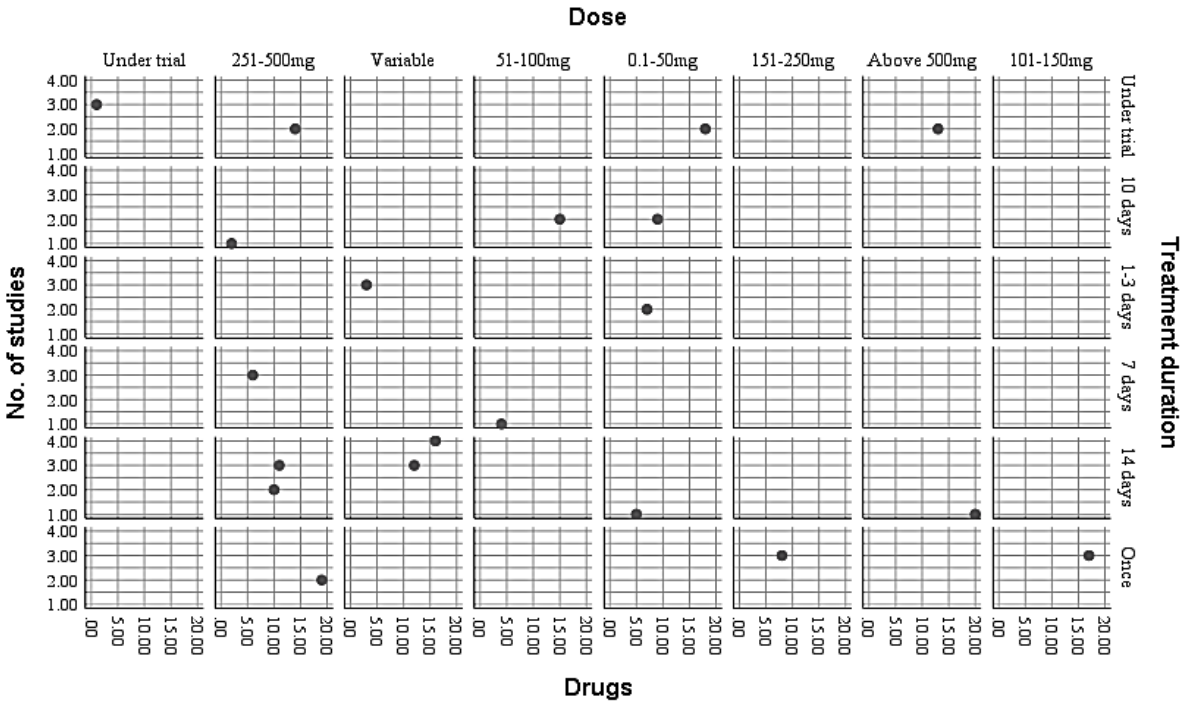



**Figure 4: Forest plots of the drugs being tested against COVID-19 to slow its spread and find effective treatment**

**Table 3: Analysis of the COVID-19 drugs included in the current review and their association with the no. of studies (n=45), treatment duration, and dose (mentioned in the selected studies) by using Bayesian Regression ANOVA[a,b].**

| Source | Sum of Squares | df | Mean Square | F | Sig.[c] |
|---|---|---|---|---|---|
| **Regression** | 201.64 | 5 | 40.32 | 1.21 | 0.35 |
| **Residual** | 463.35 | 14 | 33.09 | | |
| **Total** | 665.00 | 19 | | | |

a: Dependent Variable: Drugs. b: Model: (Intercept), No. of studies, Treatment duration, dose. c: 0.001 value was taken as significant

One of the limitations of the present study is that it was planned for November 2020, after the FDA approval of Remdesivir for the treatment of COVID-19. In several cases, antiviral EIDD-2801, Nitazoxanide, Dexamethasone, mAb, and Convalescent plasma antibodies have been in use though not officially approved. Second, no authorized SARS-CoV-2 vaccinations were available during the research design. However, there was such a rush to develop a specific cure for this fast-spreading virus and its new forms that scientists faced difficulty making decisions. As with the controversial use of medications in more than 200 global solidarity trials, the study's limitation is

the enormous pressure and controversy in the scientific community against using drugs against COVID-19.

Another drawback of this study is the cross-sectional design and the limited size of the single-center cohort, and the lack of a control group. As a result, a bigger multicenter investigation is required to determine the potential treatment of COVID-19. Furthermore, in individuals with a confirmed diagnosis of COVID-19 who are receiving prescribed treatment, it is critical to monitor the results frequently. Long-term studies are needed to determine residual lung injury after COVID-19 and steer research into future treatment possibilities, including medicinal and supportive therapies.

Given the study's limitations, the relationship of these medicines should be seen as suggestive rather than demonstrative for a possible role in the treatment of COVID-19. In addition, we suggest documenting the synergistic effect of drugs, if any, to be reported and documenting the effect of herbal medicines against COVID-19. Furthermore, the authors admit that this study gives a potential crude relationship between medicines versus COVID-19, and we urge further in-depth research. This study, however, contributes to a growing amount of suggestive data linking the medications to SARS-CoV-2/COVID-19.

## Conclusion

COVID-19 research is gathering momentum, so there is more hope for better coronavirus control because the SARS-CoV-2 are facing much better-prepared epidemic control strategies and unity worldwide. Presently Remdesivir is the only accepted drug by FDA to treat COVID-19, as the hospitalized patients recovered very quickly by taking Remdesivir. Antiviral EIDD-2801 has been found to make the SARS-CoV-2 unable to infect cells by causing genetic modifications in the virus RNA. Similarly, Nitazoxanide appeared beneficial against SARS-COV-2 in a primary intervention and severe conditions (including pregnancy) without undesirable effects on the newborns. Usually, children with mild disease cases can be handled solely by care. Although, Remdesivir (FDA approved) and dexamethasone are recommended in severe cases. Clinical trials are ongoing to investigate other possible therapies like MAb and Convalescent Plasma antibodies against SARS-CoV-2. Researchers also test older drugs (usually used to treat other conditions) to see if they are effective for COVID-19. Further tests are essential to validate whether any of the mentioned above possible therapies would be helpful for COVID-19 treatment.

## Conflicts of Interest

We all authors here declare that we have no competing and challenging interest in the publication of this article.

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