



RESEARCH ARTICLE

STUDY ON ANTIVIRAL DRUGS RAISE NEW HOPES FOR RECOVERY ON SARS-COV-2

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Manuscript Info

Manuscript History

Received: 05 February 2022

Final Accepted: 11 March 2022

Published: April 2022

Key words:-

SARS-CoV-2, Viral, Drugs, Disease, COVID-19, Medicine

Abstract

The goal of this study is to perform a systematic assessment of the literature to determine the effectiveness and safety of molnupiravir and paxlovid oral antiviral drugs in COVID-19 patients. These drugs have shown consistent efficacy against the SARS-CoV-2 virus's Gamma, Delta, and Mu versions, the firm has yet to release data on the drug's action against Omicron. COVID-19, a worldwide pandemic produced by the SARS-CoV-2 virus, has already wreaked havoc on human life and the global economy. In this study, an attempt is made to comprehend the SARS-CoV-2 life cycle, and prospective druggable targets against SARS-CoV-2 are outlined based on this knowledge. COVID-19, there are more vaccine candidates in the pipeline at the same time than there have ever been for an infectious illness. They're all attempting to accomplish the same goal: viral immunity, and some may even be able to block transmission. Whole virus, protein subunit, viral vector, and nucleic acid are the four types of vaccines now being tested in clinical studies.

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Introduction:-

With today's approval, COVID-19 will have its first oral medication – a significant step ahead in the fight against the worldwide epidemic [1]. Oral antiviral therapy works by preventing efficient virus replication within the host cell by targeting proteins on the SARS-CoV-2 virus [2]. Infectious disease experts are optimistic about the coming of oral antivirals that can be utilized in non-hospitalized patients [3]. The FDA issues an oral antiviral target against the COVID-19. Till now they are two oral antiviral targets, are being considered by the FDA for approval use under Emergency Use Authorization (EUA) those are- Pfizer's paxlovid and Merck & Co.'s molnupiravir. Pfizer's paxlovid - Paxlovid is an antiviral medication which is an orally active protease inhibitor [4]. In non-hospitalized high-risk adults and pediatric patients with COVID-19, PAXLOVID (co-packaged nirmatrelvir and ritonavir pills for oral consumption) was found to minimize the probability of hospitalization or mortality by 89 percent when compared to placebo. Where, a SARS-CoV-2-3CL protease inhibitor that has been precisely formulated which shown significant antiviral action in vitro against circulating versions of concern viruses. Paxlovid provides excellent protection against severe coronavirus illness and is also effective against the novel variant Omicron. Merck & Co.'s molnupiravir - Molnupiravir is a medicine that stops the SARS-CoV-2 virus from multiplying further by inserting faults into its genetic coding. Molnupiravir is a prodrug of the synthetic nucleoside derivative N4-hydroxycytidine that works against viruses by causing copying mistakes during viral RNA synthesis [5].

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Experimental design

Paxlovid is made up of two drugs: nirmatrelvir (PF-07321332), which stops the virus from reproducing by inhibiting a SARS-CoV-2 protein, and Ritonavir, which slows down the breakdown of nirmatrelvir and allows it to stay in the body for longer at greater concentrations. Paxlovid is a combination of two drugs: ritonavir for HIV and PF-07321332 (nirmatrelvir), an investigational medication (a pill). Ritonavir prevents nirmatrelvir from being metabolized by the body. It works by first being broken down by the body (known as a sacrificial chemical) to guarantee that enough nirmatrelvir reaches the virus undamaged. The drug nirmatrelvir is a protease inhibitor (as is ritonavir). It inhibits the replication of SARS-CoV-2 by blocking the function of a key enzyme (protease). Nirmatrelvir did not show signs of mutagenic DNA interactions in preclinical test [6].

Molnupiravir is synthesized in two steps from cytidine with a 60 percent overall yield. The hydroamination of cytidine with hydroxylamine to produce N-hydroxy cytidine (NHC) is the initial step in the manufacture of molnupiravir from cytidine. By replacing hydroxylamine with hydroxylamine sulfate and utilizing pure water instead of an isopropanol-water combination we can minimize the large amount of solvent requirement and avoid chromatographic purification. NHC is enzymatically acylated to produce the target molecule in the second synthesis step. The prior synthesis necessitated a high enzyme loading (200 wt.%) and significant amounts of the hazardous solvent 1,4-dioxane, and the yield was lowered due to the development of an oxime-ester byproduct. These problems were solved by replacing dioxane with 2-methyl THF and performing the process at higher concentrations with just 20% enzyme loading. By adding hydroxylamine to the byproduct, it was successfully converted to the desired product as shown in Table 1 [7].

Table 1:- Various drugs that target against the covid19.

DRUG	COMPANY	ROUTE OF ADMINISTRATION	APPROVED STATUS	IN-VITRO
Paxlovid	Pfizer	Oral	EUA submitted	Sars-cov-2
Molnupiravir	Merck & Co.	Oral	EUA submitted	Sars-cov-2
Remdesivir	Gilead	IV	Approved	Sars-cov-2 Hepatitis C
Chloroquine/ Hydroxychloroquine	Generic	IV/IM and Oral	Anti-malarial	HIV Sars-Cov-2 Influenza
Camostat mesylate	Ono pharmaceutical	oral	NA	Sars-Cov Mers-cov Sars-cov-2
Fluvoxamine	Solvay Pharmaceuticals	Oral	Anti-inflammatory	Sars Tricyclic antidepressant
Colchicine	Generic	Oral	Anti-inflammatory	Sars-cov-1 Sars-cov-2 Athritis
Ivermectin	Merck & Co.	Oral, Topical	Anti-parasitic agent	Influenza DENV VEEV Sars-cov-2

Patient Eligibility and Dosage

Eligibility - Molnupiravir and paxlovid are used to treat mild to moderate coronavirus disease (COVID-19) in adults who have a positive direct SARS-CoV-2 viral test and are at high risk of developing severe COVID-19, including hospitalization or death, and for whom alternative FDA-approved COVID-19 treatment options are not available or clinically. **Dosage** - Paxlovid is given as a combination of three pills (two nirmatrelvir tablets and one ritonavir tablet) taken orally twice daily for five days, for a total of 30 tablets. Paxlovid is only accessible with a prescription and should be started as soon as feasible following a COVID-19 diagnosis and within five days of the commencement of symptoms. Molnupiravir is used orally in four 200-mg capsules every 12 hours for five days, totalling 40 capsules. The usage of molnupiravir for more than five days is not recommended [8].

Mechanism of action

PAXLOVID - Manufactured by Pfizer, is the most sophisticated drug of the major protease (Mpro)inhibitors. During the propagation of a virus, SARS-CoV-2 creates lengthy polypeptides that must be divided into the viral proteins. Mpro oversees this process. As a result, inhibiting Mpro stops the virus from producing the proteins that required for replication [9].MOLNUPIRAVIR-When the RNA dependent RNA polymerase (RdR enzyme integrates the medication into viral RNA, elongation continues. Instead, the virus employs molnupiravir-containing RNAs as template strands, and when it finds molnupiravir again, it integrates the incorrect nucleotides into new viral RNA. Over time, mutations build up, resulting in an 'error catastrophe' and viral death [10].

Testing and accuracy

During clinical trials, 1,039 patients who received Paxlovid, and 1,046 patients received placebo, with 0.8 percent of those who received Paxlovid being hospitalized or dying during the 28-day follow-up period, compared to 6% of those who received placebo. Paxlovid's safety and efficacy in the treatment of COVID-19 are still being studied. Paxlovid has been used by a small number of persons. Clinical outcomes during phase I II trials for molnupiravir drug includes - Within the 29 days of time span after the drug incorporation, 6.8% of the 709 persons who took molnupiravir were hospitalized or died, compared to 9.7% of the 699 people who received a placebo. During the follow-up period, one person who took molnupiravir died, compared to nine persons who received placebo. The WHO outcome scale is an 11-point ordinal score that categorizes clinical progression. The scale runs from 0 to 10, with a higher score signifying clinical advancement [11].

Clinical Application's

Antiretroviral Drug Resistance (ARTR) is a kind of resistance to HIV, if you have an untreated HIV infection, Paxlovid might make some HIV medications less effective in the future. Paxlovid may cause the following adverse effects: mild chances of getting diarrhea, change in taste, muscular pains due to elevated blood pressure and liver problem - Loss of appetite, jaundice, dark-colored urine, pale-colored feces, itchy skin, abdominal pain. Molnupiravir is not approved for usage in patients under the age of 18 because it can interfere with bone and cartilage formation. It's possible that serious and unexpected adverse effects will occur [12].

Conclusion:-

Paxlovid is classified as experimental since it is currently being researched. There is little data on the safety and efficacy of paxlovid in the treatment of mild-to-moderate COVID-19. Paxlovid is still being studied, it's possible that not all the risks are known yet. Mpro inhibitors have a smaller spectrum since the proteases of different species have greater structural variations. The protease inhibitors, on the other hand. Protease inhibitors from Pfizer and others, on the other hand, are based on the foundations of older antiviral candidates. When COVID-19 immunization plus a booster dose is advised, these both are not a suitable substitute for vaccination. Future antivirals should focus on identification and development of such compounds and benefit from research on the architecture of essential viral proteins as well as the properties of compounds that bind them. With the use of oral antivirals in the near future, will allow patients to make things easier, cost effective and improve their standard health conditions.

Conflict of Interests

The authors declare that there is no conflict of interests exist among them regarding the publication of this paper

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