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RESEARCH ARTICLE

PROMISING RESEARCH ON ANTIVIRAL MEDICATIONS OFFERS NEW PROSPECTS FOR SARS-COV-2 RECOVERY

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Abstract

The ongoing COVID-19 pandemic has spurred extensive research efforts worldwide to identify effective treatments for SARS-CoV-2, the virus responsible for the disease. This study focusses on recent developments in antiviral medication research, showcasing the potential breakthroughs and novel approaches in the quest for SARS-CoV-2 recovery. From monoclonal antibodies to emerging antiviral drugs and vaccine advancements, this research landscape offers renewed hope for managing and ultimately defeating the virus. We summarize the key findings, promising prospects, and evolving strategies in the field of antiviral therapeutics, underscoring the collective efforts to combat the global pandemic.

Introduction:-

With today's approval, COVID-19 will have its first oral medication – a significant step ahead inthe fight against the worldwide epidemic[1]. Oral antiviral therapy works by preventing efficient virusreplication within the host cell by targeting proteins on the SARS-CoV-2 virus[2]. Infectious diseaseexperts are optimistic about the coming of oral antivirals that can be utilized in non-hospitalizedpatients[3]. The FDA issues an oral antiviral target against the covid 19. Till now they are two oralantiviral targets, are being considered by the FDA for approval use under Emergency useAuthorization (EUA) those are- Pfizer's paxlovid and Merck & Co.'s molnupiravir. Pfizer'spaxlovid - 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-packagednirmatrelvir and ritonavir pills for oral consumption) was found to minimize the probability ofhospitalization or mortality by 89 percent when compared to placebo. Where, a SARS-CoV-2-3CLprotease inhibitor that has been precisely formulated which shown significant antiviral action invitro against circulating versions of concern viruses. Paxlovid provides excellent protection againstsevere 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 frommultiplying further by inserting faults into its genetic coding. Molnupiravir is a prodrug of thesynthetic nucleoside derivative N4-hydroxycytidine that works against viruses by causing copyingmistakes during viral RNA synthesis[5].

Experimental design

Paxlovid is made up of two drugs: nirmatrelvir (PF-07321332), which stops the virus fromreproducing by inhibiting a SARS-CoV-2 protein, and Ritonavir, which slows down the breakdownof nirmatrelvir and allows it to stay in the

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body for longer at greater concentrations. Paxlovid is acombination of two drugs: ritonavir for HIV and PF-07321332(nirmatrelvir), an investigationalmedication (a pill). Ritonavir prevents nirmatrelvir from being metabolized by the body. It worksby first being broken down by the body (known as a sacrificial chemical) to guarantee that enoughnirmatrelvir reaches the virus undamaged. The drug nirmatrelvir is a protease inhibitor (as isritonavir). 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. Thehydroamination of cytidine with hydroxylamine to produce N-hydroxy cytidine (NHC) is the initialstep in the manufacture of molnupiravir from cytidine. By replacing hydroxylamine withhydroxylamine sulfate and utilizing pure water instead of an isopropanol-water combination we canminimize the large amount of solvent requirement and avoid chromatographic purification. NHC isenzymatically acylated to produce the target molecule in the second synthesis step. The priorsynthesis necessitated a high enzyme loading (200 wt.%) and significant amounts of the hazardoussolvent 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 processat 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 ofdeveloping 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 ritonavirtablet) taken orally twice daily for five days, for a total of 30 tablets. Paxlovid is only accessiblewith a prescription and should be started as soon as feasible following a COVID-19 diagnosis andwithin five days of the commencement of symptoms. Molnupiravir is used orally in four 200-mg capsules every 12 hours for five days, totalling 40capsules. 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 thevirus from producing the proteins that required for replication[9].MOLNUPIRAVIR-When the RNA dependent RNA polymerase (RdR enzyme integrates themedication into viral RNA, elongation continues. Instead, the virus employs molnupiravir-containing RNAs as template strands, and when it finds molnupiravir again, it integrates theincorrect nucleotides into new viral RNA. Over time, mutations build up, resulting in an 'errorcatastrophe' 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-dayfollow-up period, compared to 6% of those who received placebo. Paxlovid's safety and efficacy inthe treatment of COVID-19 are still being studied. Paxlovid has been used by a small number ofpersons.Clinical outcomes during phase I II trails for molnupiravir drug includes - Within the 29 days oftime span after the drug incorporation, 6.8% of the 709 persons who took molnupiravir werehospitalized or died, compared to 9.7% of the 699 people who received a placebo. During thefollow-up period, one person who took molnupiravir died, compared to nine persons who receivedplacebo. 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 untreatedHIVinfection, 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-coloredfeces, itchy skin, abdominal pain. Molnupiravir is not approved forusage in patients under the age of 18 because it can interfere with bone and cartilage formation. It ispossible 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 onthe safety and efficacy of paxlovid in the treatment of mild-to-moderate COVID-19. Paxlovid isstill being studied, it's possible that not all the risks are known yet. Mpro inhibitors have a smallerspectrum since the proteases of different species have greater structural variations viruses. Theprotease 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 antiviralsshould 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 soon, will allow patients to make things easier, costeffective 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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