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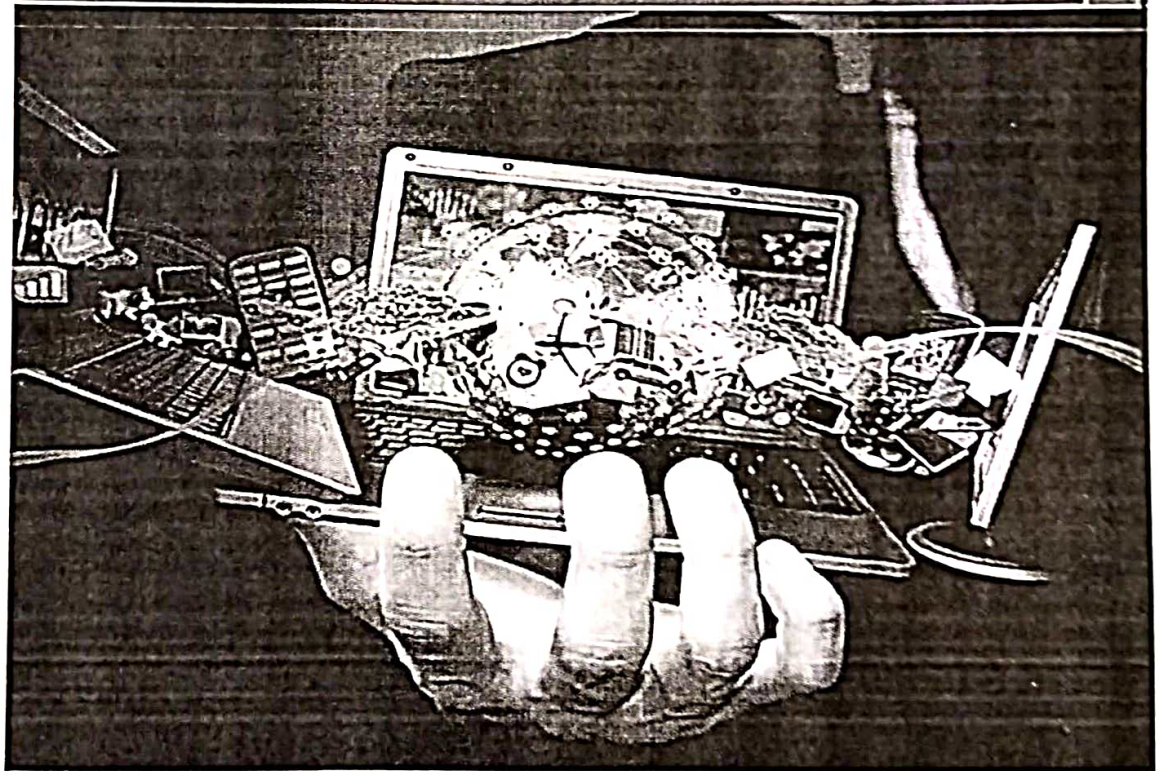
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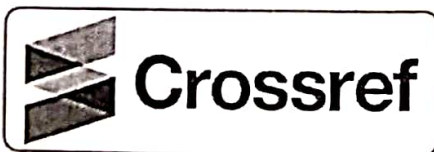
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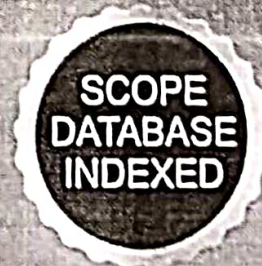


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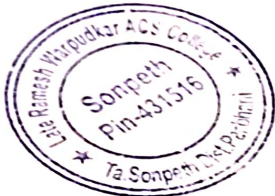
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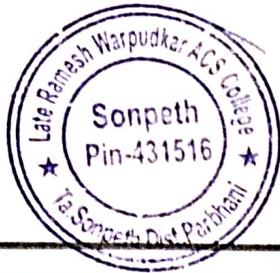
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A Review: Remdesivir and Covid-19

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PRINCIPAL

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Abstract: Remdesivir was recently approved by the Food and Drug Administration for the treatment of hospitalized patients with coronavirus disease 2019 (COVID-19). It is the prodrug of an adenosine analogue that inhibits viral replication of several RNA virus families. In this review, we have explained the structure of the coronavirus. Further it showed promising results in terms of clinical improvement, shortening the recovery time, mortality rate, and the duration of oxygen need and several studies showed positive results of Remdesivir against the new variants. Here, we provide an overview of Remdesivir, mode of action, and the current studies exploring its clinical effectiveness.

Keywords: Remdesivir, COVID-19, Corona, Virus, Drug, Efficacy, SARS-CoV-2.

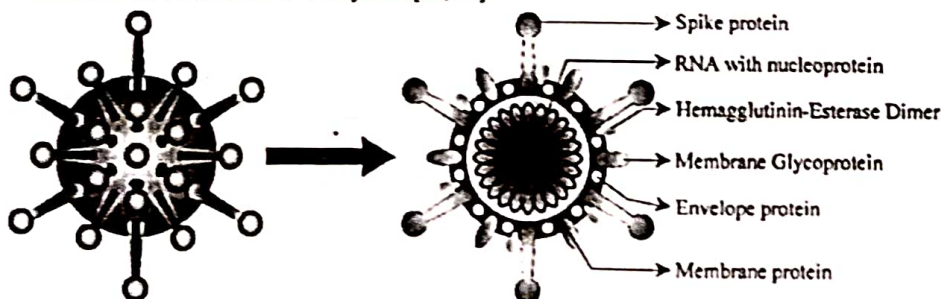
I. INTRODUCTION

SARS-CoV-2 is severe acute respiratory syndrome Coronavirus-2 which causes COVID-19 disease. This firstly found in Wuhan, China in December 2019 and in the whole world [1-5]. The virus spread in whole world and all Countries threaten by a medical emergency. In India also it spread around the March 2020 due to this The Government of India declare countrywide lockdown. Due to the lockdown every person affected and number of deaths are occurred. The aged person and the patient having heart diseases, asthma, and other serious diseases are comes under high risk. Due to this new virus workers and doctors cant gives the proper treatment to the infected person. The only way to avoid infection from Corona is to avoid contact of person to person so that wearing mask, regular hand wash, avoiding gathering of peoples and lastly the lockdown. All these steps taken by the government and researchers engaged in the finding of solution of this World wide problem. In the course of time researchers successful to made vaccine for corona virus. During this pandemic WHO suggest the use of Remdesivir against the corona virus treatment.

The corona virus transfer via respiratory aerosol and droplets by direct or indirect contacts [6-7]. Transmission of disease occurs through infected person and from asymptomatic peoples [6 & 8]. The process of synthesis and development of medicine, vaccine for treatment in COVID-19 is very lengthy and time consuming process. So that patients showing miner symptoms they cure without hospitalization but those who having major symptoms they hospitalized and they treated on the basis of their symptoms [1, 3, 9-16].

II. CORONA VIRUS (COV) STRUCTURE

The homogeneous spike protein structure of corona virus composed of 1300 amino acids which interact with host cells [17-18]. Corona virus enters through the epithelial cell membrane [18-19] the epithelial cells have angiotensin-converting enzyme-2 (ACE-2), which is the aim of virus. The detection of ACE-2 by the S- protein of the virus permits the invasion of the coronavirus into the human circulation system [18, 20].

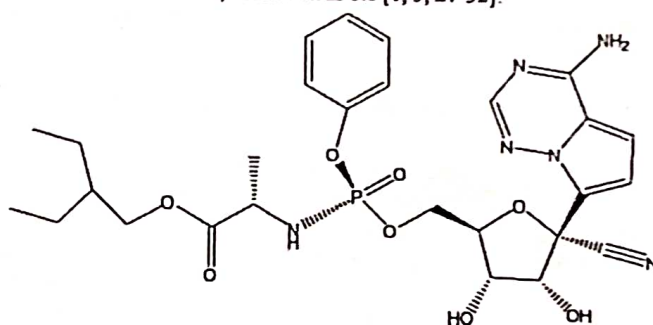


Structure of COVID-19
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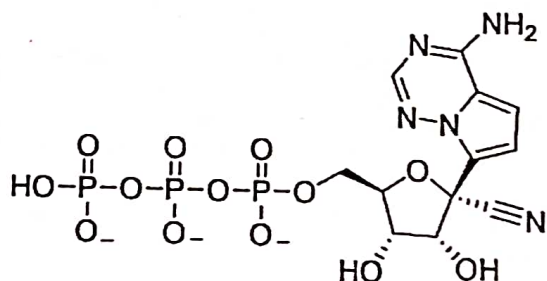
Single-strand RNA having 22–26 kilo bases viruses such as the virus family produce the virus genomes over the host cells. When corona virus comes near ribosome of the epithelial cells or host cells, it utilizes the ribosome of the host cell to replicate poly-proteins which arise in the epithelial cells [18, 21, 22]. Proteinase (3CL-pro) and papain-like protease (PL-pro) these two enzymes exhibited by corona virus whose be involved in cleaving the poly-proteins into smaller products used for replicating new viruses. RNA-dependent RNA polymerase (RdRp), which exhibited by the corona virus whose synthesize the complementary RNA strand using the virus RNA [23]. Corona virus stay at intracellular membrane of endoplasmic reticulum golgi intermediate compartment (ERGIC) after infection [24]. RNA dependent RNA polymerase (RdRp) responsible for corona virus replication [25], which is the most probable target of the investigational nucleotide analogue Remdesivir [18, 26].

MODE OF ACTION

The inhibition of RNA polymerase can be done with the help of Remdesivir which acts as a prodrug. Remdesivir also shows wide activity against viruses Ebola virus, corona virus etc [1, 3, 27-32].

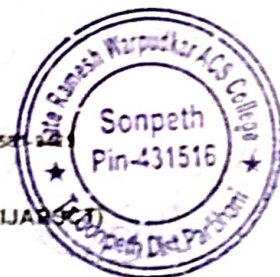


Chemical structures of Remdesivir



Chemical structures of Nucleoside Tri-Phosphate a viral inhibitor

The exact mechanism of Remdesivir about corona virus is not clear. Remdesivir generate pharmacologically active nucleoside triphosphate (NTP) that acts as an alternative substrate for RNA-chain terminator. The NTP can inhibit corona virus by incorporating active triphosphates into viral RNA. Additionally, there is a high genetic barrier to achieve resistance of corona virus to Remdesivir, which suggests that Remdesivir can maintain the effectiveness of corona virus therapies [27, 33-34]. Remdesivir shows significant activity against COVID-19 in vitro [3, 35-36]. Due to highly transmissibility of corona virus it spread among the world and WHO declared the World wide Health emergency in March 2020 [6, 37, 38]. The effective treatment against the COVID-19 nowever a hard task to the world. For the same an antiviral drug Remdesivir shows significant activity against COVID-19 [3, 38, 39]. In 2020 United State Food and Drug Administration advised the use of Remdesivir against the COVID-19 [38, 40].



IV. THE EFFICACY OF REMDESIVIR AGAINST SARS-CoV-2

The efficacy of Remdesivir against SARS-CoV-2 and associated corona viruses can be studied *in vitro* with help of animal models. Remdesivir for prophylaxis treated on mice with SARS-CoV infection which shows decrease of the viral infection in lungs and improvement of the respiratory function [30]. In 2020, Antiviral efficacy of Remdesivir against SARS-CoV-2 in infected Vero E6 cells. Which indicate that IC₅₀ and IC₉₀ values of Remdesivir against SARS-CoV-2 were 770 nM and 1760 nM, respectively (cytotoxic concentration >100 mM). From this it is clear that Remdesivir is effective agent against SARS-CoV-2 infection *in vitro* [32]. Due to mutation in the corona virus, the new variant SARS-CoV-2 it is important to know the efficacy of Remdesivir against it [41-42]. The viral spikes and RdRp are target sites of this new variant for Remdesivir. As time the corona virus muted and the mutation of Remdesivir binding residue in nsp12 was reported. This shows that there is absence of Remdesivir resistant mutation [43]. The resistant is highly conserved and no change was reported in both variants [42]. Many studies shows that significant efficacy of Remdesivir against SARS-CoV-2, B.1.351 variant and B.1.1.7 variant in intestinal epithelial Caco-2 cells and Calu-3 human lung epithelial cells [44-45]. Although several studies shows different perspectives like the absence of a statistical clinical significant in improvement within the time [46]. Remdesivir treatment not showing significant improvement and not shorten the hospitalization time [47]. Study carried by WHO shows COVID-19 patient recover shortly and have no mortality effect [48-49]. Due to poor efficacy in the rate of overall mortality against Remdesivir [50]. Although the Asian population have very poor outcome from the Remdesivir [51]. Recently it is shown that 50% of inhibitory concentration indicates exposure of Omicron to anti-viral drugs Remdesivir [52]. But due to positive role the use of Remdesivir according to WHO guidelines still used in early stages of covid-19 [53-55].

V. DISCUSSION

Remdesivir seems to be the most promising anti-viral currently available for the treatment of moderate to severe COVID-19 pneumonia based on preclinical and clinical data and represents the only treatment approved by the FDA for COVID-19 [6, 18, 33, 59]. The management in controlling a pandemic like COVID-19 must have availability of therapeutic strength. The efficacy of Remdesivir against corona virus shown in this pandemic but its need improvement [1]. As the clear data about promising drug for COVID-19 is limited however the studies ongoing on Remdesivir for COVID-19 gives some evidences the first systematic review and meta-analysis to provide evidence on the efficacy and safety of Remdesivir in COVID-19 [38]. For severely ill patient of COVID-19 which treated with Remdesivir not enough data about efficacy of Remdesivir. The data available shows need much improvement in cases which have oxygen support status observed in 68% and mortality was 13% [3]. There is need to further research on the effect of remdesivir for short and long term courses. Also need for assessing the other antiviral drugs [6, 33]. Remdesivir might useful in the COVID-19 treatment which decrease mortality and reduce period of hospitalization of Covid-19 [18, 38]. While some studies shows Remdesivir reduces the time to recovery by 31%, which is a relatively modest but clearly therapeutic effect [58]. According to clinical trials Remdesivir has not much significant against the COVID-19 while on other side the recovery time for patients oxygen need status, mortality rate, a positive effect against new variants including B.1.17 and B.1.351 according to several studies [41]. Remdesivir shows potential efficacy against moderate COVID-19 patients and compared with the care they shows clinical benefits within the five days [56]. The patients undergoing Remdesivir therapy suffer from hepatotoxicity and renal damage [57]. Immunomodulators are crucial to assess which clearly benefits from Remdesivir [60].

VI. CONCLUSION

Nucleotide analog prodrug is Remdesivir which inhibits SARS-CoV-2 RdRp. It show significant viral activity against COVID-19 *in vitro* and *in vivo*. Now a days it is used as an emergency drug for COVID-19 and shows significant clinical results [59, 61]. It need for taking significant effort towards the development of suitable therapeutic agents for this infection, a new vaccine or various therapeutics. Remdesivir as such represents one of the more promising alternatives for COVID-19 therapy [62]. In the future, studies will be necessary for the interactions of antiviral therapy with other therapies that are being investigated for COVID-19. The use of non-steroidal anti-inflammatory drugs (NSAIDs) in the treatment of COVID-19 patients are not available [63]. However in the pandemic of COVID-19 Remdesivir used as a prominent drug but recently WHO advised to health experts to stop use of Remdesivir in the treatment of COVID-19.



Researchers work on discovery and development of a prominent drug especially for COVID-19 continuously. Although now effective vaccines against the COVID-19 are available.

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