Remdesivir, A Potential Drug for COVID-19 Treatment: A New Hope

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Abstract: Objective: Coronavirus Disease-2019 (COVID-19) is a pandemic outbreak in the world and is the leading cause of Severe Acute Respiratory Syndrome (SARS).

Methods: Currently, many drugs/therapies have been tested for COVID-19, which responded sub-optimal to the patients. Remdesivir is an RNA polymerase inhibitor that found promising results in ongoing clinical trials and shows a faster recovery rate in COVID-19 patients. Currently, USFDA approves for emergent use of this drug in severe COVID-19 patients.

Results: In this review, we discussed a brief overview of biopharmaceutical and pharmacological aspects of Remdesivir. Moreover, the ongoing regulatory status of Remdesivir by official bodies has also been described.

Keywords: Remdesivir, COVID-19, USFDA, SARS, WHO, RNA polymerase inhibitor.

1. INTRODUCTION

Coronavirus Disease-2019 (COVID-19) is a viral disease which initially originated in Wuhan, China and now has spread to each country in the world. COVID-19 is a major health hazard and is classified as a pandemic in various countries [1]. Currently, millions of people are suffering from this disease and about 6 lakh deaths have been reported for this disease. Many people infected with the COVID-19 virus develop mild to moderate respiratory disease and recover without any special treatment being needed [2]. Older people with certain health conditions such as cardiovascular disease, diabetes, chronic respiratory disease and cancer are more likely to experience serious illness and respiratory burden. The transmission rate of this disease is rapidly high. When an infected person coughs or sneezes, the COVID-19 virus spreads mainly by droplets of saliva or discharge from the nose. Hence, it is important to know several day-to-day life practices to avoid infection and prevent others (for example, by coughing into a flexed elbow) [3]. There are no unique COVID-19 vaccines or therapies available at this time. However, there are also several current clinical trials testing new drugs/therapies for the potential treatment of COVID-19.

Remdesivir, or GS-5734, is an adenosine triphosphate analog that was first identified in the literature as a possible cure for Ebola in 2016 [4]. Remdesivir is a broad spectrum anti-viral drug developed by the renowned biopharmaceutical company Gilead Sciences [5]. The antiviral activity of Remdesivir was established against many RNA viruses, including Severe Acute Respiratory Syndrome (SARS) and respiratory syndrome in the Middle East.

2. REMDESIVIR: A BRIEF INTRODUCTION

Remdesivir, chemically 2-ethylbutyl (2S)-2-[[{(S)-[(2R,3S,4R,5R)-5-{4-aminopyrrolo[2,1-f][1,2,4]triazin-7-yl}-5-cyano-3,4-dihydroxyoxolan-2-yl]methoxy}(phenoxy)phosphoryl]amino}propanoate (Fig. 1), is a broad anti-viral drug developed by the renowned biopharmaceutical company Gilead Sciences [5]. The antiviral activity of Remdesivir was established against many RNA viruses, including Severe Acute Respiratory Syndrome (SARS) and respiratory syndrome in the Middle East.

![Chemical Structure of Remdesivir](Fig. 1. Chemical Structure of Remdesivir (Reproduced from Drug Bank))
3. PHYSICOCHEMICAL PROPERTIES OF REMDESVIR

The physicochemical properties of Remdesivir are enlisted in Table 1 [7-9]. Remdesivir is a white to off-white non-hygroscopic solid which is practically insoluble but soluble in ethanol and dichloromethane. The two polymorphs of Remdesivir existed in different crystalline forms, which acquired different solubility profiles [6]. This drug has five chiral centers and is produced as a single stereoisomer in racemic form. Remdesivir is a nucleotide analogue with C-linked nucleobase as a pharmacophore [7]. During the structure-activity relationship (SAR), the modification in one of the groups attached to the nucleotide base alters the activity. The adenosine nucleotide base ensures optimal activity against host polymerase enzymes [6]. Remdesivir is a thermally stable drug and its stability was not altered in high humidity (50°C/75% RH).

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Table 1. Remdesivir Physiochemical Properties.

3.3. Remdesivir Pharmacokinetics

Remdesivir is quickly decomposed into the original product (nucleoside phosphate) in rhesus monkeys by intravenous infusion at a dosage of 10 mg/kg. Within 2 hours, Remdesivir is rapidly distributed in mononuclear peripheral blood cells (PBMCs) [8]. As for the in vivo pharmacokinetic trials, it showed dose-linear pharmacokinetics after intravenous infusion of the formulation of Remdesivir solution at a single dose of 3–225 mg for 2 h. Repeated intravenous infusions of 150 mg/day of a Remdesivir solution demonstrated linear pharmacokinetics over a 14-day period [9]. Remdesivir is a lyophilized formulation which is preservative-free, white to off-white, or yellow lyophilized powder containing 150 mg of Remdesivir to be reconstituted with the 29 mL of sterile injection water and is dissolved into intravenous infusion fluids prior to intravenous administration [10]. Remdesivir is eliminated through 74% through urine and 18% in the feces. The 13.49% of the recovered amount is in the form of a GS-441524 metabolite, and 10% has recovered as the unmetabolized parent product.

3.2. Remdesivir Pharmacology

Remdesivir is an adenosine analog monophosphoramide medication with proven antiviral activity against such a number of RNA virus classes like Paramyxoviridae filoviridae (such as Ebola virus), Coronavirus and Pneumoviridae [11]. Remdesivir is also analog of adenosine, introducing into embryonic viral RNA chains and resulting in premature termination. Remdesivir is also an investigational compound with such a broad range of antiviral actions against RNA viruses, including SARS-CoV and Respiratory Syndrome of the Middle East (MERS-CoV) [12, 13]. Remdesivir is indeed a nucleotide analogue and an RNA-dependent polymerase inhibitor. A number of researches have investigated the effect of such medications on both in vitro and in vivo coronaviruses using mouse and non-human primate animal models [14]. There are presently no approved antiviral drugs for treating certain respiratory distress syndrome. Remdesivir is a promising candidate based on validated evidence, and multi-site clinical studies of Remdesivir are currently underway in COVID-19 hospitalized adults.

3.3. Remdesivir Approval Status

Remdesivir is an antiviral investigational agent undergoing clinical trials as a possible treatment for COVID-19 in a variety of countries. In January 2020, Gilead began laboratory trials for Remdesivir against SARS-CoV-2, reporting that Remdesivir was shown to be successful in animal models against SARS and Middle East respiratory syndrome (MERS) [15]. In March 2020, a small study of Remdesivir in rhesus macaque monkeys with COVID-19 infections showed that it prevents the progression of the disease [16]. On 18 March 2020, the World Health Organization (WHO) announced that it will begin a study involving one group treated with Remdesivir [17]. As of April 2020, Remdesivir was considered the most likely promising therapy for COVID-19 and was included in the International Solidarity Trial and European Discovery Trial among four therapies under evaluation [18]. The National Institute of Allergy and Infectious Diseases (NIAID) announced on 29th April 2020 that Remdesivir is better than placebo in minimizing recovery times for people hospitalized with advanced COVID-19 and lung involvement [19]. Now, US-FDA approves emergent use of this drug in patients with a severe infection in various countries. Still, more clinical trials are underway or in the pipeline.

CONCLUSION

The pandemic scenario of COVID-19 is rapidly evolving and urgently requires combinational therapies to tackle this health crisis. Various drugs/therapies have been investigated from which Remdesivir shows promising results in COVID-19 viral load and replication. Remdesivir has proved activity against both SARS and MERS, which also
belong to coronaviruses in vitro and animal models, and potentially supports its efficiency in the treatment of COVID-19. We hope that the future treatment of COVID-19 will come as soon as possible, and the world will be free from COVID-19 illness.

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CONFLICT OF INTEREST
The authors have no conflicts of interest, financial or otherwise.

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REFERENCES