

DEALING WITH SARS COV-2 PANDEMIC: PERUSING REMDESIVIR AND HYDROXYCHLOROQUINE AS THERAPEUTIC ALTERNATIVE

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Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) emerged from the Wuhan city of China and came up with a global emergency as a pandemic. It made millions of human lives infected, and thousands of deaths around the globe have alarmed various health organizations regarding the urgent need to find out its effectual treatment. Although, at present, there is no treatment or vaccine for this novel coronavirus, there are several drugs under trial to find the most promising one. Remdesivir, a broad-spectrum antiviral drug and hydroxychloroquine, an antimalarial and immunomodulatory drug, have been a matter of interest due to the various researches where they have proved their efficacy against the SARS CoV-2. Here we review the current invitro and invivo evidence of remdesivir and hydroxychloroquine as an effective treatment for SARS CoV-2. Some studies have also been done based on previous experiences of SARS CoV and MERS CoV which share structural similarities with the recent SARS CoV-2 and are also of the same β -coronavirus category. Our finding says, both the drugs have reported to play inhibitory role against SARS coronavirus with very low EC_{50} values, indicating better potency and less toxicity for future aspects. Although, both the drugs have suggested having beneficial outcomes whether tested on cell lines or few patients tested positive with the virus, however completion and results of clinical trials will prove their potency and efficacy beyond any doubts.

Keywords: SARS CoV-2, COVID-19, 2019-nCoV, treatment, invitro, invivo, remdesivir, hydroxychloroquine

Abbreviations: SARS CoV-2, severe acute respiratory syndrome corona virus 2; COVID-19, SARS CoV-2 infection; 2019-nCoV, novel coronavirus 2019; α -CoV, alpha coronavirus; β -CoV, beta coronavirus; γ -CoV, gamma coronavirus; δ -CoV, delta coronavirus; MERS-HCoV, middle-east respiratory syndrome human coronavirus; SARS-HCoV, severe acute respiratory syndrome

human coronavirus; WHO, world health organization; MoHFW, ministry of health and family welfare; N protein, nucleocapsid protein; M protein, membrane protein; E, envelope; S, spikes, ORFs, open reading frames; ORF1a, open reading frame 1a ; ORF1b, open reading frame 1b; NSPs, non-structural proteins; RTC, replication/transcription complex; RBDs, receptor binding domains; CTD1C-terminal domain 1; ACE 2, Angiotensin-converting enzyme-2 receptor; *invitro*, outside the living organism; *invivo*, inside living organism; GS-5734, chemical name for remdesivir; EBOV, ebola virus; Huh-7 cells, human hepatic epithelial cell line; EC₅₀, half maximal effective concentration; Vero E6 cells, cell lines derived from African green monkey kidney epithelial; Calu-3 2B4, human lung epithelial cell line; IC₅₀, half maximal inhibitory concentration; FFRA, Focus Forming Reduction Assay; μ M, micromolar; *Ces1c*^{-/-}, carboxylesterase 1c mouse; HCoV-OC43, human coronavirus OC43; s.c, subcutaneous; i.v, intravenous; ICU, intensive care unit; CDC, centers for disease control and preventions; CQ, chloroquine; HCQ, hydroxychloroquine; DMARDs, disease modifying antirheumatic drugs; TLR 7 & TLR 9, Toll-like receptors; CCK8, cell counting kit-8 assay; ATCC-1586, African green monkey kidney VeroE6 cells, GS-704277- Alanine metabolite of remdesivir.

1. Introduction

The year 2019, December ended with an upsurge of a disease COVID-19 caused by the novel coronavirus 2019-nCoV, which forewarned the world health organization regarding the consequences on the way.^[1] The disease emanated from the Wuhan city in China, the worldwide escalation of the severe acute respiratory syndrome (SARS CoV-2) in the humans declared it as a pandemic.^[2,3] The subfamilies of Coronaviruses (CoV) are branched into four types, including α -CoV, β -CoV, γ -CoV and δ -CoV. The α - and β -CoV can infect mammals, while γ - and δ -CoV can infect birds.^[4] They are commonly seen in animals and rare in humans. The rare ones seen in humans were MERS-CoV, SARS-CoV, which originated from bats and transmitted to humans.^[5] Being in the category of Betacoronavirus, SARS-CoV-2 shares structural parallelism with Severe Acute Respiratory Syndrome Human coronavirus (SARS-HCoV) and the Middle-East Respiratory Syndrome Human coronavirus (MERS HCoV).^[6] As the disease came into existence abruptly, it became challenging to attain a grip over its mechanism of

spread. All the coronaviruses similar to it have helped to procure knowledge about SARS CoV-2.^[7]

As on 20 July, 2020 reported by WHO; people from 216 countries, areas/territories around the world have suffered from the disease with 14,348,858 confirmed cases and 603,691 confirmed deaths worldwide.^[8] According to MoHFW, Government of India, this disease can spread from one person to another through mouth or nose droplets exhaled by the infected and by touching the surface of objects, eyes, nose or mouth carrying the virus.^[9] Also, the symptoms of COVID-19 may vary from mild to a severe form, having an incubation period of 2-14 days. Common symptoms extend from fever, cough, sore throat, difficulty in breathing, muscular pain, severe pneumonia to asymptomatic cases (which are infected with the pathogen but do not show symptoms). Severe pneumonia may also lead to the death of the person.^[10]

2. Structural organization & receptor binding of coronavirus

The structure of coronavirus consists of mainly four parts. The innermost genome part covered inside the capsid made up of nucleocapsid protein (N), the membrane protein (M) and outermost envelope (E) on which the glycoprotein spikes (S) protrudes. Coronaviruses have the largest genome of all RNA virus, with approximately 32 kilobase size.^[11] The homotrimeric spikes glycoprotein (S) play their vital role in identifying and binding with cellular receptors. The fusion of host cell and spikes of viral membrane helps viral entry into the host cell, leading to a series of events.^[12]

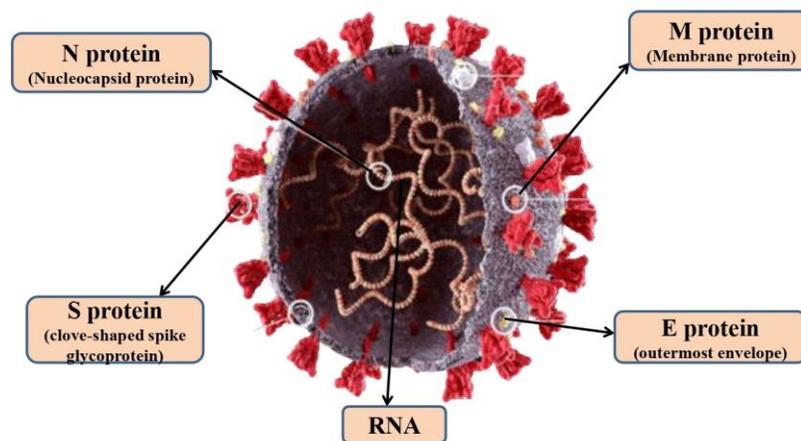


Figure 1.0 Structure of coronavirus Source- (The Week, 2020)^[13]

In a microscopic study, the spike protein has observed as a clove shaped structure, which consists of three S1 head and S2 stalk.^[14]The S1 subunit and S2 subunit made up of ~700 and ~600 amino acids, where former plays its role in receptor binding, and the latter helps in viral genome entry into the host cell. ^[15]The 5-methylated cap of the genome consists of two open reading frames (ORFs), typically ORF1a and ORF1b which are together responsible for the encoding of all non-structural proteins (NSPs) which leads to the formation of coronavirus (RTC) replication/transcription complex.^[16] It is done by the production of polyproteins pp1a and pp1b by translation of replicase gene (composed of ORF1a and ORF1b) and creates an environment for RNA synthesis.^[17, 18] Out of various receptor binding domains (RBDs), (mainly betacoronavirus) S1 subunit, the C-terminal domain (CTD1) is primarily responsible for identifying Angiotensin-converting enzyme-2 (ACE 2) receptor.^[19] ACE 2 protein is present over the cell surface of various endothelial cells, one of which is lungs. It helps to illustrate more about the disease and its routes. ^[20] Studies reveal betacoronavirus SARS CoV-2 showing 79.5% structural resemblance with another betacoronavirus i.e., SARS-CoV. Therefore, it may say that SARS CoV-2 utilizes Angiotensin-converting enzyme-2 (ACE 2) receptor, same as SARS-CoV to infect the host cell (more precisely human cell). ^[21]

3. Therapeutics of SAR CoV2 (COVID-19):

The current situations are like struggling with two issues generated from one problem. Not only the world is trying to control the spread of the disease, but also treatment is much needed to save lives.^[22] The outbreak of SARS CoV2 occurred abruptly, giving no time to the healthcare system for the development of its treatment. But the way towards the development of its vaccine/drug is going with a speedy pace worldwide. These studies have developed the roots from the earlier experiences of SARS-CoV and MERS-CoV treatments, and the healthcare system is trying to repurpose the drugs used previously for their therapeutic effects. ^[23]

3.1 Remdesivir: Trials & Testings (An antiviral drug repurposed)

3.1.1 *In-vitro* studies

Treatment of novel coronavirus is a big challenge worldwide, and every country is trying to develop the drug/vaccine for it. Several drugs are being tested and repurposed for the same.

Remdesivir (GS-5734), being a prodrug and 1'-cyano-substituted adenosine nucleotide analog has shown a broad-spectrum antiviral activity against a lot of RNA viruses.^[24]

Remdesivir being in the broad-spectrum antiviral category was already tested effective against Ebola virus (EBOV) earlier only; efficient enough to interrupt the RNA chain termination process. Reported in an article that, remdesivir showed its inhibitory or antiviral effects in a test conducted on human cell lines (Huh-7 cells) infected with EBOV. Also when incubated human macrophage, with GS-5734 caused speedy piling up of cells with the active metabolite of GS-5734 i.e, nucleoside triphosphate (NTP) for about 24 hours. The drug showed its antiviral effects against many forms of EBOV, infecting different types of the human cell with EC₅₀ values ranging from 0.06 to 0.14 μM.^[25] Getting effective and efficient results in the *in-vitro* studies, it interprets that remdesivir could also be a suitable treatment for another virus SARS CoV-2 in the future.

A recent study which drew attention towards itself conducted against the recently emerging human coronavirus SARS-CoV2, where the studies were done on a cell line (Vero E6 cells) of African green monkey kidney epithelial cells. Seven different drugs were analyzed here and the EC₅₀ of maximum drugs found to be high. Still, the EC₅₀ of remdesivir reported being 0.77 μM which was the lowest concentration among all to inhibit the viral activity. Considering the result of *In-vitro* studies can serve as one step forward for remdesivir towards the development of an efficient drug for novel coronavirus.^[26]

GS-5734 is a prodrug getting metabolized within the host cell forming active metabolite, which is a triphosphate (TP), inhibiting the viral replication process and responsible for the antiviral activity.^[27] Another *In-vitro* research reported on the human lung epithelial cell line (Calu-3 2B4) to detect the antiviral activity of GS-5734 against MERS-CoV. The results reported the inhibition of MERS-CoV replication on 2B4 cells with the IC₅₀ value of 0.025 μM. Also, they observed that upto 10 μM concentrations, there was no quantifiable cytotoxicity. Provided with suitable conditions and temperature to 1 μM GS-5734 in Calu-3-2B4, the average concentration of its pharmacologically active metabolite triphosphate (TP) was 2.79 μM, in 48 hours. Also, on evaluating the antiviral activity of the same drug for SARS-CoV and MERS-CoV on human airway epithelial cell cultures in a dose-dependent manner, the results were showing the reduction in replication. The study manifests the efficiency of GS-5734 against SARS-CoV and

MERS-CoV, which mainly infect the human. SARS CoV-2, also a human coronavirus having structural similarities with both the above-mentioned viruses, can be considered to study GS-5734 for its pharmacological activity on SARS-CoV2.^[28]

According to a published study conducted on HCoV-OC43, which affected the upper and lower respiratory system of children and adults,^[29] the nucleocapsid viral messenger RNA and protein was found profusely. These genomic and subgenomic mRNA and protein products produced during replication of the virus. During this study, they developed Focus Forming Reduction Assay (FFRA) in 96 well plates, based on nucleocapsid antigen staining. Their research on remdesivir resulted in depletion of HCoV-OC43 antigenic foci in a dose-dependent manner. Also, the EC₅₀ values determined for every experiment was consistent (0.14, 0.17, 0.16 μM), respectively.^[30] The *in-vitro* effects of remdesivir on various types of human coronaviruses have successfully lead to the *in-vivo* studies.

3.1.2 *In-vivo* studies

In an *in-vivo* study performed on *Ces1c*^{-/-} mouse SARS model, GS-5734 is an effective prophylactic treatment against SARS disease. Due to the secretion of an enzyme carboxylesterase 1c (*Ces1c*) in mice, the plasma stability of GS-5734 was much less than human.^[31] To improve the plasma stability and perform the studies, mice with genetically removed carboxylesterase 1c (*Ces1c*^{-/-}) taken. The pharmacokinetic profile analyzed by subcutaneous (s.c.) dosing with 50 mg/kg once daily or 25 mg/kg twice daily. The studies performed on mentioned doses improved the SARS CoV induced weight loss compared to the control group. Reducing viral titers in the lungs showed a significant effect. The prophylactic study drew attention and lead to therapeutic studies, which also proved to be equally effective against SARS CoV.^[28]

In 2019 another study conducted to assess the prophylactic and therapeutic efficacy of remdesivir against MERS-CoV by rhesus macaque model.^[32] Total 9 male rhesus macaques were taken for the prophylactic study, categorized 6 into the treated group and 3 into a control group. The former treated with 5 mg/kg i.v. Injection of remdesivir and the latter received vehicle solution of the same volume, 24 hours before the virus inoculation and which extended up to 6 days post-inoculation. Further therapeutic studies performed on observing a satisfactory response. The procedure followed was the same as above; the only difference was dosing, which was done 12

hours after inoculation with MERS-CoV. A decrease in respiratory rate and infiltration of lungs revealed its significant effects.^[33]

Another study reported remdesivir trial against Covid-19 positive patients. The study took place in 10 hospitals in Wuhan city in China. It has been a randomized, double-blind, placebo study, performed on adult males and non-pregnant females. The patients were administered with 200mg remdesivir intravenously (i.v.) on 1st day of treated, followed by 10mg daily, from day 2 to 10. The analysis of patients was done and recorded daily from day 0-day 28 or death by the experienced nurses. The gender was distributed group wise; on one side it was 56% men and 44% woman in remdesivir group and on the other hand, the placebo group had 65% men and 35% women. However, the study did not show any therapeutic effects, but numerically better than the placebo group.^[34]

Another study for COVID-19 and remdesivir has reported on 5 cases in Europe during January & February 2020. The criterion for patient selection was according to the French National Health Agency. The study performed authentically, approved by the French ethics committee along with written consent from the patients. Samples collected from nasopharyngeal or oropharyngeal swabs, blood, urine and stool. The selected five patients had different stages of infection while they got admitted. Patient 1 and 2 had mild condition at the time they got admitted, which grew into the severe secondary type shifting them to ICU. Patient 3 was already severely infected and directly admitted to ICU with respiratory failure. Patient 4 and 5 had mild infection diagnosed earlier only. The patients treated with loading and maintenance dose of remdesivir, which improved their condition and was effective against the COVID-19 virus. After the whole treated, all the patients recovered except patient 3, who was an 80-year-old man diagnosed at the critical stage. Due to the severe acute respiratory syndrome leading to multi-organ failure, patient 3 died on the 14th day of his illness. Although, the study cannot justify the effectiveness of remdesivir in such a small number of cases, the recovery of 4 out of 5 cases can be taken as a base for further studies on a large number of patients to get more precise results.^[35]

Another case has reported in January 2020, a 35 years old man who had returned back to U.S. from Wuhan city, China. Apart from cough and fever, he had no other symptoms, with all the vital activities running smoothly. Due to the growing cases of 2019-nCoV, it was not possible to ignore his condition. His nasopharyngeal & oropharyngeal samples collected according to CDC, where he was found 2019-nCoV positive. Apart from the earlier symptoms, the patient had

nausea, vomiting and abdominal discomfort, for which he was given supportive therapy. With the progression of days, his radiography indicated the development of pneumonia. This initiated the treatment with remdesivir, an antiviral drug which is under trial for its repurposing. Treating the patient with intravenous remdesivir improved the condition of the patient, also there were no adverse effects seen. His symptoms started to descend day by day, along with the oxygen saturation values from 94-96%.^[36] The study cannot decide the complete safety and efficacy of remdesivir in only one patient; however, it can draw the attention of researchers and clinical trials towards more comprehensive analysis. Also, circumstantial data will work as independent corroboration for remdesivir worldwide.

3.2 Hydroxychloroquine: Trials & Testings (A DMARD repurposed)

3.2.1 *In-vitro* studies

hydroxychloroquine (HCQ) was formed by introducing a hydroxyl group to the chloroquine (CQ) structure, a less toxic (~40%) analog known as d. In comparison to CQ, it was found to be much less toxic in animals.^[37] HCQ is one of the disease modifying antirheumatic drugs (DMARDs), acting strongly on rheumatic diseases and also acting as an immunomodulatory drug.^[38] Being a weak base like CQ, HCQ can alter the pH of intracellular organelles like endosomes or lysosomes, which are acidic in nature, thereby affecting the membrane fusion process.^[39] Suppression of the T cell activation, differentiation, expression^[40] and reduction in the cytokines produced by these T cells, itself explains the immunomodulatory mechanism.^[41] The alteration in endosomal pH has also hindered the binding of Toll-like receptors (TLR 7 & TLR 9) to their DNA/RNA ligand, impeding the transcription of pro-inflammatory genes.^[42,43]

It reported in an *invitro* study, where hydroxychloroquine has found to be effective against the SARS-CoV-2. The cytotoxicity and efficacy of the drug tested by CCK8 Assay in African green monkey kidney VeroE6 cells (ATCC-1586). Comparative study of chloroquine and hydroxychloroquine performed, but here we have only discussed HCQ. Cytotoxic concentration (CC₅₀) of hydroxychloroquine found to be 249.50 µM. The selectivity index values of HCQ at various multiplicities of infections (MOIs) found to be 55.32, 61.45, 14.41 and 19.25. Resulted, HCQ was found to be effective against SARS-CoV-2 infection and could be an efficient treatment for the same. But a detailed study could be an answer to the more defined results.^[44]

A recent study reported another *invitro* activity to analyze the potency of Hydroxychloroquine (HCQ) and Chloroquine (CQ) on African green monkey kidneyvero cells. The study was divided into two sections: the treatment study and the prophylactic study. Cells were grown in 96-well plates for 24 hours, density 1×10^4 cells/well. In treatment study, the Vero cells were first infected and then treated, whereas in the prophylactic study, vice-versa. The study results showed better potency of HCQ as compared to that of CQ. The EC_{50} values of HCQ for treatment study found to be 6.14 and 0.72 μM at 24 and 48 hours and that of CQ was 23.90 and 5.47 μM respectively. In prophylactic research EC_{50} values were 6.25, 5.85 μM for HCQ >100, 18.01 μM for CQ at 24 and 48 hours.^[45] So the study suggests that hydroxychloroquine is more potent as compared to chloroquine at its maximum safe doses. And it could prove to be a better treatment for SARS-CoV-2 than chloroquine.^[46]

3.2.2 In-vivo studies

As reported in some *invitro* studies, hydroxychloroquine has been an efficient drug against SARS CoV-2. To further investigate the drug, an open-label non-randomized clinical trial on 36 patients (20 under drug-treated and 16 under control group) performed in France. The effect of drug against the disease and the viral load was the prime concern. The drug-treated group patients were given hydroxychloroquine 200mg each orally, thrice a day and observed from starting to 14 days. On day-6, the study reported a reduced viral load to about 70% in hydroxychloroquine treated patients as compared to a control group, which showed a 12.5% reduction ($p=0.001$). The study also took a step ahead by doing a distinguishing between the effects of hydroxychloroquine administered alone and in combination with azithromycin. The result of hydroxychloroquine in combination with azithromycin showed 100% virological clearance and sets a great example of synergistic effect.^[47]

Another recent study conducted in New York was done to find out therapeutic effectiveness of hydroxychloroquine on moderate to severely ill patients of COVID-19 who had tested positive through nasopharyngeal or oropharyngeal sample. Out of 1376 patients taken for the study, 811 (58.9%) received hydroxychloroquine, and 565 (41.1%) did not receive. The initial vital sign recorded at the time of admission was the ratio of the partial pressure of arterial oxygen and inspired oxygen. The dose suggested for hydroxychloroquine administration was 600mg twice on day 1, followed by 400mg for next 4 days. At the end of the study, 1025 patients had survived and got discharged from the hospital, 232 died, and 119 were still left hospitalized to recover

completely. According to the authors, the study did not show a clear one-sided judgement about the effectiveness of hydroxychloroquine on a large population, and he also suggested that randomized clinical trials could serve to be a better option for the same. Maybe the ongoing trials worldwide could bring out more clarity to the findings.^[48]

4. Discussion

The review aims to find out the possible therapeutic or prophylactic effects of remdesivir and hydroxychloroquine against the novel coronavirus (SARS CoV-2) through various *invitro* and *invivo* studies done on the same. Since December 2019, from the detection of the very first case to its spread globally, it brought up a significant health issue worldwide.^[49,50] As the host ACE-2 receptors play an essential role in the binding of SARS CoV-2 and viral entry, they have been under rigorous analysis by various means.^[51]

The novel coronavirus SARS CoV-2 has a major resemblance or structural similarities with that of SARS CoV^[52] and to get the treatment for such a speedy growing virus in shortest time period is a difficult challenge for the researchers. To find a way, researchers are trying to repurpose various antiviral and other drugs showing their efficacy against this novel coronavirus, as there is a critical need for the drug an effective treatment to control the pandemic situations.^[53] There are many studies which push researchers to think of drugs like remdesivir and hydroxychloroquine which can be an effective treatment for COVID-19 in the coming period.

Invitro study for remdesivir against EBOV, done on the human cell line, have shown good results with EC₅₀ values ranging from 0.06 to 0.14 μM^[25] Another study against MERS-CoV resulted in the inhibition of MERS-CoV replication on 2B4 cells with the IC₅₀ value of 0.025 μM.^[28] Having structural resemblance with SARS-CoV and MERS-CoV is another reason to choose the drug for studies against SARS-CoV-2. It might serve an effective treatment for SARS CoV-2. Also, remdesivir found to be efficient against SARS CoV-2 in a comparative study of seven drugs, where cell line (Vero E6 cells) used, and the lowest EC₅₀ value (0.77 μM) was reported to be of remdesivir.^[26] This particular comparative study has not only given a hint for its potency against SARS-CoV-2 but also has been in the top list out of the seven drugs. Remdesivir (GS-5734) is a prodrug, gets metabolized into an alanine metabolite (GS-704277) within the cells. Its mechanism of action plays its role in the viral replication process within the host, where it targets RNA-dependent RNA polymerase.^[54]

In an *invivo* study performed on *Ces1c*^{-/-} mouse SARS model, GS-5734 found to be an effective prophylactic treatment against SARS disease. The experiment initiated on those mice who had genetically removed carboxylesterase 1c (*Ces1c*^{-/-}). A subcutaneously (s.c.) dosing of 50 mg/kg once daily or 25 mg/kg twice daily explains the pharmacokinetic profile. The efficient results of the prophylactic study lead to further therapeutic studies.^[28] Another study in 2019 on rhesus macaques treated with 5mg/kg i.v. injection of remdesivir showed significant effects against MERS-CoV by decreasing the respiratory rate and infiltration of lungs.^[33] Human trial^{[34], [35], [36]} have also shown some positive sights of remdesivir against SARS CoV-2, but the detailed 100% results still awaited as there is a huge difference between the small sample size as well as large sample size study and clinical trials are going worldwide to define its potency. It may prove to be an effective treatment in future.

Hydroxychloroquine (HCQ), an analogue of antimalarial drug chloroquine (CQ) has been used since long time and it is considered to be less toxic than chloroquine. Along with this antimalarial effect, it has been a potent drug for autoimmune diseases like rheumatoid arthritis. Ever since HCQ turned out to be a direct inhibitor of the viral entry process; it has also been in the list of drugs which could be an efficient treatment for viral infections.^[55] Reported in a study on African green monkey kidney Vero cells, the EC₅₀ values of HCQ for treatment study as well as the prophylactic research found to be very much less as compared to chloroquine. The author has suggested HCQ to be more potent as compared to CQ and also it can be a better treatment for SARS CoV-2.^[46]

Hydroxychloroquine was administered 20 out of 36 patients, doses of 200mg each orally, thrice a day were analyzed for 14 days. The study reported a reduced viral load to about 70% in hydroxychloroquine treated patients as compared to a control group, which showed 12.5% reduction (p=0.001) on day 6. And when combined with azithromycin, 100% virological clearance was observed depicting the synergistic effects.^[47] The antiviral mechanism of HCQ has suggested to be alteration in lysosomal pH,^[56] decreasing cytokine production by inhibiting the toll-like receptors as well as T cells & B cells^[57] and Phospholipase A2 inhibition^[58]

Reported in a study conducted in New York, 1376 patients were involved in a study to find out therapeutic effectiveness of hydroxychloroquine on moderate to severely ill patients of COVID-19. A total of 811 (58.9%) received hydroxychloroquine and 565 (41.1%) did not receive was done. The administered dose for drug-treated patients was 600mg twice on day 1, followed by

400mg for next 4 days. The end of the study was neither against or in favour of hydroxychloroquine efficacy as in the end, 1025 patients survived and got discharged from the hospital, 232 died and 119 were still left hospitalized to recover completely.^[48] The results did not show clear evidence, maybe more studies on the same drug may help to draw a conclusion on the potency of HCQ on severely ill patients. Along with the clinical efficacy, dosing regimen and therapeutic levels are still a matter of concern to be studied and analyzed thoroughly. ^[59-61]

5. Conclusion

SARS CoV-2 emerged as a pandemic within no time and took away the lives of so many people worldwide. Its fast spread gave no time to the researchers for an effective treatment discovery. There are still several trials going on to find out the effective treatment for the newly emerged novel coronavirus. Remdesivir and hydroxychloroquine which have reported to be efficient against SARS CoV-2 in various *invitro* and *invivo* studies have been effective in treating cell lines or smaller population. Still, when it comes to a larger community, its potency needs to be analyzed more. Researches have to be more detailed to identify the complete efficacy and potency of Remdesivir and hydroxychloroquine against SARS CoV-2. Our finding suggests that remdesivir and hydroxychloroquine have given numerous favourable results; however, outcomes of a clinical trial are still awaited for any result to deduce.

Declaration of Competing Interest

The authors declare that they have no competing interest.

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