



Risk Factors on Covid-19 Drugs

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ABSTRACT

To increase the success in Covid 19 treatment, many drug suggestions are presented, and some clinical studies to are shared in the literature. There have been some attempts to use some of these drugs in combination. However, using more than one drug together may cause serious side effects on patients. Therefore, detecting drug-drug interactions of the drugs used will be of great importance in the treatment of Covid 19. In this study, the interactions of 8 drugs used for Covid 19 treatment with 645 different drugs and possible side effects estimates have been produced using Graph Convolutional Networks. As a result of the experiments, it has been found that the hematopoietic system and the cardiovascular system are exposed to more side effects than other organs. Among the focused drugs, Heparin and Atazanavir appear to cause more adverse reactions than other drugs. In addition, as it is known that some of these 8 drugs are used together in Covid-19 treatment, the side effects caused by using these drugs together are shared. With the experimental result obtained, it is aimed to facilitate the selection of the drugs and increase the success of Covid 19 treatment according to the targeted patient. In this review, we conclude some AEs of vitamin-D, zinc, Remdesivir, Hydroxychloroquine or chloroquine, azithromycin, dexamethasone, amantadine, aspirin reported in different papers and we continue the rest of the drugs in second part of our review article.

Keywords: Mechanism, Treatment, Side effects of covid -19 drugs

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INTRODUCTION

COVID-19 is an infectious disease caused by SARS-CoV-2, the coronavirus that was discovered in December 2019 and has caused a huge pandemic in the world. The disease is spread primarily through inhaled drops when coughing, sneezing, or talking to infected people in addition, infection may occur by touching an infected surface as a result of contact with the face. SARS-CoV-2 is a positive, single stranded RNA virus (~30 KB in length) with a nucleocapsid, which undergoes endocytosis or membrane fusion to enter infected cells and can cause respiratory and intestinal diseases, liver and nerve in different species, including humans and some animals SARS-CoV-2 contains spike (S) glycoproteins, which are composed of two functional subunits called S1 protein, which binds to the host cell receptor and S2 protein, which fuses viral and cell membranes [3]. Angiotensin II converting receptor (ACE2) is known as a functional receptor for SARS-CoV-2 entry into cells and ACE2 expression is high in lung, heart, ileum, kidney and bladder So far, many efforts have been made to develop a vaccine, but at this time, there are some specific vaccine or treatment for COVID-19, and the elderly with underlying diseases are at higher risk for severe disease Therefore, the important information for most people is to know how they can boost their immune system to prevent SARS-CoV-2 infection or control the severity of disease progression. There is a lot of research around the world every day trying to find an effective drug that shows promising results in preventing or treating and controlling COVID-19. Some drugs are found helpful for the treatment of COVID 19. Here, we try to investigate some of them include vitamin-D, zinc, Remdesivir, Hydroxychloroquine and chloroquine, azithromycin, dexamethasone, amantadine, aspirin. Besides the clinical efficacy of these drugs, there have been some adverse effects (AE) reported in experimental studies and clinical trials. For the first COVID-19 time, to the best of our knowledge, in this review article, we aimed to briefly describe mechanisms of actions of these drugs and then conclude the AE of them. It should also be explained that this systematic review over these drugs was done using PubMed and Google Scholar research engine and searching for different clinical trials and review articles all around the world. That would be a very long review article if we wanted to bring all these Drug complications in only one article. ^(1,2)

TYPES OF DRUGS:

1. Vitamin-D
2. Zinc
3. Azithromycin
4. Aspirin

5. Dexamethasone

6. Remdesivir

VITAMIN – D:

Vitamin D is a group of fat-soluble steroids that are the most common forms of vitamin D supplementation: colecalciferol (vitamin D3) and ergocalciferol (vitamin D2), precursors 1, 25 (OH) 2D3 (active form of vitamin D) Vitamin D plays important (classical) biological roles including bone metabolism, calcium and phosphorus homeostasis, and more recently (non-classical) roles including immune system modulation, lung and muscle function, cardiovascular health, and infection prevention has been. In fact, vitamin D reduces the risk of respiratory infections through three main mechanisms: maintaining tight connections to prevent immune cells from penetrating the lungs and other respiratory tissues, killing some viruses by stimulating antiviral mechanisms, and reducing the synthesis of pro-inflammatory Cytokines by modulating the immune system and preventing the development of pneumonia.⁽²⁾

Mechanism :(Figure 1) ⁽³⁾

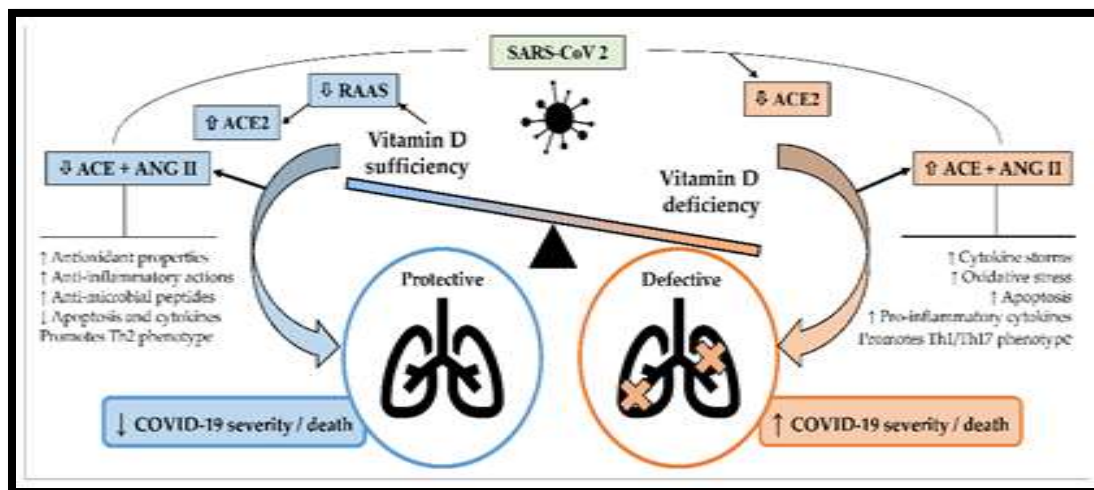


Figure: 1 Mechanism of Vitamin-D against Covid-19

Treatment:

- Vitamin –D is crucial for bone and mineral metabolism because the vitamin D receptor is present on immune cells such as B cells, T cells, and antigen-presenting cells and because these cells can synthesize the active vitamin D also has the potential to modulate innate and adaptive immune responses.
- It is postulated that these immunomodulatory effect of vitamin D could potentially protect against SSRS-COV 2 infections or decrease the severity of COVID-19.

Side effects:

Vitamin D is taken orally and in shots. Vitamin D may be unsafe for long periods of time in doses above 4,000 units (100 micrograms) per day and may cause very high levels of calcium in the blood and can cause side effects. Have their own. For example: includes weakness, fatigue, drowsiness, headache, loss of appetite, dry mouth, metallic taste, nausea, vomiting and more. This can lead to kidney stones and other problems. In patients with the hyperparathyroidism, vitamin D may increase calcium levels in people with hyperparathyroidism. Vitamin D may also increase calcium levels in people with lymphoma.⁽²⁾

ZINC:

Zinc is an essential mineral that the body cannot produce on its own. Zinc has effect on some parts of the body such as immune function, protein synthesis, wound healing, DNA synthesis, and cell division It appears that zinc have antiviral effects against viruses such as influenza and coronavirus due to the increasing of immune system function and also zinc can prevent coronavirus replication by inhibiting RNA synthesis Therefore, we assume that due to its antiviral properties of zinc, it can protect the body against coronavirus.⁽²⁾

Mechanism :(Figure 2)⁽⁴⁾

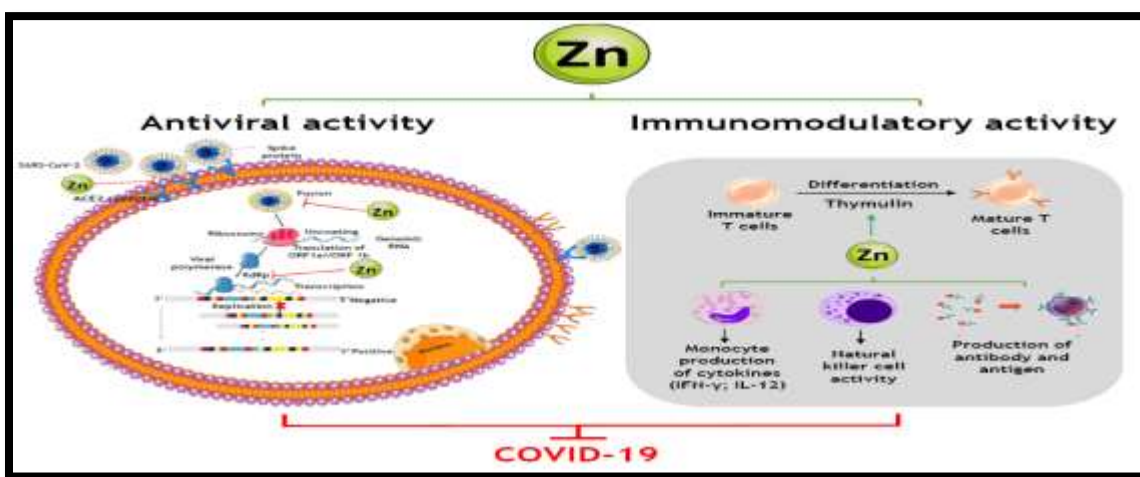


Figure: 2 Mechanism of Zinc against Covid – 19

Treatment :(Figure 3)⁽⁵⁾

Side Effects: The most common side effects of zinc which is usually due to its high dose can be referred to as head ache, nausea and vomiting.

When taken by mouth: Zinc is likely safe when used in amounts no greater than 40 mg daily. But taking doses higher than 40 mg daily might decrease how much copper the body absorbs.

When applied to the skin: Zinc is likely safe. Using zinc on broken skin may cause burning, stinging.

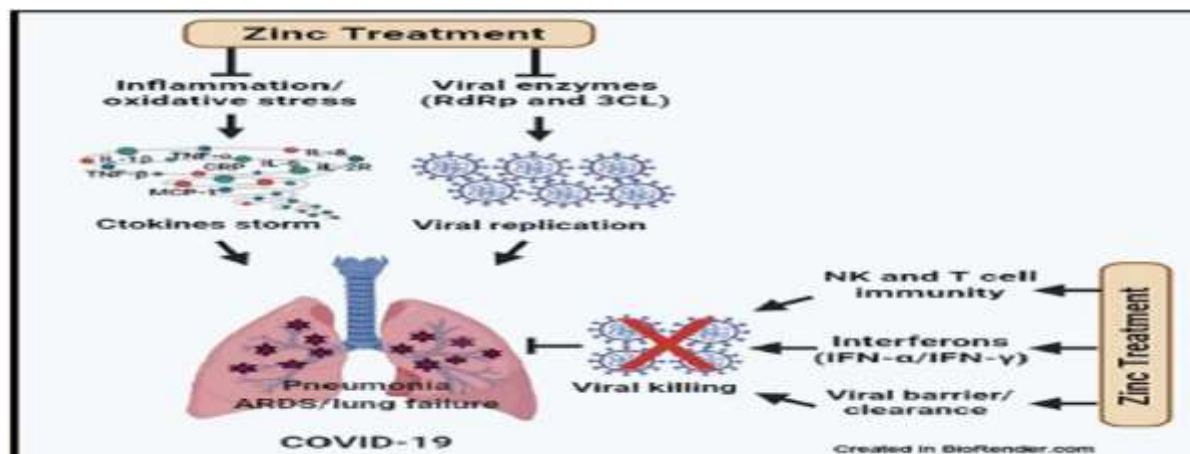


Figure 3: Treatment of zinc against Covid-19

AZITHROMYCIN:

Azithromycin (Azi) belongs to the large family of macrolide antibiotics, an important class of first-line antimicrobial agents. Azi belongs to the second generation of macrolides, as a semisynthetic derivative of erythromycin with a modified macrolactone ring with 15 members instead of 14 members as in erythromycin. Although Azi did not exhibit improved activity against Gram-positive bacteria compared to the mother compound erythromycin, it was selected for further development due to its enhanced pharmacokinetic profiles. Clarithromycin is another key second-generation 14-membered macrolide with similar features and structure, and while it was initially included in a few trial schemes as a potential therapeutic drug for COVID-19, it was rapidly discontinued. Azi, like most of the other macrolides, is not only known for its antimicrobial activity, but it also has additional actions as either anti-inflammatory or antiviral agents. ⁽²⁾

Mechanism: (Figure 4) ⁽⁶⁾

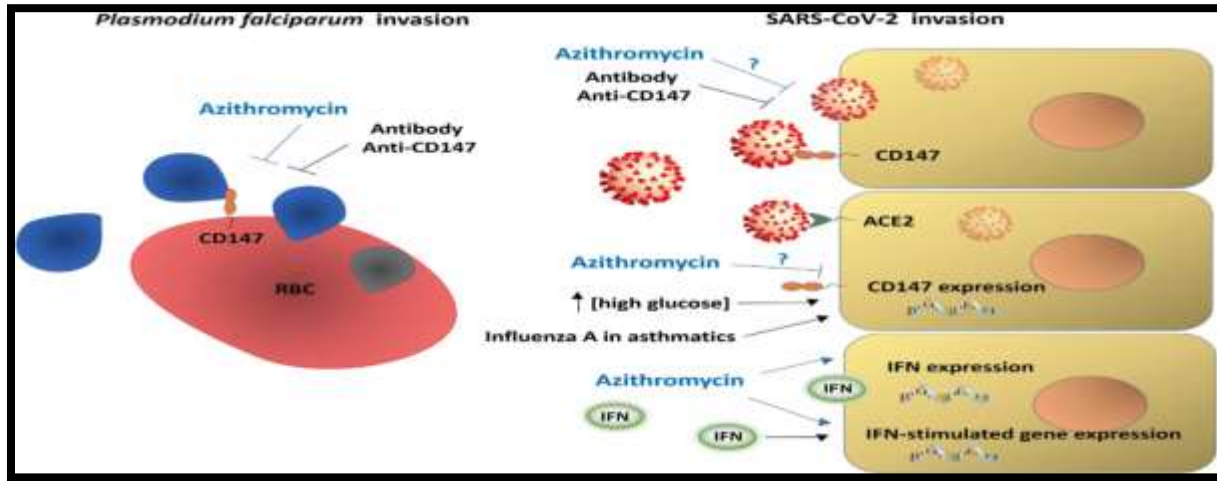


Figure 4: Mechanism of Azithromycin against Covid-19

Treatment: (Figure 5) ⁽⁷⁾

Side effects:

The most common side effects of azithromycin are diarrhea, nausea, abdominal pain, and vomiting. Allergic reactions such as anaphylaxis, QT prolongation, or *Clostridium difficile* infection have been reported with azithromycin. (Figure 6)

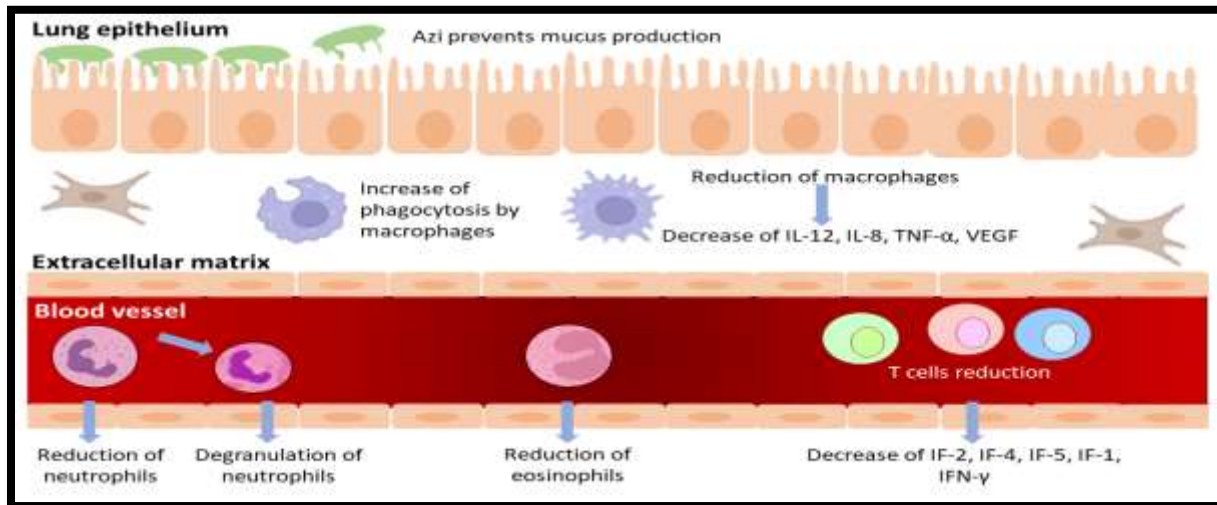


Figure 5: Treatment of Azithromycin against Covid-19

ASPIRIN:

Aspirin, also known as acetylsalicylic acid (ASA), is a drug used to reduce pain, fever, or inflammation. Acetylsalicylic acid (ASA) inhibits prostaglandin synthesis. It is not selective for COX-1 and COX-2 enzymes. Inhibition of COX-1 leads to inhibition of platelet aggregation. Recently, some articles have suggested that aspirin is useful for patients, which can help improve patients. Because one of the leading causes of death from COVID-19 is cardiovascular problems and pulmonary embolism. ⁽²⁾

Azithromycin common side effects:

- Fatigue
- Nausea
- Diarrhoea
- Impaired sense of taste
- Headache
- Loss of appetite
- Dizziness

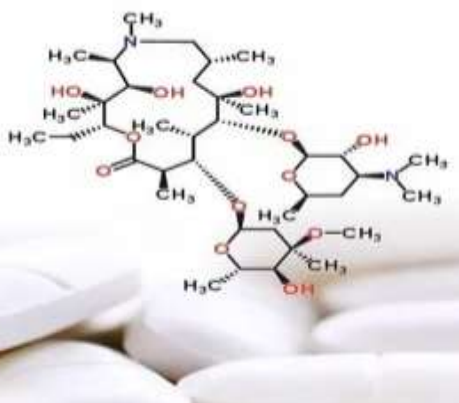


Figure 6: Side effects of Azithromycin against Covid-19

Mechanism:(Figure 7)⁽⁸⁾

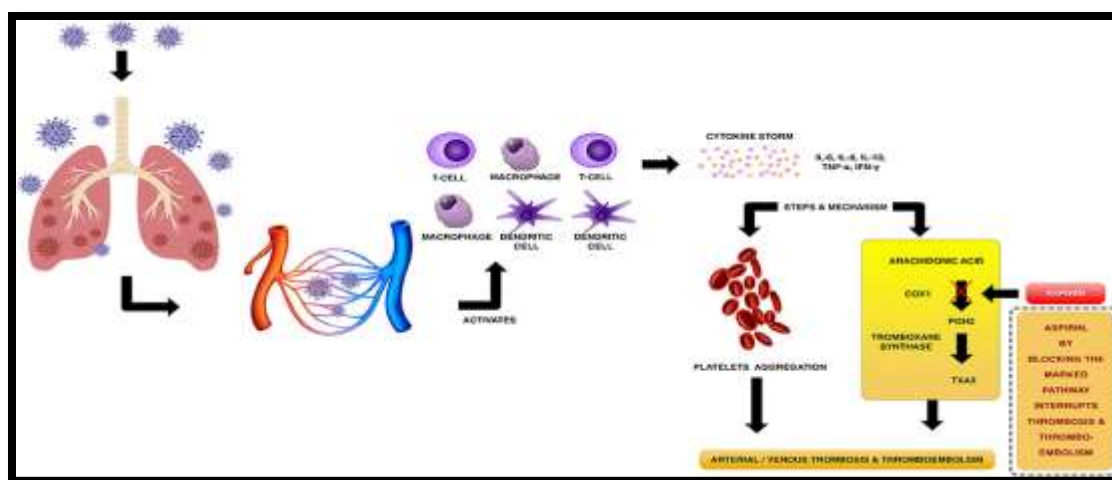


Figure 7 : Mechanism of Aspirin against Covid - 19

Treatment: (Figure 8)⁽⁹⁾

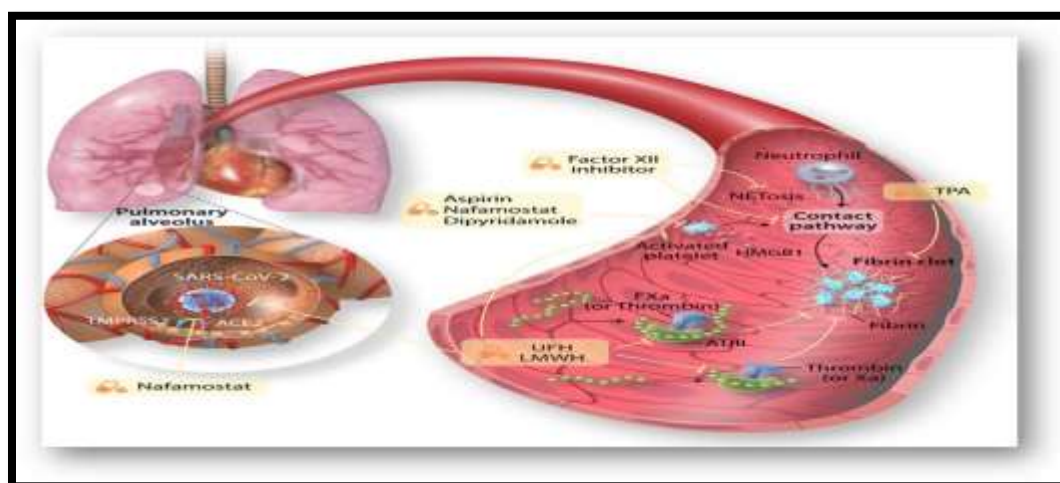


Figure: 8 Treatments of Aspirin against Covid - 19

Side effects:

Aspirin common side effects such as cramping, nausea, bleeding, upset stomach, abdominal pain. Recently, the side effect of its use in COVID-19 patients has been controversial, as the drug irreversibly inhibits platelet cyclooxygenase, and its effect continues for life on circulating platelets (7-10 days). There has been some concern that the delay between a positive SARS-CoV-2 test and its clinical deterioration is similar to the delay between the last aspirin dose and the end of its clinical effect. ⁽²⁾

DEXAMETHASONE:

Dexamethasone is a type of corticosteroid. The mechanism of dexamethasone is mainly due to its anti-inflammatory and immunosuppressive effects. The anti-inflammatory effects are complex, but primarily through inhibition of inflammatory cells and suppression of expression of inflammatory mediators. It is intended for use in the treatment of inflammatory and immune diseases. Dexamethasone is usually given orally, as an intramuscular injection, or as an intravenous injection, and the effect may last for up to a week. ⁽²⁾

Mechanism: (Figure : 9) ⁽¹⁰⁾

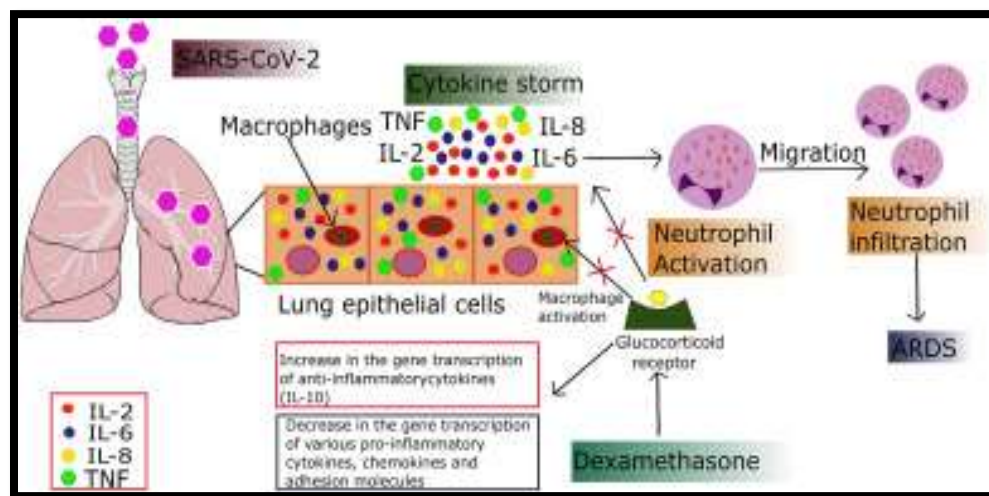


Figure : 9 Mechanism of Dexamethasone against Covid-19

Treatment:(Figure : 10) ⁽¹¹⁾

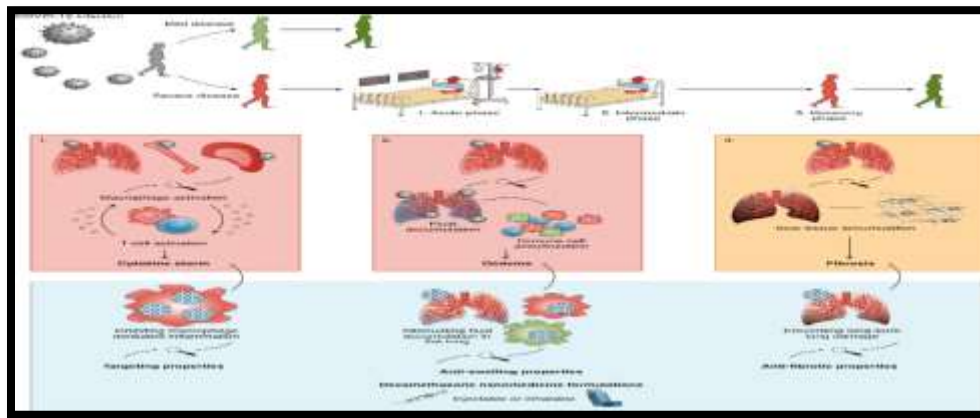


Figure : 10 Treatment of Dexamethasone against Covid-19

Side Effects:(Figure :11) ⁽¹¹⁾

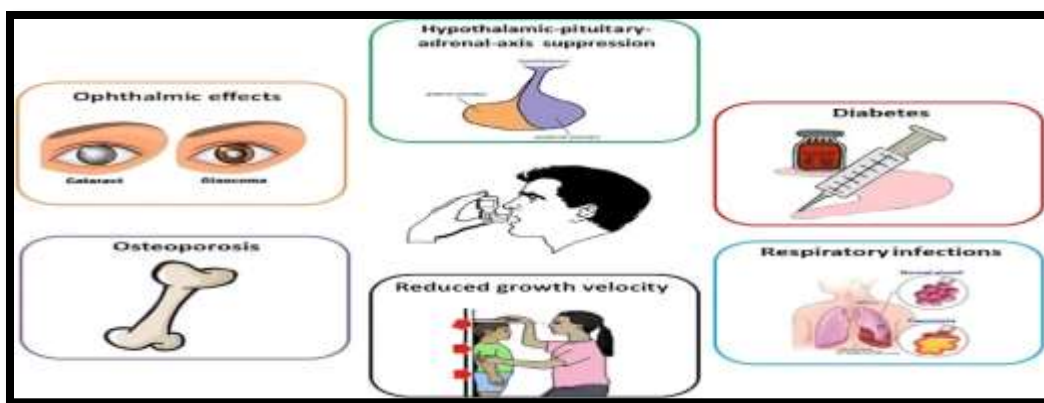


Figure : 11 Side effects of Dexamethasone against Covid-19

REMEDSIVIR:

Remdesivir is an antiviral drug from the family of nucleoside analogues developed by the Gilead Pharmaceutical Company to treat Ebola virus and Marburg virus infections. Due to its antiviral properties, it has also been used against other single-stranded RNA viruses such as respiratory syncytial virus, blood virus, lasa gna virus, NIPA virus, Hendra virus and corona virus family (including coronavirus Mers and SARS) . ⁽²⁾

Mechanism :(Figure 12) ⁽¹²⁾

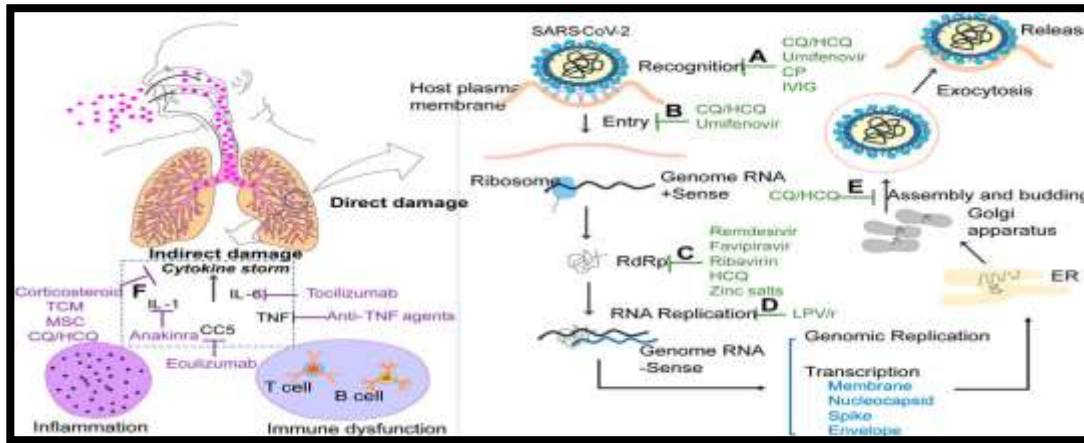


Figure :

12 Mechanism of Remdesivir against Covid-19

Treatment :(Figure 13) ⁽¹³⁾

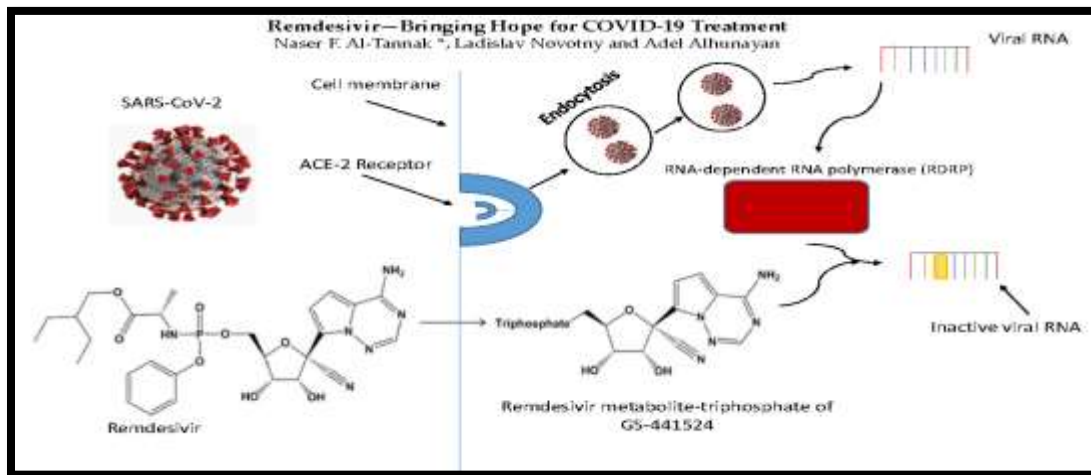


Figure : 13 Treatment of Remdesivir against covid-19

SIDE EFFECTS:

The most common side effects in Remdesivir studies for COVID-19 include respiratory failure and organ dysfunction, including low albumin, low potassium, low red blood cell count, low platelet count, which helps clots, and yellow skin discoloration. Reported side effects include gastrointestinal upset, increased levels of transaminases in the blood (liver enzymes), and injection site reaction. Other possible side effects have been reported with Remdesivir due to its injection reactions; During or around the time of Remdesivir injection, it has been observed that the signs and symptoms of injection-related reactions may include: low blood pressure, nausea, vomiting, sweating and chills. ⁽²⁾

CONCLUSION:

There are some drugs reported that can be helpful for COVID-10, different kinds of drugs are 106 used to improve the disease. Each of these drugs has its own efficacy and indication of usage

but the important issue is that some patients confront different AEs during treatments. In this review article, we had a survey on different AEs associated with some COVID-19 drugs which can be a great helpful when choosing a drug. Taken together, along with specific 4 characteristics of drugs, their AEs should also be noticed in order to prevent serious problems for patients. ⁽²⁾

REFERENCE:

1. İrfan Aygün, Mehmet Kaya & Reda Alhajj, Identifying side effects of commonly used drugs in the treatment of Covid 19, *Journal of Scientific Reports*, 2020, 10(21), 508-514.
2. Nadia Mohammad Zadeh, Nazli Sadat Mashinchi Asl, Khatereh Forouharnejad, Keyvan Ghadimi, Sara Parsa, Sima Mohammad, *International Journal of Physiol Pathophysiol Pharmacol* 2021; 13(4):102-109.
3. Drishti Ghelani, Simon Alesi and Aya Mousa, Vitamin-D and covid-19: An overview of Recent evidence, *international journal of molecular sciences*, 2021, 22(19), 105-159
4. Dilina do Nascimento ID, kyira jayanne, Climaco cruz, Anaraquli saoes de Olivera, Rodrigues, de Sousa Melo Loanna Rocha dos. Santos, Bruna Emanuele Pereira Cardoso and Thaline Milany da Silva, dias, Anti-Viral and immunological activity of Zinc and Possible role in covid-19, *British Journal of Nutrition*, 2021, 22(19),105-159
5. Anand S. Prasad, Agnes Malysa, Gerold Bepler, Andrew Fribley and Bin Bao, The Mechanism of zinc action as Potent anti-viral agent: The chemical therapeutic implication in covid -19, *Journal of antioxidants*,2022, 11(10), 862-868.
6. Henning Ulrich &Micheli M. pillat, CD147 as a Target for COVID-19 treatment: suggested effects of azithromycin and stem cell engagement, *Journal of stem cell reviews and reports*, 2020,16, (2), 434-440.
7. Georgia G. kournoutou, George Dinos, Azithromycin through the lens of the COVID-19 treatment, *Journal of antibiotics*, 2022, 11(8), 163-169.
8. Temistocles Diaz, Samuel J.K Abraham, Armando A. Durant – archibold, Barry H. Trachtenberg, Rao kosagisharaf, Aspirin Bio activity for preventions of cardio vascular injury in covid-19, *Journal of frontiers in cardio vascular medicine*, 2020,7(10), 389-395.
9. James D. Mc fadyen, Hannah, stevens, and Karlheinz. Peter, The emerging threat of (micro) thrombosis in covid-19 and it's therapeutic Implications, *Journal of AHAIASA*, 2020, 127(4), 1-30
10. Twann Lammers, Alexandros Marios Sofias, Roy Van der Mell, Raymond Schifferlers, Gurt strom, Frank, Tacke Stefen Koschmieder, Tim.H. Brummendorf, Fabian kiessling&

- Josbert M. Metselaar, Dexamethasone Nano medicine for covid-19, Journal of nature Nanotechnology,2020, 15(5), 622-626
11. Sobia Noreen, Irsah Magbool, Asadullah Madni, Dexamethasone: Therapeutic potential, risks, and future projection during COVID-19 pandemic, European journal of Pharmacology, 2021, 894(4), 122-128.
 12. Katya uzunova, Elena Filpora, velichka Pavlavas, Toni vekav, in sights in to anti- viral mechanisms of Ramdesivir, lopinavir/ritonavir and chloroquine / hydroxy chloroquine affecting the News SARS-COV-2, Bio medicine and pharmacotherapy, 2020, 131(11),668-674.
 13. Naser F.Al. Tannak, Ladislav Nortony, Adel Alhuagan, Remdesivir-Bringing Hope for covid-19 Treatment, Journal of Scientia Pharmaceutica, 2020, 88(2), 29-34.



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