

Review on Ayurvedic and Investigational Drugs For covid-19

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Submitted: 11-03-2024

Accepted: 21-03-2024

ABSTRACT:

The novel coronavirus (SARS-Cov-2) infection, more commonly it is worldwide known as Coronavirus or COVID-19. It has rapidly spread worldwide pandemic with a significant health burden. Coronavirus became evident in Wuhan, China, and then spread rapidly all over the world. The aim of this systemic review was to discuss about investigational and new as well as repurposed drugs currently under the trial for COVID-19 infection. A huge number of drugs and vaccines are under clinical trials for investigational drugs for the treatment of COVID-19. In the pandemic of coronavirus disease (COVID-2019), ANTIVIRAL drugs are at the centre of attraction/attention because of their critical role against severe acute respiratory disease syndrome coronavirus 2 (SARS-CoV-2). Most early clinical trials have the defects of study design, small sample size, non-randomized design, or different timings of treatment initiation. However, well-designed studies on asymptomatic or mild, or pediatric case of COVID-19 are scarce and desperately needed to meet the clinical need. However, a trend could be observed based on current clinical evidence. Remdesivir and favipiravir may shorten the recovery time; lopinavir/ritonavir does not demonstrate treatment efficacy in severe patients. Triple therapy of ribavirin, lopinavir, and interferon β -1b showed early viral negative conversion, and the major effect may be related to interferon. Currently there are no therapeutics approved by the US Food and Drug Administration (FDA) for the treatment of COVID-19. In this review we will discuss investigational treatments, both repurposed and novel, early data regarding their use in the treatment of COVID-19, and key clinical trials that are currently underway.

Keywords: Coronavirus, COVID-19, severe acute respiratory syndrome coronavirus 2, antiviral drugs, US Food and Drug Administration, clinical trial.

I. INTRODUCTION:

Coronavirus disease (COVID-19) is an infectious disease caused by the SARS-CoV-2 virus. It mainly attacks on the respiratory system of human beings. It was firstly found in the year 2019 that's why it is named as COVID-2019, and 'D' for disease. 'CO' stands for corona, 'VI' for virus. The disease caused by the novel coronavirus first identified in Wuhan, China[1].

This disease is mainly caused due a virus name CORONAVIRUS, which directly attacks on the respiratory system i.e. on the lungs. Patients fail to identify the symptoms of this disease at the initial stage, but when the severity of the disease increases; patients become seriously ill and require medical emergency. This disease spreads very quickly from person to person. It transmits from one infected person through droplets which travel through air. It also transmits by touching contaminated surfaces with the virus. The coronavirus survives on a particular surface for several time of period but it can be easily killed simple disinfectants.

The symptoms of coronavirus include common cold or cough (after some days the severity of cough increases; as the virus increases its activity), low to high fever, and difficulty in breathing. These all symptoms are similarly observed in FLU (influenza), which are lot more commonly seen in patients with both flu and covid-19. That's why medical tests are required for the confirmation of covid-19; whether the patient is suffering from covid or not.

SARS-CoV-2, the virus that causes COVID-19, enters your body through eyes, nose or mouth through air droplets which carry the virus in it. It travels through the nasal passages and mucous membrane present in the throat. It gets attached to the cells and starts to multiply and moves towards tissues of lungs. Gradually it starts to spread towards the other body tissues[2].

Transmission of this disease can also occur due to touching sensory organs such as eyes, nose or mouth after touching contaminated surfaces

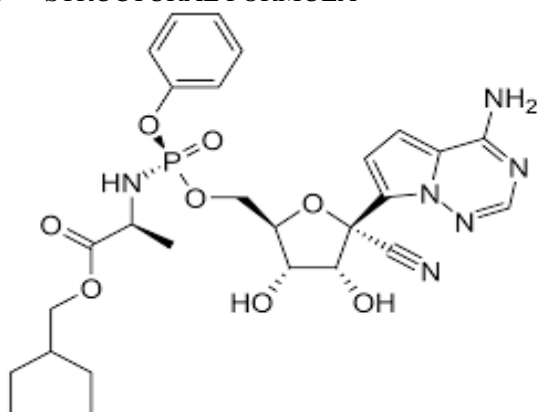
containing the virus. When the virus passes through lung tissues, it starts to multiply with the cells and increases its effect and therefore patient experiences shortness of breath. About 81% of people develop mild to moderate symptoms, while 14% develop severe symptoms that require hospitalization, and about 5% require ICU emergency admission[3].

DRUGS PROFILE WHICH WERE INVESTIGATED FOR THE TREATMENT OF COVID-19:

1. REMDESIVIR:

Remdesivir is a broad-spectrum antiviral drug/medication which was approved to use for emergency treatment in the coronavirus pandemic.

- GENERIC NAME- Remdesivir
- BRAND NAME- Veklury
- IUPAC NAME- (2S)-2-[(2R,3S,4R,5R)-[5-(4-Aminopyrrolo[2,1-f][1,2,4]triazin-7-yl)-5-cyano-3,4-dihydroxy-tetrahydro-furan-2-ylmethoxy]phenoxy-(S)-phosphorylamino}propionic acid 2-ethyl-butyl ester
- MOLECULAR FORMULA- C₂₇H₃₅N₆O₈P
- STRUCTURAL FORMULA-



Structure No. 1

- MOLECULAR WEIGHT- 602.585 g/mol
- MECHANISM OF ACTION-

COVID-19 is caused by the positive-sense RNA virus severe acute respiratory syndrome coronavirus-2 i.e SARS-CoV-2. Remdesivir enters cells before being cleaved to its monophosphate form through the action of either carboxylesterase 1 or cathepsin A; it is subsequently phosphorylated by undescribed kinases to yield its active triphosphate form remdesivir triphosphate (RDV-TP or GS-443902).[4]

- ADMINISTRATION OF DRUG- It is administered intravenously through one any vein.
- PHARMACOLOGY-
 1. Class- antiviral drug
 2. Formulations- 100 mg single dose vials containing lyophilized powder and 100 mg/20 mL solution in single dose vials.
 3. Route- Intravenous
 4. Metabolism- Prodrug metabolized by carboxyesterase 1 and capthepsin A, then phosphorylated by cellular kinases to the active metabolite.
 5. Half life- Remdesivir 1 hr following a single 30 minute intravenous infusion.

SIDE EFFECTS:

- Back pain
- Headache
- Dark coloured urine
- Difficulty in swallowing
- Chest tightness
- Increase in speed of heartbeat
- Hives,etc.[5]

TOXICITY: Developmental toxicity of remdesivir, an anti-COVID-19 drug, is implicated by in vitro assays using morphogenetic embryoid bodies of mouse and human pluripotent stem cells.[6]



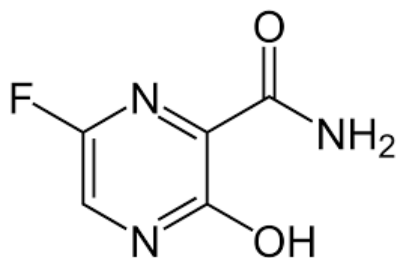
Figure No. 1

2. FAVIPRAVIR:

Favipiravir is an antiviral drug used to manage influenza. And it has capacity/potential to target other viral infections.

- GENERIC NAME- Favipiravir
- BRAND NAME- Fabiflu, Ferawell
- IUPAC NAME- 6-fluoro-3-hydroxypyrazine-2-carboxamide
- MOLECULAR FORMULA- C₅H₄FN₃O₂

➤ STRUCTURAL FORMULA-



Structure No. 2

➤ MOLECULAR WEIGHT- 157.104 g·mol⁻¹[7]

➤ MECHANISM OF ACTION-

The mechanism of action of favipiravir primarily prevents the entry or exit of the virus from cell. Favipiravir-RTP is a nucleoside analogue. It mimics both guanosine and adenosine for the viral RdRP. Incorporating two such bases in a row stops primer extension, although it is unclear how as of 2013.[8]

➤ ADMINISTRATION OF DRUG- It is administered both intravenously or orally as per patients convenience.

➤ PHARMACOLOGY-

Pharmacological actions are presented in the figure below

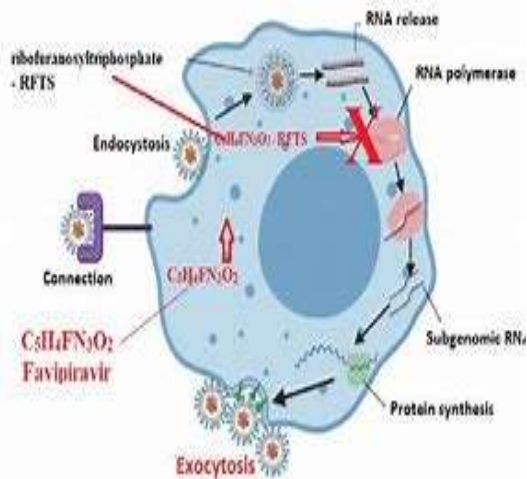


Figure No. 2

SIDE EFFECTS:

- Abdominal pain
- Vomiting
- Nausea
- Diarrhea
- Increased uric acid level in blood
- Neutrophils
- Increased liver enzymes



Figure No. 3



Figure No. 4

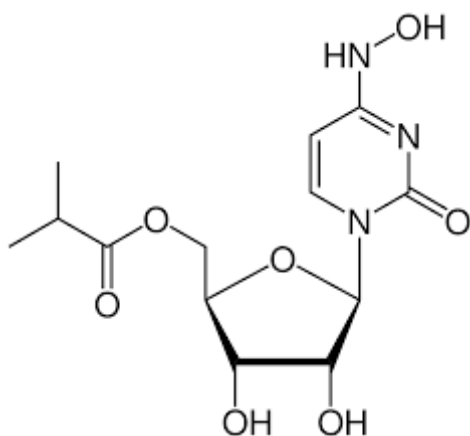
3. MOLNUPIRAVIR:

Molnupiravir is a orally administered isopropylestercytidine analog used to treat COVID-19.

- GENERIC NAME- Molnupiravir
- BRAND NAME- Lagevrio
- IUPAC NAME- N-Hydroxy-5'-O-isobutyryl-3,4-dihydrocytidine

[(2R,3S,4R,5R)-3,4-Dihydroxy-5-[4-(hydroxyamino)-2-oxypyrimidin-1-yl]oxolan-2-yl]methyl 2-methylpropanoate (

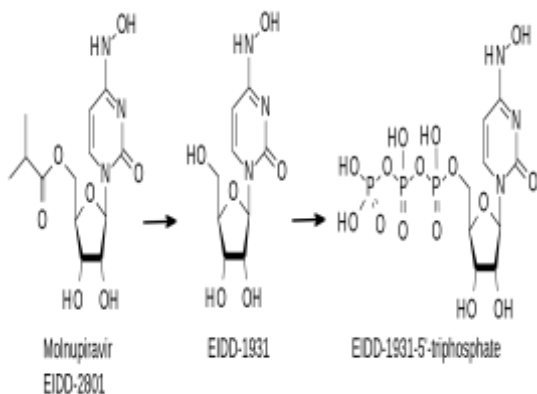
- MOLECULAR FORMULA- C₁₃H₁₉N₃O₇
- STRUCTURAL FORMULA-



Structure No. 3

- MOLECULAR WEIGHT- 329.309 g·mol⁻¹
- MECHANISM OF ACTION-

Molnupiravir inhibits viral reproduction by promoting widespread mutations in the replication of viral RNA by RNA-directed RNA polymerase. It is metabolized into a ribonucleoside analog that resembles cytidine, β-D-N4-hydroxycytidine 5'-triphosphate (also called EIDD-1931 5'-triphosphate or NHC-TP). During replication, the virus's enzyme incorporates NHC-TP into newly made RNA instead of using real cytidine. Molnupiravir is turned into NHC-TP, the active form.[9]



Structure No. 4

- ADMINISTRATION OF DRUG- Molnupiravir is taken by oral route, twice daily for 5 days.
- PHARMACOLOGY-

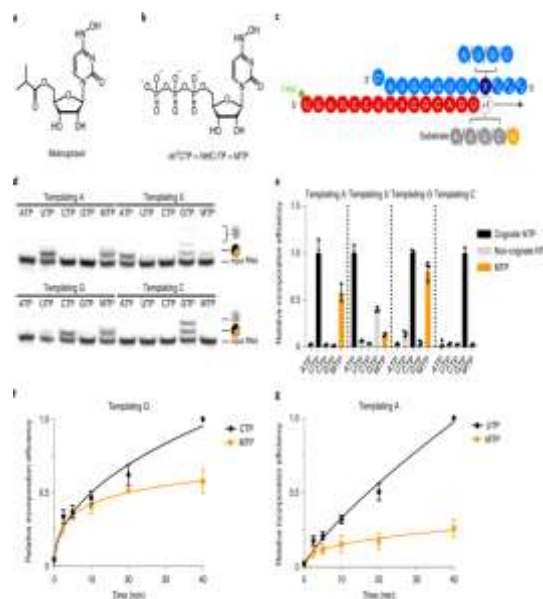


Figure No. 5

- SIDE EFFECTS:
 - Nausea
 - Diarrhea
 - Vomiting
 - Dizziness



Figure No. 6

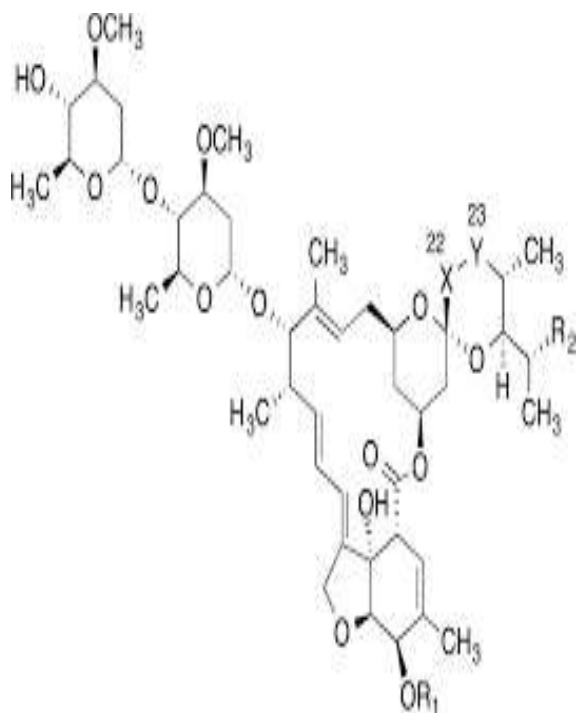


Figure No. 7

4. IVERMECTIN :

It belongs from the drug class known as anthelmintics. Basically, it kills parasites by paralyzing them.

- GENERIC NAME- Ivermectin
- BRAND NAME- Sklice, Soolantra, Stromectol
- IUPAC NAME- 22,23-dihydroavermectin B1a + 22,23-dihydroavermectin B1b
- MOLECULAR FORMULA- C₄₈H₇₄O₁₄
- STRUCTURAL FORMULA-



Structure No. 5

- MOLECULAR WEIGHT- 875.106 g·mol⁻¹
- MECHANISM OF ACTION- The safety and efficacy of ivermectin for the prevention and treatment of COVID-19 have been evaluated

in clinical trials and observational cohorts. Ivermectin inhibits replication of SARS-CoV-2 in cell cultures. It helps or tries to prevent the doubling of SARS-CoV-2 cells in the body.

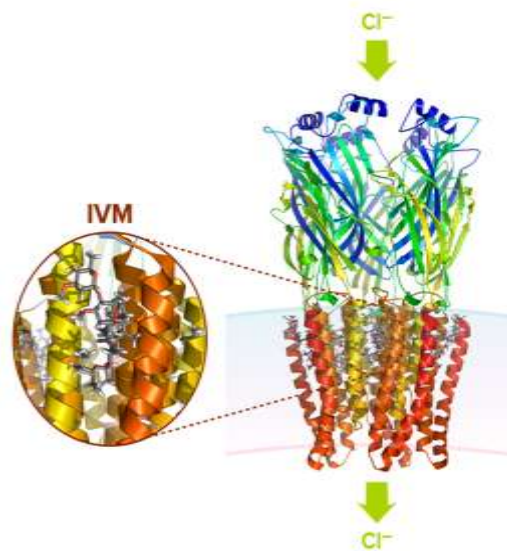


Figure No. 8

(Mechanism of action of IVM)

- TOXICITY-Ivermectin including products such as ivermectin creams and lotions causes significant toxicity. If the ivermectin products are administered in unusual or wrong quantities or significant exposure ivermectin is practiced repeatedly, patients have experienced rash, edema, headache, dizziness, asthenia, nausea, vomiting, and diarrhea.
- ADMINISTRATION OF DRUG- Ivermectin tablets are taken by oral route. It is recommended to take 1 hour before the meal or 2 hours after the meal. It should be taken with full glass of water.
- SIDE EFFECTS-
 - Blistering, peeling, or loosening of the skin.
 - burning, dry, or itching eyes.
 - change in consciousness.
 - confusion about identity, place, and time.
 - dark urine.
 - diarrhea.
 - discharge, excessive tearing.
 - light-colored stools.[10]

5. PHARMACOLOGY:

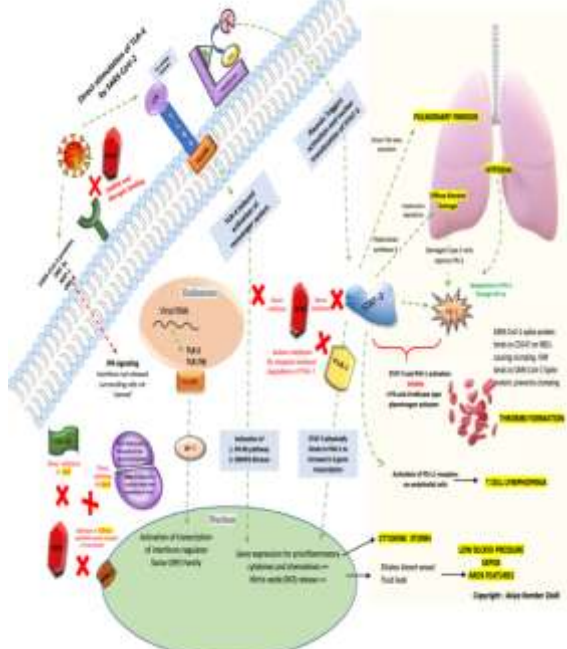


Figure No. 9

IVERMECTIN TABLETS AND DROPS:



Figure No. 10



Figure No. 11

HOME REMEDIES FOR COVID-19

1. GINGER:

Ginger has anti-inflammatory and antibacterial properties. Due to these properties, ginger is used in Ayurveda from a long time as a home remedy ingredient to treat cough. Ginger also has a number of terpene compounds such as β -bisabolene, α -curcumene, zingiberene, α -farnesene, and β -sesquiphellandrene etc. which make it a strong antioxidant. It also gives it a strong aroma.

It can be boiled in water and consumed twice daily. It creates heat in the body and kills cough-causing bacteria. Ginger can be used to treat COVID-19 because cough is one of the most common symptoms of it.

An experiment stated that ginger comprises phytochemicals that help in prevention of Covid-19 transmission and its Ayurvedic formulation helped reduce SARS-CoV-2 transmission. It also moderated COVID-19 symptoms.

GRAPHICAL REPRESENTATION:

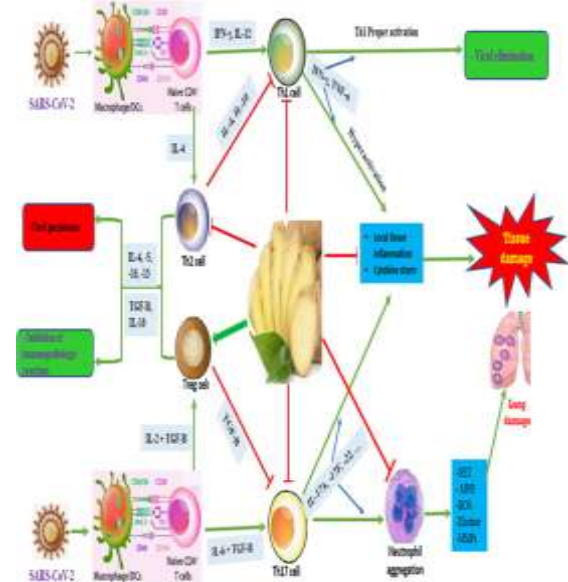


Figure No. 12

2. TURMERIC:

Turmeric is the most common used ingredient in Indian kitchens from so long due to its anti-inflammatory properties. Turmeric has a special address in Ayurveda. One-time dose of 1000 mg of turmeric is effective for patients with anosmia following COVID-19 infection.

Curcumin has been shown to bind and block the active site of Mpro, the main protease

utilized by COVID-19 to produce proteins required for viral replication from viral genomic RNA [11] Turmeric helps to reduce inflammation in the body thus helping to increase immunity. Turmeric includes natural killer cells and dendritic cells which enhances the overall body's antibody response, which in turn helps in treating COVID-19.

Turmeric powder can be boiled in water and consumed twice or thrice a day. Turmeric root tea is also a great option for sore throat or runny nose which common symptoms of COVID-19.

How to make TURMERIC ROOT TEA:

Ingredients-

- 2 cups water
- 1-inch fresh turmeric root
- ½ tsp pepper powder
- Raw honey

Method-

Add a small piece of fresh turmeric root and ½ tsp pepper powder to two cups of boiling water. Boil it until it reduces to half and turn off the heat. Add raw honey if required, and consume hot. This tea can be consumed twice or as per the severity of symptoms. But its intake should be in control as it can cause severe inflammation if consumed in excess quantity.

GRAPHICAL REPRESENTATION

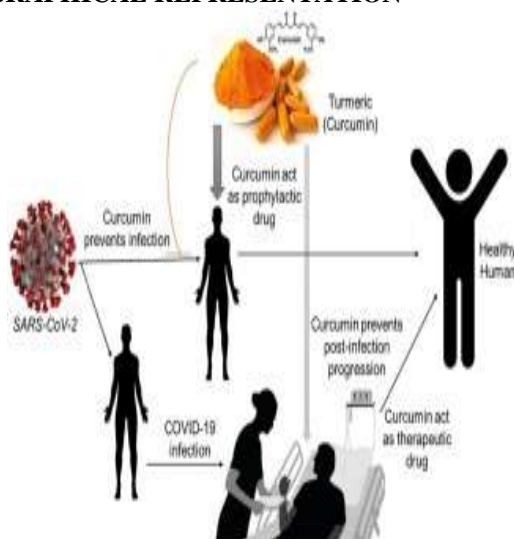


Figure No. 13

3. CINNAMON:

As per some scientific statements, cinnamon can be effective for treating coronavirus due to its anti-obstructive properties/effect. It is

also effective in lung obstruction. It is also useful in chills and fevers. Cinnamon has high penetration in the chest, due to which it cleans all the mucus and other material stuck in it. In this way it clears the chest and helps to get relief from chest and lung related diseases.

It prevents pathogens entry into the human body organs by its astringent effect and enhances organs' properties, making them less prone to damage.

A molecular docking analysis on key protein targets of SARS-CoV-2 predicts interaction of *C. zeylanicum* essential oil components (eugenol, linalool, (E)-cinnamaldehyde, (E)-cinnamyl acetate, β-caryophyllene) with the virus targets in the body.[12]

HOW TO MAKE CINNAMON (effective for COVID-19)

Ingredients:

- Cinnamon bark
- Water
- Honey
- lemon

Method-

Boil the water. Add 1 bark of cinnamon to it. Strain it. Drizzle half spoon of honey into it. Squeeze 4-5 drops of lemon onto it. Mix well. Sip hot.

This drink can be consumed empty stomach in the morning or after the meals.

GRAPHICAL REPRESENTATION-

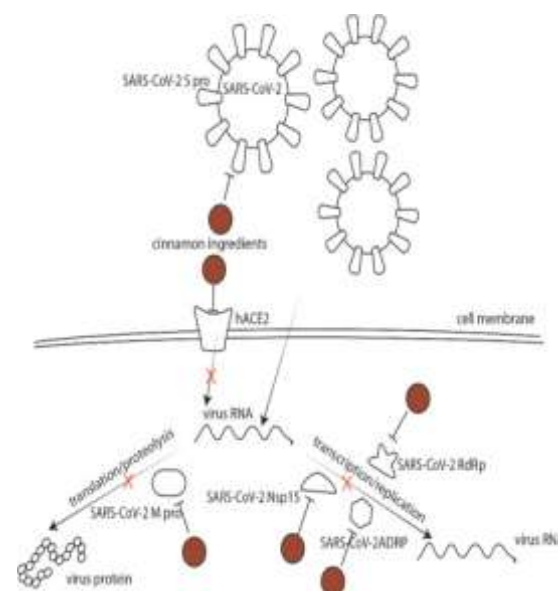


Figure No. 14

4. TULSI:

Tulsi is the most ancient indian herb used for boosting immunity. Tulsi has antioxidant properties. It helps to combat free radicals. Tulsi also contains antifungal and antimicrobial properties which has the potential to cure various infective diseases.

Tulsi leaves are enriched with vitamins A, C and K and minerals like calcium, magnesium, phosphorus, iron and potassium etc. It also has high amount of protein and fibre in it.

Tulsi is also known as queen of herbs and worshipped from ancient times in indian homes. Nanoparticles in tulsi can help in boosting immune system, as improving immune system is the most important part in treating COVID-19.

One can chew raw tulsi leaves empty stomach in the morning, which works wonders in keeping immune system healthy.

TULSI KADHA:

Ingredients-

- Fresh tulsi leaves
- 6 cups water
- 4 tbsp jiggery or jiggery powder
- Grated ginger- half tbsp.

Method-

Wash the tulsi leaves properly. Boil 6 cups of water. Add few tulsi leaves to it. Then add 4 tbsp jiggery and boil until it changes the colour. Strain it and sip hot.

It can be taken twice a day. Don't overconsume as it can cause inflammation in the body.

GRAPHICAL REPRESENTATION:



Figure No. 15

REVIEW PAPER BENEFITS-

In this review paper all the necessary information related treatments and drugs used in COVID-19 are covered. One who will read this will get an basic idea about the quick and effective

treatments used for coronavirus disease. This review paper includes allopathic as well as ayurvedic drugs effective for COVID-19. All the basic information regarding the drugs is included in this review paper. The language in this paper is simplified because an individual without any knowledge of medicines and drugs can also easily understand it.

Detailed drug profile is also included to get clarity about the efficacy and effectiveness of the particular drug. Marketed preparations are also mentioned in the form of images to understood well.

Overall the paper summarizes the current state of the drugs used in COVID-19.

II. CONCLUSION:

COVID-19 progressively became global pandemic and has caused more than 468,308 deaths worldwide; which a huge number! This review has concluded an overview on the main medicines/drugs which have been investigated in clinical trials for the effective treatment of COVID-19.

Despite the drugs mentioned in this paper there is a need of more drugs, which have lesser side effects; to improve patient compliance. It is stated that remdesivir is the most effective drug against COVID-19 but it has immense number of side effects such as it gave birth to mucormycosis disease which is an severe eye infection.

Therefore, this paper includes some home remedies which are effective in boosting immunity; which in turn reduces the symptoms and covid causing bacteria. Also healthcare professionals should pay attention on the administration of the drugs and vaccines as per directions provided by WHO.

Overall this review article gives and basic idea about the on-going clinical trials, drugs used in the pandemic, all the directions related to the particular drug and its efficacy in treating COVID-19.

REFERENCE:

- [1]. All you need to know about Corona virus in India. UNICEF India. (n.d.). <https://www.unicef.org/india/coronavirus/covid-19>
- [2]. Professional, C. C. medical. (n.d.). Coronavirus disease (COVID-19): Symptoms, causes & prevention. Cleveland Clinic.

- <https://my.clevelandclinic.org/health/diseases/21214-coronavirus-covid-19>
- [3]. Wikimedia Foundation. (2023, December 9). Covid-19. Wikipedia. <https://en.wikipedia.org/wiki/COVID-19>
- [4]. Remdesivir. Uses, Interactions, Mechanism of Action | DrugBank Online. (n.d.). <https://go.drugbank.com/drugs/DB14761#:~:text=Remdesivir%20enters%20cells%20before%20being,TP%20or%20GS%2D443902>
- [5]. Mayo Foundation for Medical Education and Research. (2023, August 1). Remdesivir (intravenous route) side effects. Mayo Clinic. <https://www.mayoclinic.org/drugs-supplements/remdesivir-intravenous-route/side-effects/drg-20503608?p=1>
- [6]. Y.; K.-J. L. (n.d.). Developmental toxicity of remdesivir, an anti-covid-19 drug, is implicated by in vitro assays using morphogenetic embryoid bodies of mouse and human pluripotent stem cells. Birth defects research. <https://pubmed.ncbi.nlm.nih.gov/36349436/#:~:text=pluripotent%20stem%20cells-Developmental%20toxicity%20of%20remdesivir%2C%20an%20anti%2DCOVID%2D19%20drug,Birth%20Defects%20Research>
- [7]. Wikimedia Foundation. (2023a, December 3). Favipiravir. Wikipedia. <https://en.wikipedia.org/wiki/Favipiravir>
- [8]. Jin Z;SmithLK;RajwanshiVK;KimB;Deval J; (n.d.). The ambiguous base-pairing and high substrate efficiency of T-705 (Favipiravir) ribofuranosyl 5'-triphosphate towards influenza A virus polymerase. PloS one. <https://pubmed.ncbi.nlm.nih.gov/23874596/>
- [9]. Molnupiravir mutations | science | AAAS. (n.d.-a). <https://www.science.org/content/blog-post/molnupiravir-mutations>
- [10]. Ivermectin (oral route) side effects - mayo clinic. (n.d.-a). <https://www.mayoclinic.org/drugs-supplements/ivermectin-oral-route/side-effects/drg-20064397>
- [11]. Das S;SarmahS;LyndemS;Singha Roy A; (n.d.). An investigation into the identification of potential inhibitors of SARS-COV-2 main protease using molecular docking study. Journal of biomolecular structure & dynamics. <https://pubmed.ncbi.nlm.nih.gov/32362245/>
- [12]. WN; S. J. P. K. (n.d.). Essential oils as antiviral agents. potential of essential oils to treat SARS-COV-2 infection: An in-silico investigation. International journal of molecular sciences. <https://pubmed.ncbi.nlm.nih.gov/32408699/>