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DRUG TREATMENT FOR COVID-19

Enlisted Methods:- Allopathic drugs, Ayurvedic drugs, Homeopathic drugs.

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Abstract:- Coronavirus Disease 2019, also known as COVID-19, is caused by a coronavirus that causes severe acute respiratory syndrome (SARS-CoV-2). The global spread of disease caused the COVID-19 pandemic. Variable COVID-19 symptoms include fever, coughing, headaches, tiredness, breathing problems, loss of smell, and loss of taste. The purpose of this article is to review the published literature on the efficacy of these drugs against COVID-19 methods. New treatments are currently being investigated, and the results will be published to provide evidence-based guidance to prescribers and policymakers.

Keywords:- COVID19, SARS-Cov2, Immune-modulatory, Antiviral, RNA, DNA

INTRODUCTION

The disease COVID19, which has spread across the globe since December 2019, was discovered to be caused by SARS-Cov2. There aren't any particular treatments or vaccinations for COVID-19 yet. Many medications have been repurposed, including allopathic medicines like lopinavir/ritonavir, remdesivir, chloroquine, and ivermectin, as well as azithromycin, molnupiravir, and sorocomimab. Samshamani vati, Ayush-64, cinnamon, cloves, turmeric, flax seeds, and other ayurvedic medicines are among them. Arsenicum album30, camphora 1M, and brayonia alba are examples of homeopathic medications. With an emphasis on their antiviral, immune-modulatory, and/or anti-inflammatory effects, this paper covers the key pharmacological characteristics of such medications given to patients with COVID-19. Data from clinical trials involving people with COVID-19 are

published when they are available. Clinical trials in preliminary stages appear to confirm their value. These medications have distinctive safety profiles in COVID-19 patients, though. Therefore, these medications require proper clinical trials. Even Nevertheless, several clinical trials on medicines from various therapeutic groups are now in progress as we wait for effective preventive strategies, such as vaccines. Their findings will aid in determining the most effective course of treatment for COVID-19 and minimising its symptoms and effects.

ALLOPATHIC

1. Chloroquine-

Synonyms - Antimalarial , proguanil.

Classification – Antimalarial , amebicides.

Biological source - extracted the bark of the Cinchona .

Structure – Chloroquine | $C_{18}H_{26}ClN_3$

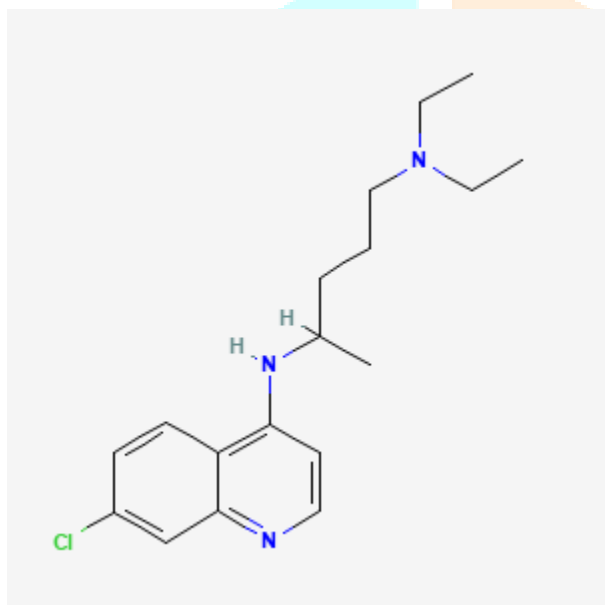


Figure No.1 Structure of Chloroquine [1]

Mechanism of action –

Viral enzymes or processes such viral DNA and RNA polymerase, viral protein, glycosylation, virus assembly, new virus particle transit, and virus release may all be inhibited as part of the mechanism. Inhibition of the ACE2 cellular receptor, acidification of the cell membrane surface that prevents virus fusion, and immunomodulation of cytokine release are additional potential mechanisms.[26]

Uses –

Chloroquine may have immuno-modulating characteristics and exhibits in-vitro efficacy against SARS-COV2.[26]

Safety concern-

Due to the possibility of a significant adverse event and drug interaction, using the drug in COVID-19 patients outside of clinical trials or in a setting other than a hospital is not advised. heart arrhythmia risk (eg : QT Prolongation) Serious arrhythmias are more likely to occur in very sick patients with comorbidities. When possible, stay away from other QT prolonging substances. damage to the retina, especially with prolonged use. Patients with G6-PD deficiencies and diabetics should exercise caution.[26]

Lopinavir / Ritonavir –

Synonyms – Ritonavir 155213-67-5

Classification – Protease inhibitor.

Structure – Lopinavir | C₃₇H₄₈N₄O₅

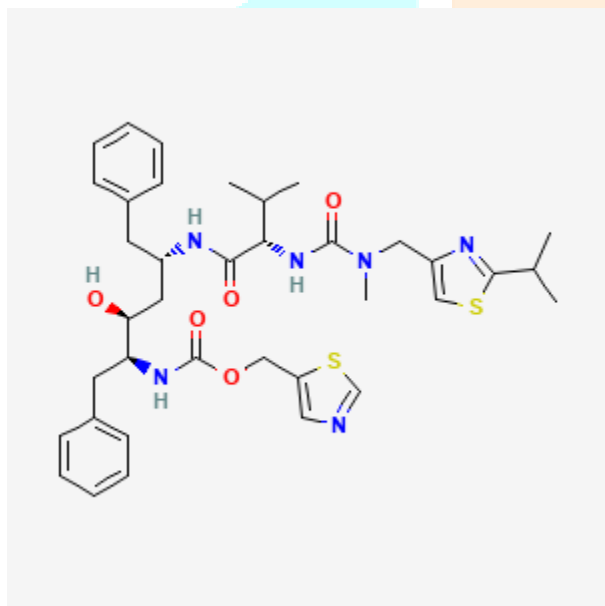


Figure no. 2 Structure of Lopinavir [2]

Mechanism of action –

Mpro, a vital enzyme for corona virus replication, is bound by lopinavir and ritonavir. This could reduce the activity of the Corona virus.[26]

Use –

Studies using in vitro and animal models suggest that more Corona viruses may be active (SARS-COV and MERS-COV).[26]

Safety concern –

heart arrhythmia risk (eg : QT Prolon gation). Serious arrhythmias are more likely to occur in very sick patients with comorbidities. When possible, stay away from other QT prolonging substances. Bradycardia, Patients with hepatic illness or hepatitis should use caution. Substantial medication interaction. [26]

Ivermectin –

Synonyms – Stromectol

Classification – anthelmintics

Structure – Ivermectin | C₄₈H₇₄O₁₄

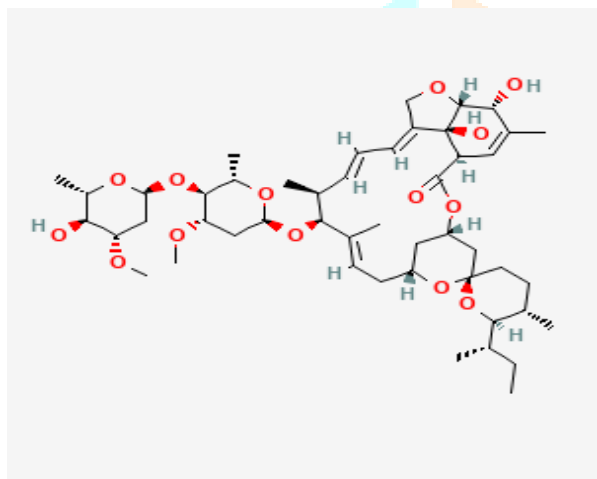


Figure no. 3 Structure of Ivermectin [3]

Mechanism of Action –

Ivermectin inhibits the host alpha/beta one nuclear transport proteins, which are a component of a crucial intracellular transport route that viruses exploited to promote infection by stifling host defence mechanisms. [26]

Use –

Inhibits SARS-COV2 replication in cell culture, but pharmacokinetic and pharmacodynamic investigations indicate that dosages up to 100 times greater than those currently permitted for use in humans would be needed to reach the plasma concentration required for the antiviral action shown in vitro. [26]

Safety concern –

Ivermectin intended for use in animals should not be used to treat COVID-19 in people, according to a caution from the FDA. Patients with asthma or hepatic problems should use caution. [26]

Azithromycin –

Synonyms – Zithromax

Classification – Macrolides antibiotics.

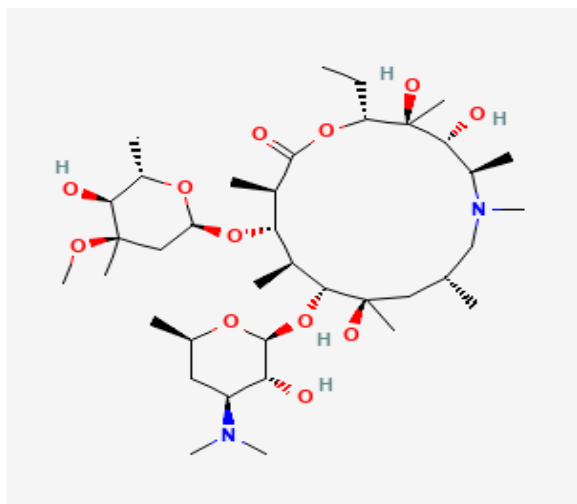


Figure no 4. Structure of Azithromycin [4]

Structure – Azithromycin | C₃₈H₇₄N₂O₁₃

Mechanism of Action –

When it comes to pulmonary inflammatory diseases, macrolides may have immunomodulatory characteristics. Although their direct effects on viral clearance are unclear, they may downregulate inflammatory responses and lessen the excessive cytokine production linked to respiratory viral infections. Immunomodulatory techniques could limit cytokines like IL-8, mucus hypersecretion, produce less reactive oxygen species, hasten neutrophil apoptosis, and prevent the activation of nuclear transcription factors in order to diminish the chemotaxis of neutrophils (PMNs) to the lungs.[26]

Use –

As an additional therapy, macrolides may have immunomodulatory effects similar to how azithromycin prevents bacterial superinfection.[26]

Safety Concerns –

Cardiac arrhythmia risk is 0 (e.g., QT prolongation) Serious arrhythmias are more likely to occur in severely unwell patients with concomitant conditions. When possible, stay away from additional QT prolonging medications. No notable medication interactions.[26]

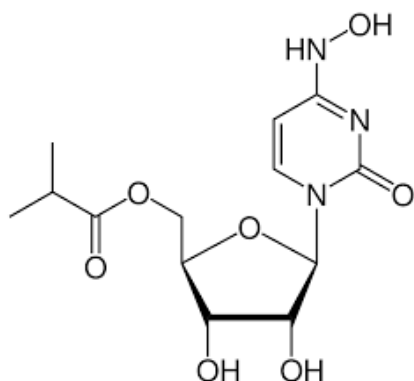
Molnupiravir –**Classification** – Antiviral**Structure** – Molnupiravir |C₁₃H₁₉N₃O₇

Figure no 5. Structure of Molnupiravir [5]

Mechanism of Action –

A process known as viral error catastrophe occurs when molnupiravir is hydrolyzed in vivo to N4-hydroxycytidine, which is then phosphorylated in tissue to the active 5-triphosphate form and integrated into the genome of new virions. It has also been demonstrated that a mutant mouse hepatitis virus that is resistant to remdesivir is more sensitive to N4-hydroxycytidine.[26]

Use –

The FDA has approved the drug molnupiravir for administration in cases of COVID-19. Adults who are at least 18 years old, have recently tested positive for the coronavirus, have mild to moderate symptoms lasting no longer than five days, and are not in the hospital should use it. You must also be at a high risk for COVID-19 problems due to advanced age, obesity, or persistent medical disorders in order to get this medicine (such as lung or heart disease or diabetes, among others). Discuss the risks and advantages of molnupiravir therapy with your doctor. The way that molnupiravir works is by stopping the COVID-19 virus' development. The FDA Fact Sheet for Patients, Parents, and Caregivers for Emergency Use contains more details about molnupiravir.[26]

Safety Concerns –

The safety of a medicine that causes mutations has been questioned by some specialists. There are worries that asmolnupiravir causes viral RNA to change, it might also alter host cells. In one investigation using animal cell cultures, cells treated with molnupiravir exhibited mutations. Worries that the medicine can cause cancer or birth defects have arisen as a result of this. The authors of the study on animal cells advise evaluating this mutagenesis potential in vivo with an emphasis on quickly dividing cells.[26]

Sotrovimab –

Classification – Monoclonal antibody .

Mechanism of Action –

A recombinant human IgG1 monoclonal antibody called sotrovimab works by attaching to a conserved epitope on the spike protein receptor-binding domain of COVID-19 virus SARS-CoV-2. Since the epitope is so conserved, viral resistance to the antibody is less likely to arise.[26]

Use –

The FDA and Health Canada have approved the use of sotrovimab as an emergency/provisional treatment for COVID-19. It is prescribed to patients 12 years of age and older who have recently tested positive for the coronavirus, who have mild to moderate symptoms that have lasted no more than 10 days, and who have not been admitted to the hospital. You must also be at high risk for COVID-19 problems due to advanced age, obesity, or persistent medical disorders in order to receive sotrovimab (such as lung, kidney, or heart disease, diabetes).[26]

Safety Concerns –

The adverse events, significant adverse events, and adverse events of particular concern, which were characterised as infusion-related reactions, were included in the safety results (including hypersensitivity reactions). Antidrug antibody immunogenicity testing was carried out, and antibody-dependent enhancement was assessed. Serious adverse effects were defined as any hospitalizations, including those brought on by Covid-19.[26]

Remdesivir

Classification – Antiviral Nucleoside Analogue

Structure – Remdesivir | C₂₇H₃₅N₆O₈P

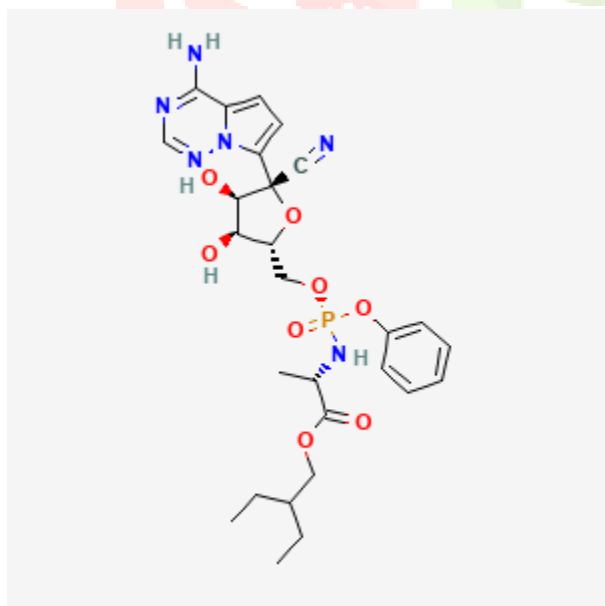


Figure no 6. Structure of Remdesivir [6]

Mechanism of Action –

Remdesivir is a monophosphoramidate prodrug of the adenosine analogue remdesivirtriphosphate (RDV-TP), which inhibits RNA-dependent RNA polymerases (RdRps). Adenosine triphosphate and remdesivir-TP fight for inclusion into developing viral RNA chains. RDV-TP stops RNA synthesis at position i+3 after incorporating into the viral RNA at site i. RDV-TP does not result in immediate chain termination, hence it seems to bypass viral exoribonuclease's editing process (an enzyme thought to excise nucleotide analogue inhibitors).[26]

Use –

Remdesivir is used to treat COVID-19, commonly known as coronavirus disease, in some hospital patients. An antiviral medication is remdesivir. Remdesivir may also be used to treat COVID-19 patients in the United States who are not hospitalised but are at a high risk for COVID-19 problems because of advanced age, obesity, or preexisting medical disorders (such as lung, kidney, or heart disease, diabetes).[26]

Safety Concerns –

Betacyclodextrin sodium with sulfobutyl ether formulation should be used with caution in people with renal impairment (SBECD) responses associated to infusions and hypersensitivity. Risk of having increased hepatic enzymes.[26]

Ayurvedic drugs –

Samashani vati –

Synonyms - Guduchi ghana vati

Classification – Antioxidants, Antidiabetic

Chemical components –

Protein and micronutrients including calcium, phosphorus, iron, zinc, and manganese are all rich in guduchi. Terpenes, alkaloids, flavonoids, steroids, and glycosides are just a few of the many secondary plant metabolites that are also present.

Image –



Figure no 7. Samshani Vati [7]

Information-

For all types of fevers, ayurvedic medicine known as Samshamani vati (Guduchi ghana vati) is used. It is also used as an antipyretic and anti-inflammatory medication. Samshamani vati, an aqueous extract of *Tinospora cordifolia* (Willd.) Miers (family Menispermaceae), is thought to have immunomodulatory qualities as a result of the synergistic effects of the various compounds contained. It also helps with a lot of viral diseases.[17-18]

Ayush 64 –

Chemical constituents- Jwarahara (useful in fevers), Shwasa-Kaasaghna (useful in asthma, cough), Shothahara (relieves inflammation).

Image –

Figure no 8. Ayush 64

Information-

Alstonia scholaris (L.) R. Br. bark, *Picrorhiza kurroa* Royle ex Benth. rhizomes, *Swertia chirayita* (Roxb.) H. Karst. whole plant, and *Caesalpinia crista* L. seed pulp make up the ingredients of the AYUSH-64 pill. AYUSH-64 is thought to be beneficial among the high-risk coronavirus group due to its antimalarial activity. Each of its components is efficiently antiviral, anti-asthmatic, and immune-stimulating, according to research.

Garlic –

Synonyms – *Allium Sativum*

Family - Amaryllidaceae

Classification – Antipyretic

Biological source – Garlic is the ripe bulb of *Allium sativum* Linn., belonging to family Liliaceae.

Chemical constituents –

The drug's active ingredient is a yellow liquid called allicin, which gives garlic its distinctive odour. It is miscible with benzene, ether, and alcohol and breaks down during distillation. Allicin, diallyl disulphide, and allyl propyl disulphide are all present in essential oil (0.06-0.1 percent). Garlic is used to isolate glutamyl peptides. Leucine, methionine, S-propyl-L-cysteine, S-propenyl-L-cysteine, S-methyl cysteine, S-allyl cysteine

sulphoxide (alliin), S-ethyl cysteine sulphoxide, and S-butyl-cysteine sulphoxide are among the amino acids found in the bulb.

Image –



Figure no 9. Garlic [8]

Information-

Several in vivo studies have been carried out to demonstrate the role of A. sativum in immunomodulation employing garlic oil extract. The reduction in serum levels of TNF-, ICAM-1, and immunoglobulin (G and M) supported the improvement in immune system function. When embryonated chicken eggs were pre-treated with aqueous garlic extract, the velogenic strain of Newcastle disease virus was less infectious and had a lower viral titer. On Vero cells, A. sativum demonstrated antiviral activity against the H9N2 strain of the avian influenza virus. In a rodent model of allergic airway inflammation, it had a protective effect that resulted in a significant decrease in the number of inflammatory cells, eosinophil infiltration, and serum IgE-modified Th1, Th2, and Th3 cytokines, as well as an upregulation of Th-1 and Th-3 and a concurrent downregulation of Th-2 expression. Old A. sativum extract demonstrated control of airway inflammation generated in BALB/c mice by reduction in lavage and serum IgG1 levels, perivascular inflammation, and eosinophil percentage.

Cinnamon –

Synonyms – Cassia

Family - Laurels

Classification – dietary supplement.

Biological source –

Cinnamon is made of dried bark that has been stripped of its outer cork and underlying parenchyma from Cinnamomum zeylanicum Nees shoots that are growing on their cut stumps.

Chemical constituents –

Cinnamon has a 10% volatile oil content, along with sugar, tannin, mucilage, and calcium oxalate. Cinnamic aldehyde makes up 50–65 percent of volatile oil, along with eugenol, which is 5–10 percent, terpene hydrocarbons, and trace amounts of alcohols and ketones.

Image –



Figure no 10. Cinnamon [9]

Information-

By altering total protein, globulin, total antioxidant capacity, and lysozyme activity, as well as noticeably increasing phagocytic activity, *C. verum* essential oil and powder displayed anti-oxidant, immunostimulant, and antiviral action in Newcastle disease virus in chickens. According to another study, *C. zeylanicum* essential oil has significant antiviral properties against the H1N1 and HSV1 viruses when combined with other essential oils. For both H1N1 and HSV1 viruses, a reduction in virus infectivity has been noted, with 99 percent at 60-min contact time and more than 99.99 percent after 60 min. The immunomodulatory action of its bark extract led to a substantial rise in serum immunoglobulins, phagocytic index, neutrophil adhesion, and antibody titer.

Turmeric –

Synonym - *Curcuma aromatica*

Family - Zingiberaceae

Classification – rheumatoid arthritis

Biological source –

The herbaceous perennial plant *Curcuma longa*, a member of the ginger family Zingiberaceae, and a native of tropical South Asia, produces turmeric.

Chemical constituents –

Curcuminoids, a group of curcumin, demethoxycurcumin, and bisdemethoxycurcumin, make up 3–6% of the polyphenolic chemicals in turmeric.

Image –



Figure no 11. Turmeric [10]

Information-

In an in vivo immunosuppressed by cyclophosphamide model, *C. longa* aqueous extract reduced relative spleen weight and modulated haematological alterations, suggesting its potential as an immunomodulator. When spleen cells from young mice were used as a model for turmeric's immunomodulatory properties, the study found some encouraging results. In both in vitro and in vivo tests using Huh7it-1 cells, *C. longa* extract shown antiviral efficacy against dengue virus, and an in vivo model showed a notable reduction in viral load. H5N1 additionally demonstrated increased TNF- as well as IFN- mRNA expression, underlining its promising involvement in the prevention of viral replication. Water and ethanolic crude extracts have been proven to be antiviral. Mice inoculated with ovalbumin and alum showed signs of anti-allergic responses to turmeric extract. It has been observed that preserving the balance of Th1/Th2 can lessen food allergy.

Flax Seeds –

Synonym – Linseeds.

Family - Linaceae

Classification - dietary supplement

Biological Source - Linseed is the dried, ripe seed of *Linum usitatissimum*

Chemical constituents –

A neutral arabinoxylan (75%) and an acidic rhamnogalacturonan (25%).

Image –



Figure no 12. Flax Seeds [12]

Information –

Heteropolysaccharide from the flax seed hull had the potential to be anti-hepatitis B virus and immunomodulatory. It greatly increased the mRNA expression of TNF-, NO, and IL in murine macrophages that exhibit immunological responses. There have been reports of antiviral activity that interfered with DNA replication and inhibited the production of both surface and envelop antigens. Its promising potential as an adjuvant and immunostimulant was suggested by the study. It demonstrated anti-inflammatory and immunomodulatory potential in insulin resistance linked to obesity. 3T3-L1 adipocytes and their oil were co-cultured in RAW 264.

Tulsi –

Synonym - Sacred basil, Holy basil.

Family - Mints

Classification - antimicrobial

Biological Source -

Tulsi consists of fresh and dried leaves of *Ocimum sanctum* Linn., belonging to family Labiatae.

Chemical constituents –

70% eugenol, carvacrol (3%), and eugenol-methyl-ether (20%).

Image –



Figure no 13.Tulsi [12]

Information -

Ocimum sanctum hydro-alcoholic extract prevented viral intracellular replication. Additionally, it prevents H9N2 viruses from interfering with certain virus-cell interactions. At an IC₅₀ value of 73.3 g/ml, the immunomodulatory capacity of alcoholic leaf extracts reduced hepatic parasite and skewed the humoral response toward Th1 type. *O. sanctum* significantly reduces OVA-induced lung inflammation by inhibiting the activities of leukotriene-C4-synthase, leukotriene-A4-hydrolase, and cyclooxygenase-2 in cultured HL-60 cells.

Amla –

Synonym – Emblica, Indian goose berry

Family - Phyllanthaceae

Classification – anti-diabetic

Biological Source –

This consists of dried, as well as fresh fruits of the plant *Emblica officinalis* Gaerth (*Phyllanthus emblica* Linn.

Chemical constituents –

gallic acid 1.32%, tannin, sugar 36.10%; gum 13.75%; albumin 13.08%; crude cellulose 17.08%; mineral matter 4.12%; and moisture 3.83%.

Image –



Figure no 14.Amla [13]

Information –

Amla has been shown to dramatically lessen the immunosuppressive effect that chromium has on lymphocyte proliferation, which has restored the production of IL-2 and INF. Splenocyte proliferation has been observed to be increased by emblica phenolics. Amla ethanolic extract significantly decreased pro-inflammatory cytokine levels while increasing anti-inflammatory cytokine levels. One isolated substance from *P. emblica*, 1, 2, 4, 6-tetra-O-galloyl-d-glucose, demonstrated antiviral activity against HSV through HSV-1 inactivation, which prevents early infection by inhibiting intracellular growth and HSV-1 E and L gene expression along with DNA replication.

Ginger –

Synonym – Emblica, Indian goose berry

Family - Zingiberaceae

Classification – anti-diabetic

Biological Source –

This is made up of both the fresh and dried fruits of the *Emblica officinalis* Gaerth *Phyllanthus emblica* Linn plant.

Chemical constituents –

There include 1.32 % gallic acid, 36.10 % sugar, 13.75 % gum, 13.08 % albumin, 17.08 % crude cellulose, 4.12 % mineral matter, and 3.83 % moisture.

Image –



Figure no 15.Ginger

Information -

In human respiratory tract cell lines (HEp-2 and A549), fresh ginger aqueous extract exhibited antiviral activity against human respiratory syncytial virus and reduced the plaque numbers in a dose-dependent manner.

Additionally, it promoted IFN- production, which helps the body fight viral infection. Additionally, it demonstrated dose-dependent antiviral activity against the H9N2 strain of the avian influenza virus in Vero cells. Oral administration of Soft gel capsules containing *Z. officinale* in combination demonstrated immunomodulatory and anti-inflammatory effects similar to those exercised by positive controls, and gene expression results indicated generally the same transcriptional remodelling.

Homeopathic drugs –

Arsenicum album 30

Synonym - Arsenigen Saure.

Classification - anti-neoplastics.

Biological source –

High-temperature baking is used to separate arsenic from iron (as in arsenopyrite), cobalt, or nickel.[19]

Chemical constituents –

It is a trace element, arsenic. Seafood, chicken, grains (particularly rice), bread, cereals, mushrooms, and dairy products are among the foods that include it. Arsenic can be found in some medications.[20]

Structure – Arsenic trioxide | As_2O_3



Figure no 16. Structure of Arsenicum album 30 [14]

Information –

a white blood cell cancer (leukemia). Acute promyelocytic leukaemia is a special type of white blood cell cancer that can only be treated with an arsenic compound that is available only by prescription (arsenic trioxide, Trisenox). Arsenic is being considered for a variety of additional uses, but there isn't enough trustworthy data to say whether or not it would be beneficial.[20]

Camphora 1M

Synonym - camphor.

Classification - anti-flatulent

Biological source -

Some medications and incense include camphor, a terpenoid ketone classified as an isoprenoid molecule. It is a naturally occurring substance obtained from the camphor laurel tree, an evergreen (*Cinnamomum camphor*).[21]

Chemical constituents -

Between 0.05 and 0.5 percent of camphor can be found in rosemary leaves (*Rosmarinus officinalis*), while 5 percent can be found in camphorweed (*Hetero*). In Asia, camphor basil is a major source of camphor (the parent of African blue basil).[21]

Structure -

Camphor | $C_{10}H_{16}O$

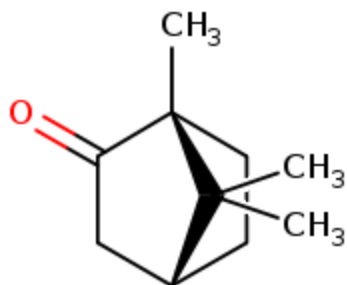


Figure no 17.Camphor 1M [15]

Information -

The bark and wood of the camphor tree were once used to distil camphor. Today, turpentine oil is mostly used to produce camphor. Vicks VapoRub is one product that uses it. Camphor is applied topically to the skin to ease discomfort and stop itching.[22]

Bryonia alba

Synonym - false mandrake, English mandrake

Classification – emetic

Biological source –

A robust herbaceous perennial vine that resembles kudzu in look and growth pattern is called *Bryonia alba*. Foliage. Each spring, vines develop from a huge, fleshy root resembling a parsnip. They grow quickly, sometimes reaching heights of 30 feet (9.1 metres) in a single season.[23]

Chemical constituents –

In addition to the alkaloid bryonicine flavonoids saponarin, vitexin, isovitexin, 5, 7, 4'-trihydroxy flavone 8-C-glucopyranoside, lutanarin, and isoorientin found in *bryonia*, it also includes glycosides. triterpenoids, cucurbitacin L, 23, 24-dihydrocucurbitacin B, 22-deoxocucurbitosides A and B, and 22-deoxocucurbitacin D.[25]

Structure –

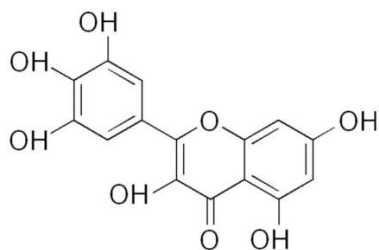
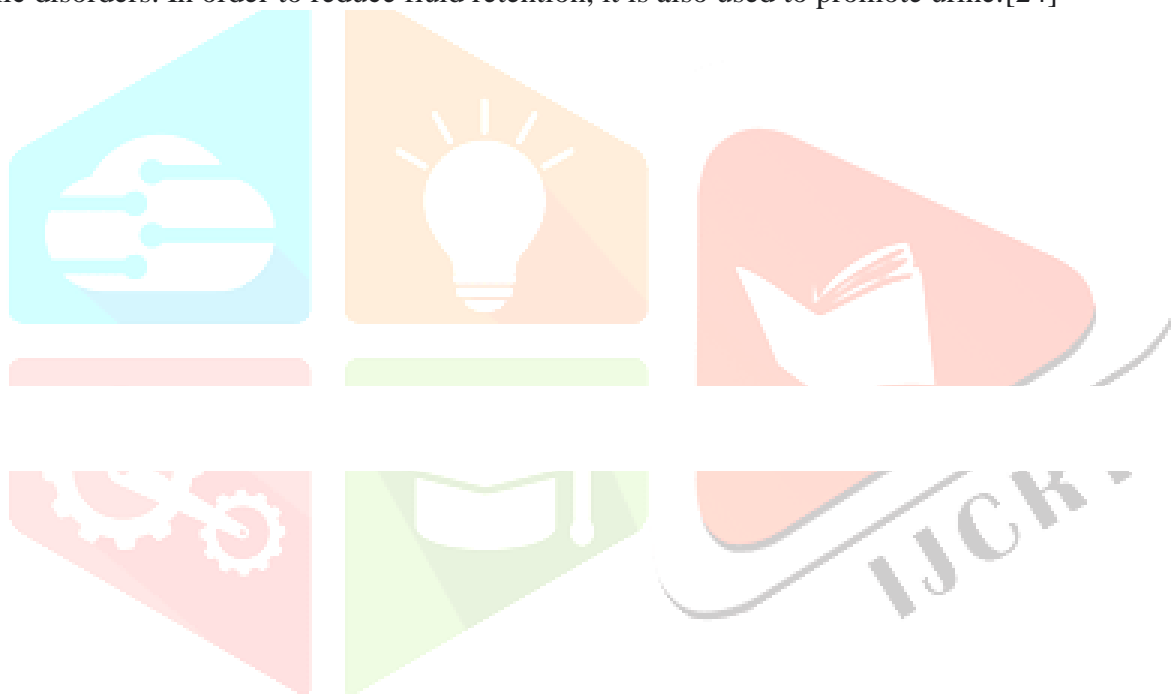


Figure no 18. Bryonia alba [16]

Information –

The bryonia plant. The root is used by people as medication. Bryonia is used as an emetic and a laxative to treat constipation despite major safety concerns. Emetics are medications that make you vomit. In addition to treating infections, bryonia is used to treat illnesses of the stomach and intestines, the lungs, arthritis, the liver, and metabolic disorders. In order to reduce fluid retention, it is also used to promote urine.[24]



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