

## A Review Article on Phytochemicals New Line of Treatment of Sars Covid-19

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**Abstract:** Coronaviruses are found in avian and mammalian species. They resemble each other in morphology and chemical structure: for example, the coronaviruses of humans and cattle are antigenically related. Coronavirus virions are spherical to pleomorphic enveloped particles. The envelope is studded with projecting glycoproteins, and surrounds a core consisting of matrix protein enclosed within which is a single strand of positive-sense RNA ( $M_r 6 \times 10^6$ ) associated with nucleoprotein. The envelope glycoproteins are responsible for attachment to the host cell and also carry the main antigenic epitopes, particularly the epitopes recognized by neutralizing antibodies. OC43 also possesses a haemagglutinin.

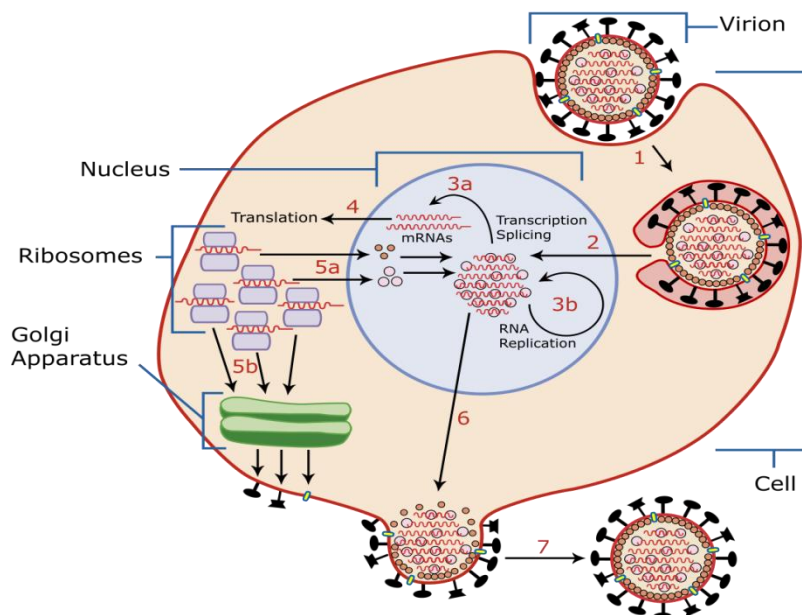
Common medications used against viral infections are often inadequate and show a variety of side effects. In the last few years, natural remedies gain more and more popularity in the field of medical science. The idea of herbal drugs is popular because of easy access, cost effectiveness, less side effects and good tolerability. Viruses are obligate intracellular parasites with a viral genome (DNA or RNA) and protein envelope (capsid). Viruses do not have an own metabolism and are not able to replicate by owner to perform bio-syntheses.

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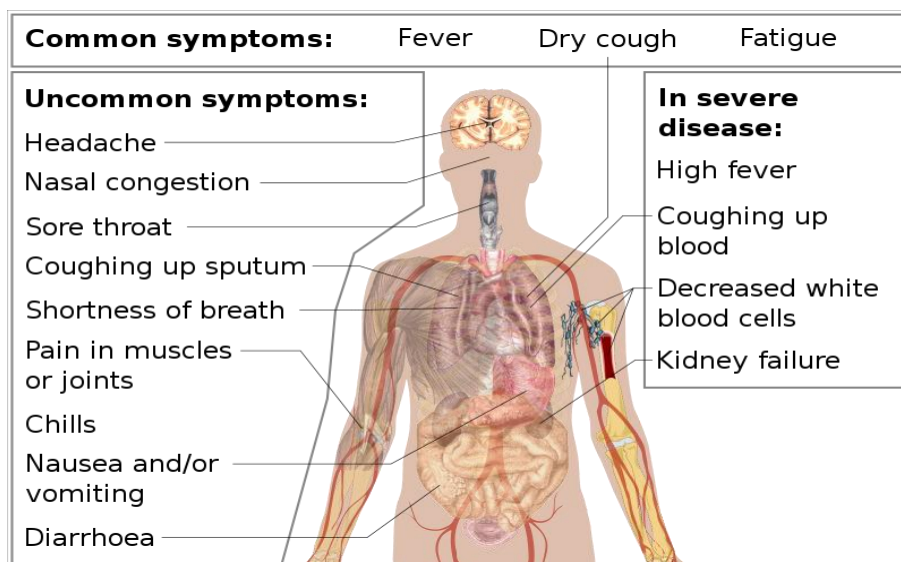
### I. Introduction

Coronaviruses are found in avian and mammalian species. They resemble each other in morphology and chemical structure: for example, the coronaviruses of humans and cattle are antigenically related. There is no evidence, however, that human coronaviruses can be transmitted by animals. In animals, various coronaviruses invade many different tissues and cause a variety of diseases, but in humans they are only proved to cause mild upper respiratory infections, i.e. common colds. On rare occasions, gastrointestinal coronavirus infection has been associated with outbreaks of diarrhoea in children.

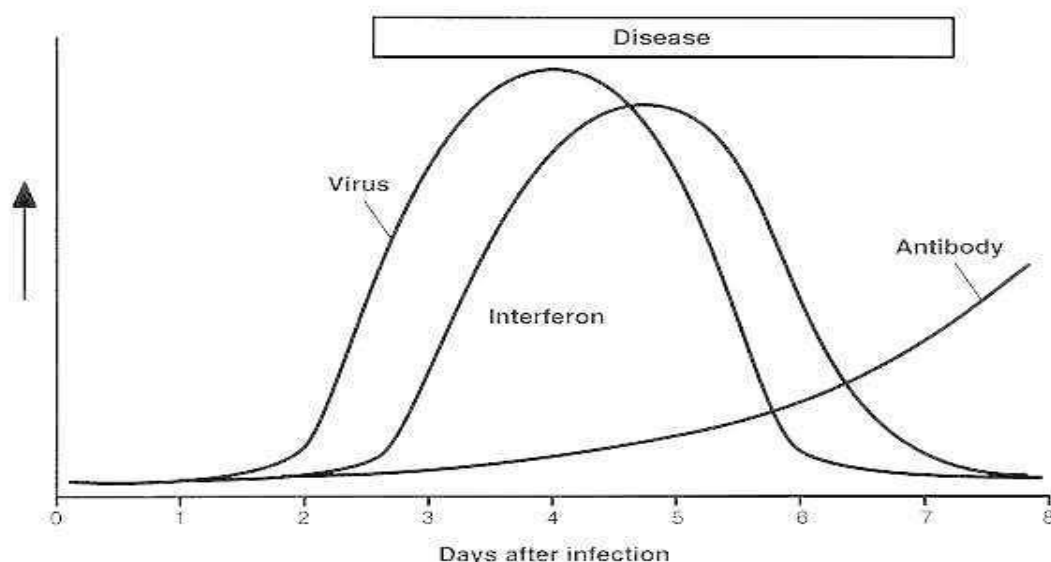


### Clinical Manifestations

• Coronaviruses invade the respiratory tract via the nose. After an incubation period of about 3 days, they cause the symptoms of a common cold, including nasal obstruction, sneezing, runny nose, and occasionally cough. The disease resolves in a few days, during which virus is shed in nasal secretions. There is some evidence that the respiratory coronaviruses can cause disease of the lower airways but it is unlikely that this is due to direct invasion. Other manifestations of disease such as multiple sclerosis have been attributed to these viruses but the evidence is not clear-cut.

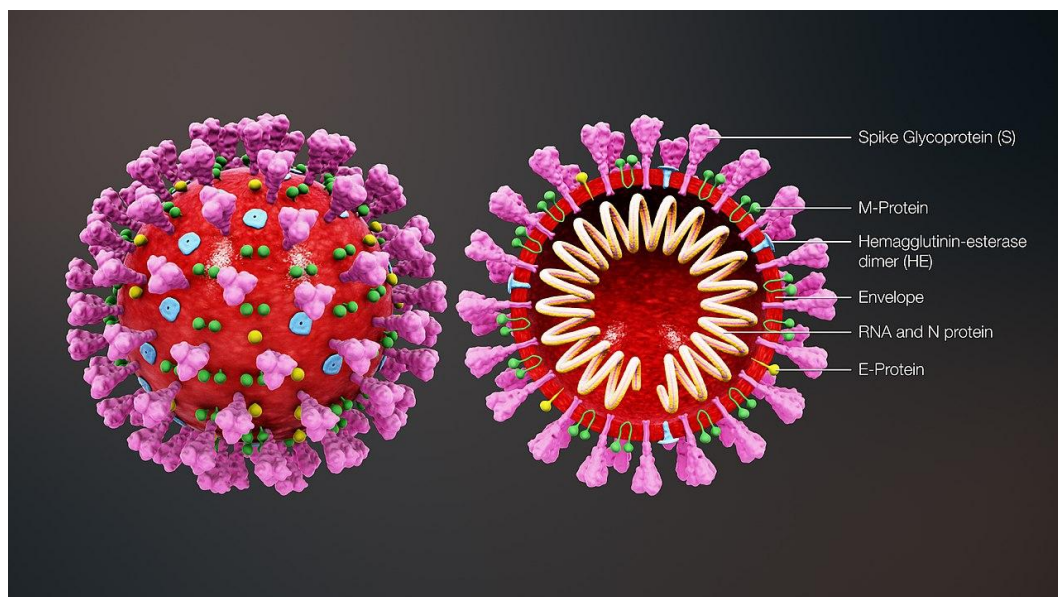


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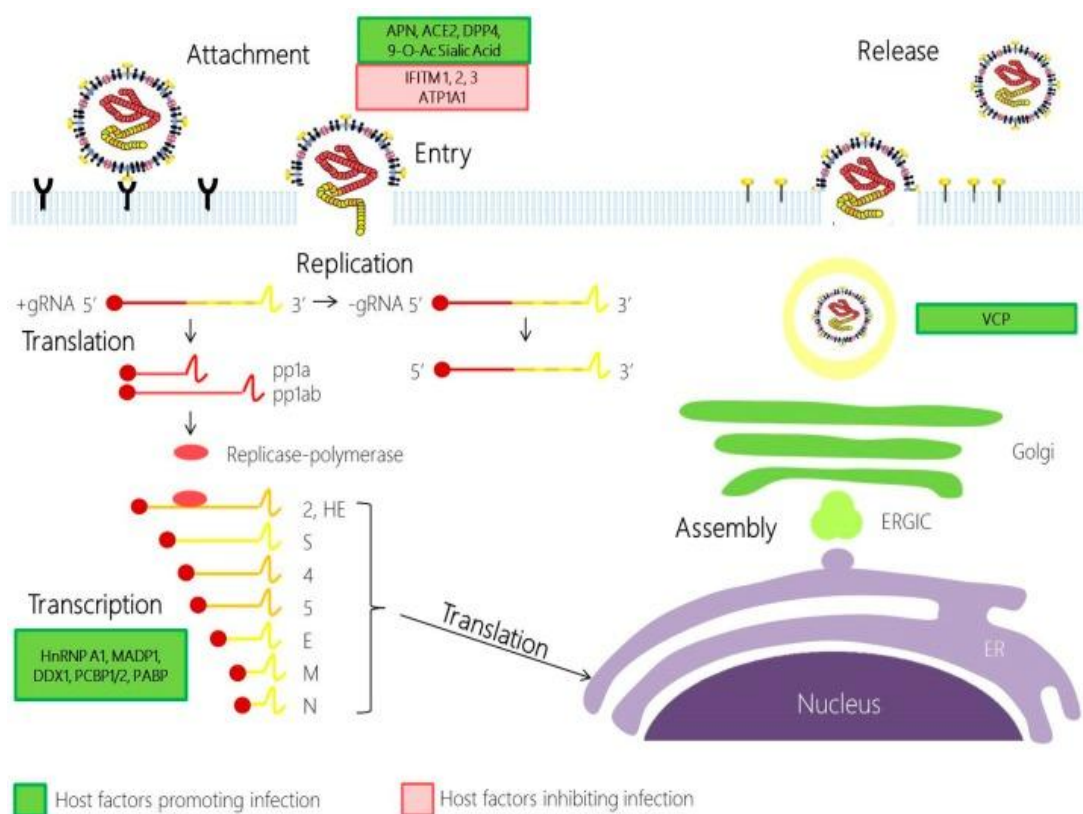
### STRUCTURE

• Coronavirus virions are spherical to pleomorphic enveloped particles. The envelope is studded with projecting glycoproteins, and surrounds a core consisting of matrix protein enclosed within which is a single strand of positive-sense RNA ( $Mr\ 6 \times 10^6$ ) associated with nucleoprotein. The envelope glycoproteins are responsible for attachment to the host cell and also carry the main antigenic epitopes, particularly the epitopes recognized by neutralizing antibodies. OC43 also possesses a haemagglutinin.



### CLASSIFICATION AND ANTIGENIC TYPES

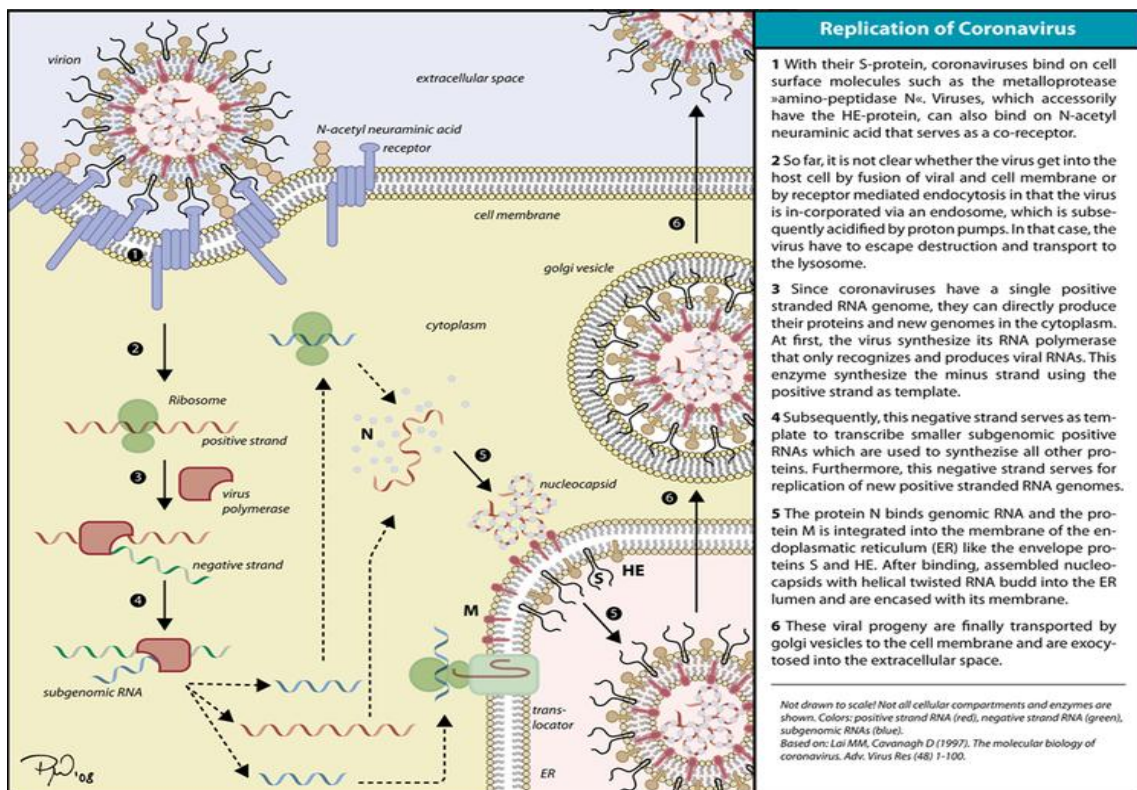
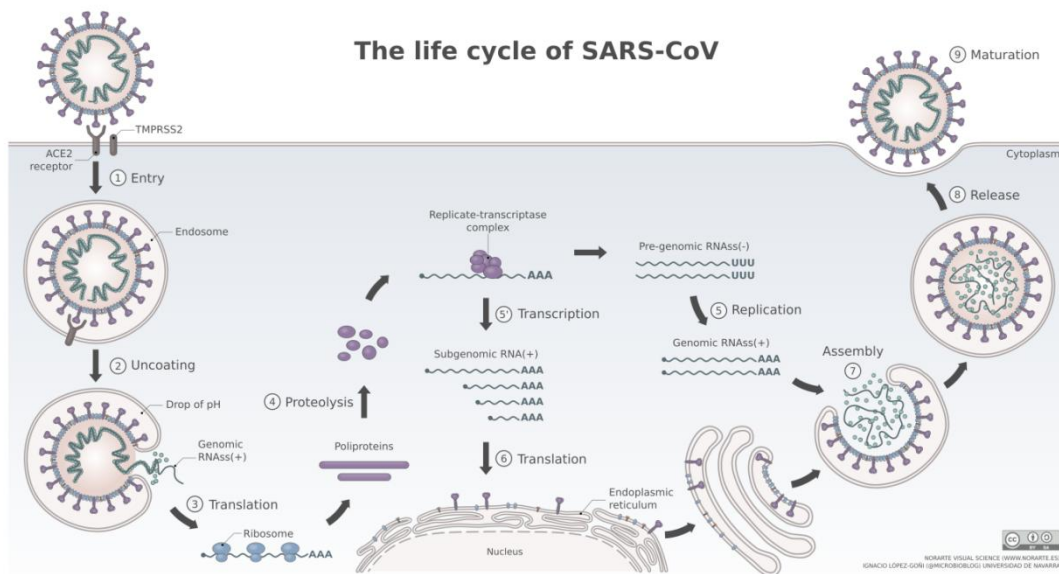
The coronaviruses were originally grouped into the family *Coronaviridae* on the basis of the crown or halo-like appearance given by the glycoprotein-studded envelope on electron microscopy. This classification has since been confirmed by unique features of the chemistry and replication of these viruses. Most human coronaviruses fall into one of two groups: 229E-like and OC43-like. These differ in both antigenic determinants and culturing requirements: 229E-like coronaviruses can usually be isolated in human embryonic fibroblast cultures; OC43-like viruses can be isolated, or adapted to growth, in suckling mouse brain. There is little antigenic cross-reaction between these two types. They cause independent epidemics of indistinguishable disease.





**Multiplication**

• It is thought that human coronaviruses enter cells, predominantly, by specific receptors. Aminopeptidase-N and a sialic acid-containing receptor have been identified to act in such a role for 229E and OC43 respectively. After the virus enters the host cell and uncoats, the genome is transcribed and then translated. A unique feature of replication is that all the mRNAs form a “nested set” with common 3’ ends; only the unique portions of the 5’ ends are translated. There are 7 mRNAs produced. The shortest mRNA codes for the nucleoprotein, and the others each direct the synthesis of a further segment of the genome. The proteins are assembled at the cell membrane and genomic RNA is incorporated as the mature particle forms by budding from internal cell membrane.



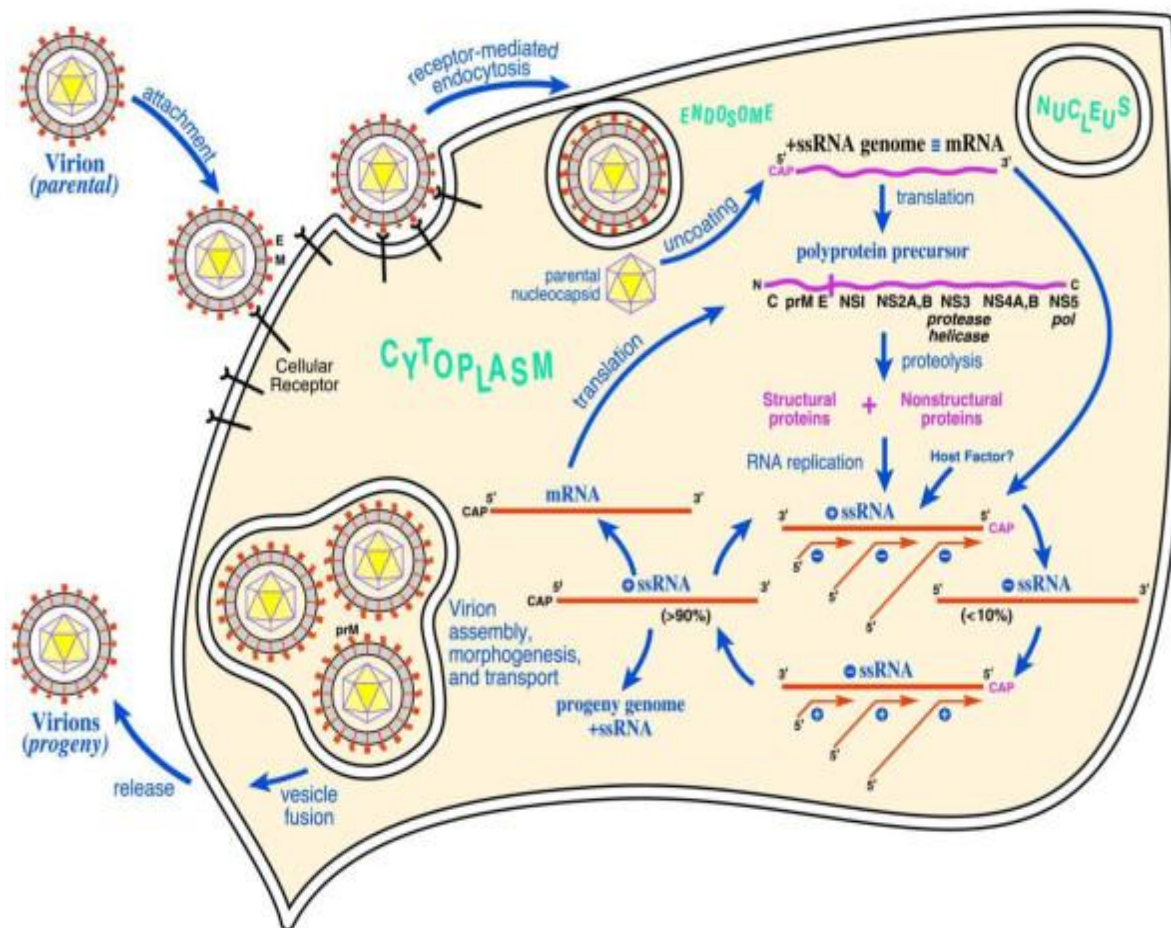
## COVID 19 : POTENTIAL DRUG THERAPY

### Antimicrobials with potential activity against SARS-CoV-2:

**Chloroquine:**chloroquine has an in vitro SARS-CoV-2 activity and can have an in vitro SARS-CoV-2 effect and Immunomodulatory properties.(3)(4)(5)(6)

**Lopinavir; Ritonavir:**In vitro and animal model studies show potential activity for other coronaviruses (SARS-CoV and MERS-CoV).(1) (19)(20)(21) •

**Remdesivir (GS-5734):**Remdesivir is a broad-spectrum antiviral with in vitro activity against coronaviruses. (2) (4) (13)(14)(15)(16)(17)



## HOLISTIC APPROACH:-PHYTOCHEMICALS NEW LINE OF TREATMENT

Viral diseases, including emerging and chronic viruses, are an increasing worldwide health concern. Due to the global disease burden caused by viral infections there is an urgent need for novel and more effective antiviral drugs. Medicinal herbs and their bioactive constituents came in the center of interest, since they may provide feasible treatment options for the population of developing countries, where the majority of the population cannot afford for expensive chemical drugs of western medicine. Now a day, viral infection is becoming a great danger to humans and often causes death. In the past, deadly viruses caused pandemics in the world. Due to the metabolic properties of viruses, they are difficult to control and there are still relatively few drugs for treatment of viral diseases. The major problem encountered in the treatment against viruses is their rapid adaptation and development of drug-resistance as well as the emergence of new hybrid viruses.

Common medications used against viral infections are often inadequate and show a variety of side effects. In the last few years, natural remedies gain more and more popularity in the field of medical science. The idea of herbal drugs is popular because of easy access, cost effectiveness, less side effects and good tolerability. Viruses are obligate intracellular parasites with a viral genome (DNA or RNA) and protein envelope (capsid). Viruses do not have an own metabolism and are not able to replicate by own to perform biosyntheses. To this end, they exploit and control the host cell. They are transmitted by droplet infection, exchange of body fluids, contact infection and blood-sucking insects.

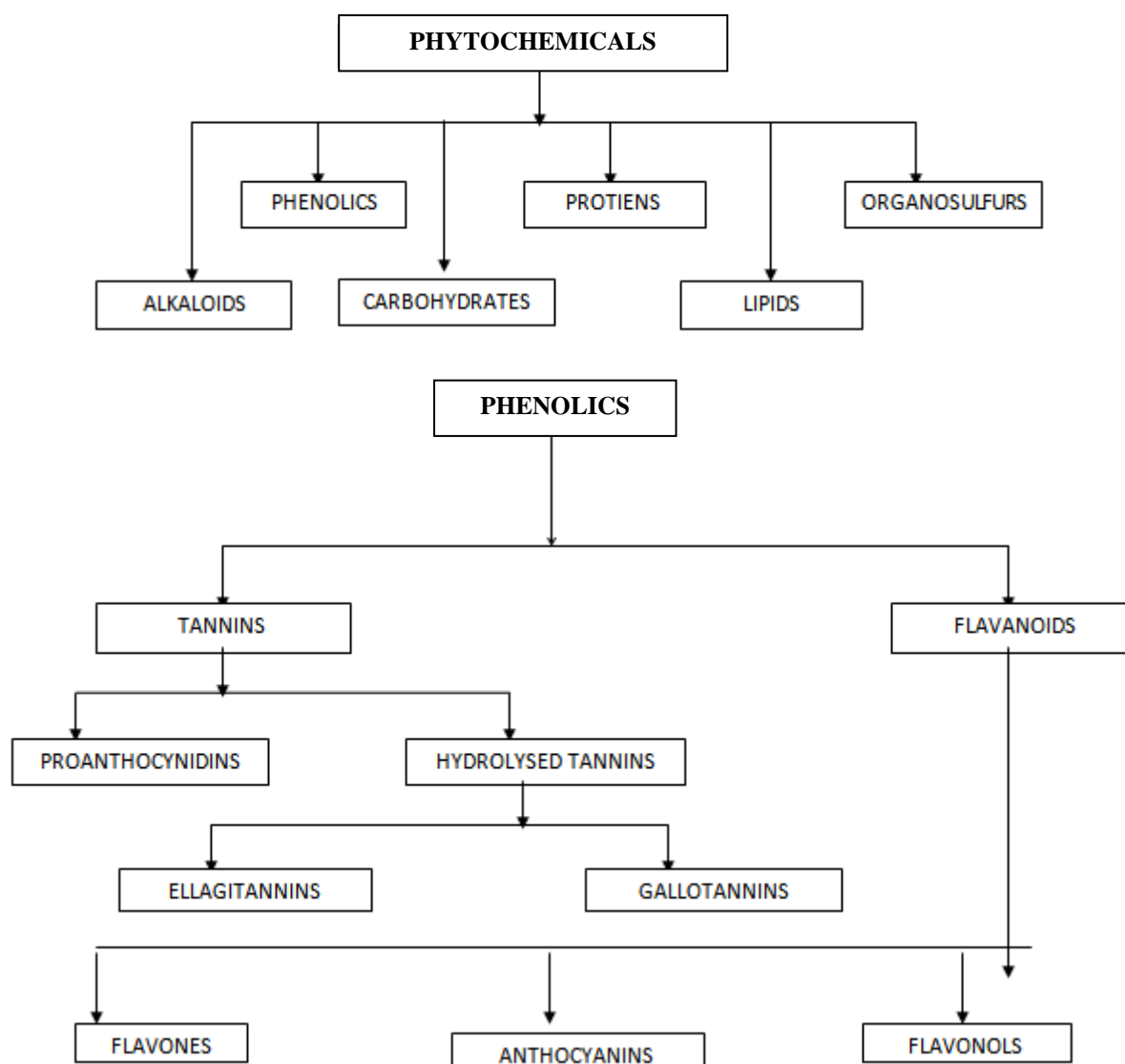
The viral life cycle can be divided in various sections -

- ♣ During adsorption, the virus attaches to the host cell.
- ♣ The virus penetrates the cell and releases genetic material during uncoating.
- ♣ The genome of the virus exploits the cell and takes control over it.
- ♣ The cell begins to synthesize virus particles.
- ♣ Then, new viruses are formed, and finally leave the cell.
- ♣ The new viruses are now able to infect other cells.

**Mechanisms of action of existing antiviral drugs:-**

To prevent viral entry into the cell, adsorption of the virus has to be avoided, e.g. by antibodies or specific ligands.

1. Inhibit viral uncoating after endocytosis by Capsid-stabilizing agents and blocking of endosomal ion channels.
2. DNA or RNA replication can be suppressed by inhibition of DNA- or RNA-polymerases, by endonucleases, or by nucleoside analogues.
3. Virus replication can be interfere with Nucleoside analogs
4. Protease inhibitors prevent virus maturation and discharge. These substances are peptides that block protease substrates. This leads to suppression of maturation and interruption of the viral replication cycle



### Antiviral activity of Indian plants

Plants contain a wide variety of phytochemicals, such as alkaloids, phenolic compounds, tannins, saponins, flavonoids, terpenoids, lignans, coumarins, and many other active components. The mechanisms of action of the substances are multi-faceted and often not yet extensively explored. The focus of the present review is particularly on Indian medicinal herbs and plants used to treat viral diseases, which are cheap and easily accessible since viral infections can be one of the biggest nightmares for Medical Practitioners and patients.

1. Black tea
2. Clove
3. Rubarb
4. Swertiachirata
5. kalmegh

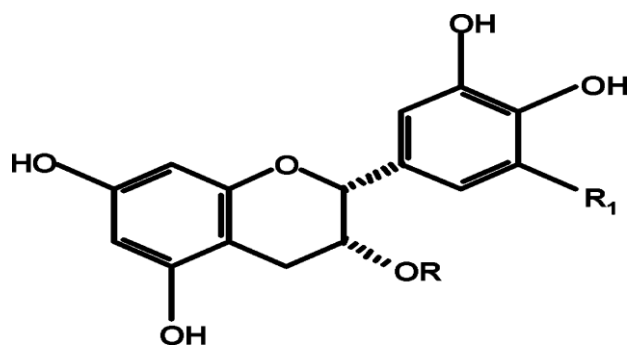
### BLACK TEA

Tea is the most widely used ancient beverage in the world. Tea, consumed as a beverage worldwide, is prepared from systematically processed dried tea (*Camellia sinensis*) leaves by boiling in water (milk and/or sugar are added sometimes). *C. sinensis* an evergreen bushy plant, initially from China and is now widely distributed. The origin can be traced to East Asia.

Black tea is fully fermented. Withered leaves undergo biochemical reactions during distortion and fermentation stages in the manufacturing process, after which they are subjected to drying. This type of tea has a different composition than fresh tea leaves as oxidation, polymerization, and other modifications of original components take place during processing.

### Chemical Composition

- Catechins
- Simple polyphenols
- Flavonols
- Oxidised polyphenols
- Theanine
- Aminoacids
- Peptides/proteins
- Lipids/Organic acids
- Carbohydrates
- Caffeine
- Minerals/ash
- Pectins
- Chlorophyll and other pigments
- Volatile compounds



### BENEFICIAL BIOLOGICAL ACTIVITIES

Black tea possesses many biological activities. It acts as an effective antioxidant, active against inflammation, and some types of cancer. It reduces DNA damage and mutagenesis. It may have a role in preventing cardiovascular diseases. Besides this black tea has an effect on the gastrointestinal tracts, it affects motility, absorption, micro flora etc., By influencing the hormonal balance and antioxidant function black tea improves bone mineral density. It is also antiviral due to its enzyme inhibiting and receptor blocking properties. This review specifically deals with the health effects reported for black tea. In some of the studies, even minor



components in black tea such as catechins (which are present in much higher concentrations in other products e.g. green tea), have been shown to have biological activity. A broader perspective on the activity of such components is provided by a review on the effects of tea catechins and polyphenols on health by Higdon and Frei.

### Antiviral Activity

Theaflavins present in black tea were found to have anti HIV-1 activity. These polyphenols inhibited the entry of HIV-1 cells into the target cells. HIV-1 entry into the target cell involves fusion of glycoprotein (GP) and envelope of the virus with the cell membrane of the host cells. Haptad repeat units present at N and C terminals of GP41 (membrane protein) on the viral envelope, fuse to form the fusion active GP41 core, which is a six-helical bundle. Theaflavins were found to block the formation of this six-helix bundle required for entry of the virus into the host. Galloyl moieties may have a role in the inhibition effect as a higher number of galloyl groups correlated with greater inhibition.(23)

Theaflavin3, 3\_ -digallate>theaflavin3\_gallate  
>theaflavin 3 gallate>theaflavin

Theaflavins may interact with the membrane protein through ionic interactions as theaflavins possess negatively charged groups. The anti HIV activity of theaflavins was found to be stronger than the activity of catechins. This may help in drug design. Theaflavin 3 3\_ digallate, and theaflavin 3\_ gallate were found to inhibit Severe Acute Respiratory Syndrome (SARS) corona virus. The antiviral activity was due to inhibition of the chymotrypsin like protease (3CL Pro) which is involved in the proteolytic processing during viral multiplication. Tannic acid may also have anti 3 CL Pro activity. Consumption of black tea may therefore affect multiplication of enteric corona viruses. This could be useful in designing drugs. An antiviral mask that contains tea extract applied to electric filter was developed and it can scavenge and inactivate the viruses and prevent the viruses from drifting out.(24)

### CLOVE

**Cloves** (*Syzygium aromaticum*) are the aromatic flower buds of a tree in the Myrtaceae family. They are native to the Maluku Islands in Indonesia and are commonly used as a spice, sold both whole or ground. For its high anti-microbial, anti-fungal, **antiviral**, antiseptic and stimulating properties, **clove** oil is a popular home remedy for various ailments. Here are some benefits you can reap by using **clove** oil.

There are three types of clove oil:- bud oil, leaf oil and stem oil.

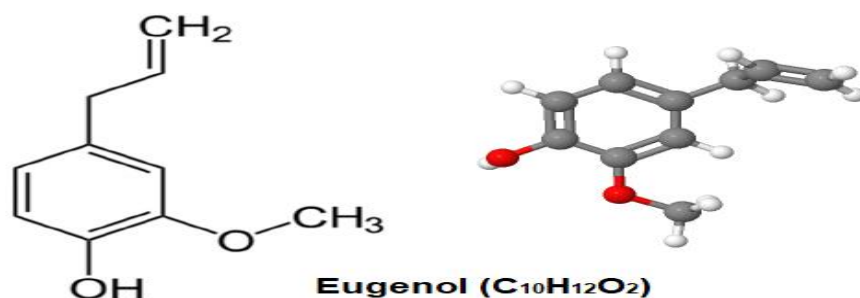
Bud oil is derived from the flower-buds of *Eugenia caryophyllus*. It contains mainly of 60-90% eugenol, eugenyl acetate, caryophyllene and other minor constituents.

Leaf oil is derived from the leaves of *Eugenia caryophyllus*. It consists of 82-88% eugenol, little amount of eugenyl acetate, and other minor constituents.

Stem oils are evolved from the twigs of *Eugenia caryophyllus*.

#### Chemical constituents

- Eugenol
- Beta-caryophyllene
- Vanillin
- *Cratogenic acid*
- Tannins such as bicornin, gallotannic acid, methyl salicylate (painkiller),
- The flavonoids eugenin, kaempferol, rhamnetin, and eugenitin, triterpenoids such as oleanolic acid, stigmasterol.





### Anti viral activity

**Eugenol** exhibited **antiviral activity** against herpes simplex ( HSV-1) and herpes simplex -2 (HSV-2) by preventing viral replication and reducing the viral infection . **Eugenol** isolated from *S. aromaticum* extracts and their essential **oils** has shown its free radical scavenging, antioxidant, and antimicrobial **properties.**(29)(28)

### RHUBARB

Indian rhubarb, which is official in Indian Pharmacopoeia, consists of the dried rhizomes of *R. emodi* and *R. webbiana* and other species of *Rheum*. Rhizomes and roots of *R. moorcroftianum* and *R. spicifolium* are also reported to be mixed with the drug. The plant grows wild at an altitude of about 4000 to 12000 feet . Rhubarb has been successfully grown in certain parts of Assam also. Indian rhubarb occurs in sub-cylindrical or irregular pieces, ranging from 2 to 20 cm in length and 1.5 to 2.0 cm in diameter, much shrunk and light in weight. It is somewhat dark in colour, almost odourless or somewhat fragrant with a bitter and astringent taste. It contains anthraquinone derivatives and yields about 25-30 per cent of extract soluble in 50 percent aqueous alcohol. In ayurvedic preparations, rhubarb has long been used as an ingredient of purgatives , laxatives and stomachic-tonics. It is hoped that the review would be useful to those working in the field of phytochemical investigations of rhubarb.

Tart rhubarb is a Canadian favourite, and our cool northern climate has the perfect growing conditions for it. If you're thinking about planting a rhubarb root (*Rheum rhabarbarum*) be sure to give it moist, well-drained soil and a bit of room to grow. Let the root establish itself for one year before harvesting the stalks. Be sure never to eat the greens as they are high in oxalic acid, which can contribute to kidney stones if consumed in large amounts.

Rhubarb's main health benefits are its ability to promote detoxification, and its power of astringency. An astringent substance is a chemical compound that shrinks or contracts body tissues, thereby diminishing discharges of mucus or blood.

### Rhubarb may help treat hepatitis B

The antiviral effects of rhubarb have been used for many years in traditional Chinese medicine. These antiviral compounds are now being researched by western medicine to specifically treat hepatitis B as well as severe acute respiratory syndrome (SARS).(30)

### SWERTIA CHIRATA

The antiviral activity of Indian Medicinal plant extract *Swertia chirata* was tested against Herpes simplex virus (HSV) type-1, using multiple approaches both at cellular and molecular level.

*Swertia* plant crude extract (1gm/mL) at 1:64 dilution inhibited HSV-1, plaque formation at more than 70% level. HSV antigen expression and time kinetics experiments conducted by indirect immunofluorescence (IFA) test, revealed a characteristic pattern of small foci of single fluorescent cells in *Swertia* extract treated HSV-1 infected cells at 4 hours post infection dose, suggested drug inhibited viral dissemination. Infected cell cultures treated with *Swertia* extract at various time intervals, tested by PCR, failed to show amplification at 12, 24-72 hours. HSV-1 infected cells treated with Acyclovir (antiviral drug) did not show any amplification by PCR.

Medicinal plant products have been used as folk remedies for different kinds of ailments including viral diseases. There is a need to search for new compounds for treatment of viral infections since there is an increasing resistance to antiviral drugs. The problems of viral resistance and viral latency leading to recurrent infections in immunocompromised patients has been documented earlier. Recently, a number of medicinal plant products have been shown to have antiviral activity. Traditional plant extracts having anti-infective properties, have been screened for their antiviral activity.

Acute and recurrent herpes simplex virus (HSV) infections are distributed worldwide and cause wide range of diseases from mild to severe and in some cases they may become life threatening in immunocompromised patients. Also, several antiviral compounds have been tried as therapeutic use in earlier decades. Nucleoside derivative drugs such as acyclovir (AVC), gancyclovir (GCV) and pencyclovir have been widely approved drugs for the treatment of HSV infections. However, widespread use of these drugs has shown resistance especially in immunocompromised and bone marrow transplant recipients. In order to circumvent the problem of viral resistance, development of new antiviral products with different mechanism of action are very much required.(31)

### Virus infectivity and antigen expression

To determine the time kinetics of *Swertia* extract on HSV-1 antigen expression, indirect immunofluorescence assay was carried out. Infected Vero E6 cells were treated with *Swertia* plant extract (1:64 dilution) at 4, 8 and 24 hours of post infection dose (PID) and results were represented in Maximum reduction in number of

fluorescent cells was observed at 4 hours PID, a characteristic pattern of small foci of positive cells and even single fluorescent cells observed suggested the drug inhibited viral dissemination. *Swertia* plant extract subsequently added at 8 and 24 hour PID showed a significant reduction of positive fluorescent cells. Also, HSV-1 infected cells treated with acyclovir indicated a gradual reduction of infected cells and a complete inhibition was observed at a concentration of 0.1 mg/mL compared with controls

### **KALMEGH**

Andrographispaniculata (*A. paniculata*) used in ancient oriental and ayurvedic medicine. *A. paniculata*, commonly known as King of Bitters. *A. paniculata* has various compounds in its aerial parts and roots and these are often used in extracting its active principles.(32)

#### **ACTIVE CONSTITUENTS**

Flavonoids (flavones)

Noroidoides,

Xanthones,

Polyphenols

Trace elements (cr, mn, co, ni, zn, cu, se, rb, sr, and pb)

Macro-element (potassium and calcium).(33)(34)

#### **PHARMACOLOGICAL ACTIVITY**

The use of the different parts of *A. paniculata* plant in folk medicine, especially, in Asia led scientists to study its pharmacological properties to validate its use as a therapeutic agent in the remedy of various ailments. Several studies showed that this plant exhibited various biological activities such as anti-microbial, cytotoxicity, antiviral, anti-protozoan, anti-inflammatory, anti-oxidant, immunostimulant, anti-diabetic, anti-infective, anti-angiogenic, hepato-renal protective, sex hormone modulatory, liver enzymes modulatory and insecticidal and toxicity activities.(34)(35)

#### **ANTIVIRAL PROPERTY**

Andrographispaniculata is a medicinal plant which have anti HIV, anti pathogenic bacteria and immunoregulatory activities. The research purpose was to investigate the activity of Andrographispaniculata ethanol extract as antiviral and immunostimulant. *A. paniculata* leaves oven-dried, then grinded and macerated with ethanol 90%, and the extract then analyzed using High Performance Liquid Chromatography (HPLC) to determine the content of active compounds andrographolide. The antiviral activity of the extract was determined by observing its ability on inhibiting virus load in A549 cells transfected with Simian Retro Virus (SRV) by Real Time – Polymerase Chain Reaction (RT-PCR) analysis. The immunostimulant activity of extract was determined by its ability to induce lymphocytes cell proliferation using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. result indicated that the *A. paniculata* ethanol extract inhibited the SRV virus titer similar to the positive control Lamivudine, and it was not toxic to the A459 cell line. Furthermore, low concentration (1 µg/mL) of *A. paniculata* extract could stimulated lymphocyte cell proliferation about 38% compared to the control lymphocyte cell without any treatment.(34)(35)(36)(37)

## **II. Conclusion**

On the basis of above study we conclude that the phytochemicals are useful for the treatment of SARS COVID-19 BY Enhancing the immunity of infected people and they also have antiviral activity as we mentioned above. blacktea, clove, rhubarb, swertiachirata and kalmegh have antiviral property so we can use these phytochemical(drugs) as a new line of treatment of SARS COVID-19.

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PRASHANT VATS, et. al. "A Review Article on Phytochemicals New Line of Treatment of Sars Covid-19." *IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS)*, 15(3), (2020): pp.36-46.