Potential of plant based active pharmaceutical moieties in combating SARS-CoV2 novel corona (Covid-19) virus infection

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Introduction

Novel corona virus is also known as severe acute respiratory syndrome corona virus (SARS-CoV-2). Nowadays, it has become life threatening for human race and whole world is facing crisis due to novel corona virus also called as Covid-19. It has great capacity of transmission from human to human that's why it is threat for human species. The virus had disseminated to the world due to international air travel facilities and lack of awareness in infection control **(Cheng, Lau, Woo, & Kwok, 2007)**. Covid-19 is a respiratory tract infection originated from novel corona virus comes under beta-corona virus class and similar to the viruses belonging t the severe acute respiratory syndrome (SARS) and middle east respiratory syndrome (MERS) **(Chang, 2020),(Perlman, 2020)**.

Corona family: Corona viruses are the broad group of viruses which belongs to order Nidovirales, which includes Coroniviridae, Roniviridae and Arteriviridae family. Corona virus family is further subdivided into four groups- alpha, beta, gamma and delta coronavirus. Nidovirales viruses are enveloped, positive sense ribonucleic acid (RNA) viruses having very large genome approximately 30 Kb **(Maier, Bickerton, & Britton, 2015)**.

Genetic structure: Gene makeup consists of single stranded RNA (single stranded ribonucleic acid) containing 29891 nucleotides, which encodes 9860 amino acids. From the present reports it is known that probably Covid-19 evolved from bats. Since the genetic structure is made up of single stranded RNA that's why it can mutate at much faster speed than other genomes **(Cascella, Rajnik, Cuomo, Dulebohn, & Di Napoli, 2020).**

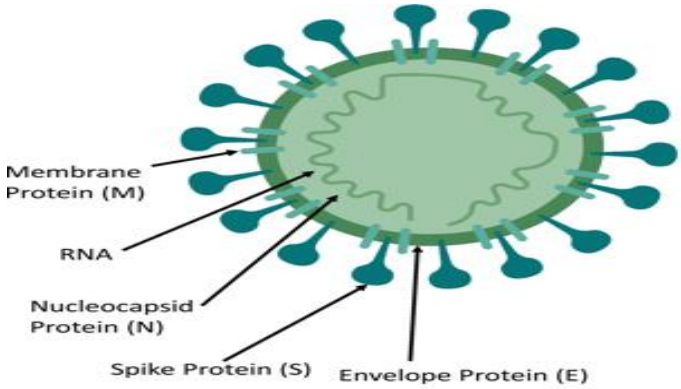

Fig: Corona virus genetic structure **(Seah, Su, & Lingam, 2020)**

Origin: Covid-19 is newly emerged corona virus. Whole world is facing Covid-19 as big challenge for human beings as it is spreading rapidly nowadays. According to the research study done by **Andersen *et.al*** in first scenario it was found that corona virus has evolved from bats and pangolins. The spike proteins of corona virus had undergone mutation to bind with human ACE-II (angiotensin converting enzyme II) protein. In the second scenario corona virus is transmitted from animals to humans and thus causing corona virus disease **(Andersen, Rambaut, Lipkin, Holmes, & Garry, 2020).**

Life cycle of virus

1. Attachment and entry: In host cell, Covid-19 life cycle begins when spike protein binds with ACE-II receptor. After this binding spike protein will undergo conformational change which results in fusion of viral envelope with the cell membrane of ACE- II receptor. The next step is release of genome which is RNA into host cell.

2. Replication and transcription: In the next step RNA is translated into polyprotein pp 1a and 1ab. These polyproteins are cleaved by viral proteinases. The polymerase enzyme produces several copies of mRNA by discontinuous transcription process which is further translated into viral proteins.

3. Assembly and release: Viral protein and RNA assembles to form virus copies in endoplasmic reticulum and golgi which are then released out of the cell and transported in the form of vesicles **(Shereen, Khan, Kazmi, Bashir, & Siddique, 2020),(Maier *et al.*, 2015).**

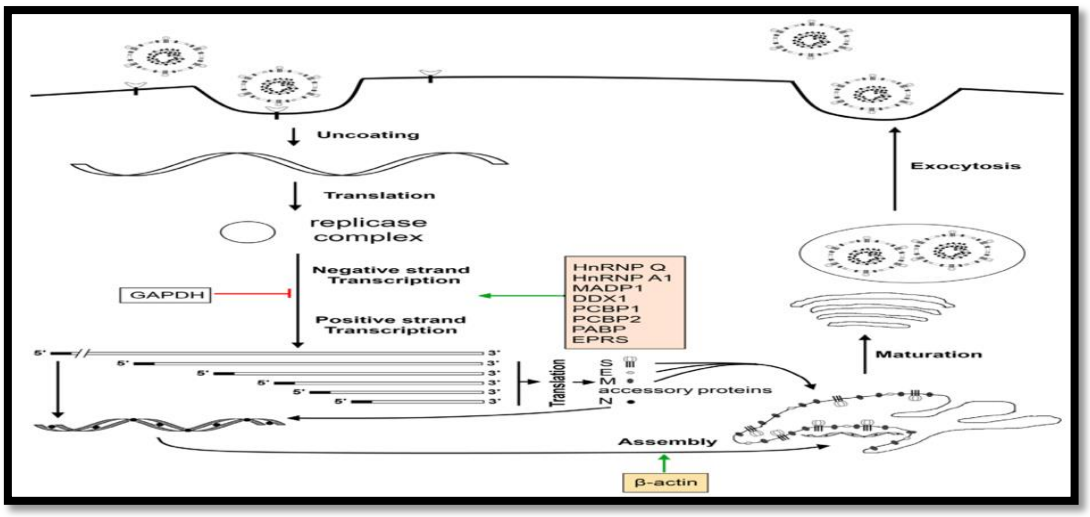

Fig: Life cycle on corona in host cell **(Zhong, Tan, & Liu, 2016)**

Pathogenesis

Animal coronaviruses

Several diseases are caused by corona viruses in animals and they have ability to infect various animals like pigs, cows, chickens, dogs and cats etc. which may lead to severe disease. That's why in the last half of 20th century significant research is done. Transmissible gastroenteritis virus (TGEV) is efficient in causing severe gastroenteritis in young piglets, whereas porcine epidemic diarrhoea virus (PEDV) and Porcine hemagglutinating encephalomyelitis virus (PHEV) can cause enteric infection **(Perlman & Netland, 2009)**. Recently SW1 (novel corona virus) is found in beluga whale **(Mihindukulasuriya, Wu, St. Leger, Nordhausen, & Wang, 2008)**. This virus affects respiratory system and liver which may result in acute liver failure and severe respiratory problems. More recently a novel corona virus is also found in bats which are sources for SARS-CoV (severe acute respiratory syndrome corona virus) and MERS-CoV (middle east respiratory syndrome corona virus).(He et al., 2014) Another novel virus of Nidovirales group comes under mesoniviridae family are responsible for infecting insect host **(Nga *et al.*, 2011),(Lauber *et al.*, 2012).** Murine hepatitis virus (MHV) is most interesting topics for study of animal corona viruses which are responsible for infection in mice.

Human coronaviruses

Before SARS-CoV-2 outbreak, corona viruses were thought to cause only mild respiratory infection in humans. Corona viruses which can affect human are of alpha and beta class.

Examples of alpha class corona viruses are HCoV-229E and HCoV-NL63 while examples of beta class corona viruses are HCoV-OC43 and HCoV-HKU1. HCoV-OC43 and HCoV-229E was also known fifty years ago but HCoV-HKU1 and HCoV-NL63 are recently identified after Covid-19 outbreak **(McIntosh, Becker, & Chanock, 1967),(Bradburne, Bynoe, & Tyrrell, 1967),(Van Der Hoek *et al.*, 2004),(Woo *et al.*, 2005),**(Medicine, 1962) These viruses affect respiratory system resulting in dry cough, fever, difficulty in breathing, common flu etc. Another interesting feature of these viruses is change in gene makeup which is calld mutation with time and environmental condition **(Vijgen *et al.*, 2005).** In 2002-2003 SARS-CoV was found as infecting agent of SARS in Guangdong city of china. This is most dangerous disease caused by corona virus that time resulting in 8098 cases and 774 deaths having mortality rate of 9%. SARS-CoV's primary target organ is lung's epithelial cells. This virus enters in macrophages and thus destruction of lymphocytes which results in a drastic decrease of immune power **(Peiris *et al.*, 2003),(Spiegel, Schneider, Weber, Weidmann, & Hufert, 2006),(Law *et al.*, 2016).**

Causes of Covid-19

1. Infection may develop by direct contact with novel corona virus
2. Disease is highly contagious and can be transmitted from person to person very easily by respiratory droplets **(Peterfalvi *et al.*, 2019),(Adhikari *et al.*, 2020).**
3. Infection spreads by direct contact with infecting environmental surface, faecal and oral.
4. Risk factors associated are age (old age person are at high risk as compared to adults), sex (from the study it was observed that males are more affected with the virus) and contact with infective person **(Perlman, 2020),(Andersen *et al.*, 2020), (Shereen *et al.*, 2020),(Zhong *et al.*, 2016).**

Modes of transmission: On the basis of size of droplets there are of two types of transmission mode:

1. Respiratory droplets are of size more than or equals to 5-10µm. Transmission of droplets occurs when the person is within 1m area with the other person who is infected and shows symptoms like cough, sneezing etc. Transmission can also take place by direct contact with the objects having pathogen on their surface.

2. Droplet nuclei are of size less than 5µm and can remain in air for longer time and that's why can be transmitted to persons which separate to each other by more than 1m. Airborne transmission is not observed till now for the virus **(American Nurses Association, 2020).**

Symptoms of Covid-19

Most common symptoms are shortness of breath, dry cough which may get more severe with time and mild fever which also increases with time. If the symptoms become severe then immediately call the emergency medical services. Followings are the symptoms which are indication that the disease is getting severe and person must call ambulance:

1. Difficulty in breathing.
2. Face and lips turned blue.
3. High pressure in chest and continuous pain.
4. Immoderate drowsiness.
5. Confusion

Table : Difference between flu and Covid-19 (White & Kandola, 2020)

S.No.	**Flu**	**Covid-19**
1.	Incubation period is 1-4 days.	Incubation period is 1-14 days
2.	Symptoms appears suddenly.	Symptoms appear gradually and get severe with time.
3.	Bodyache is common.	Bodyache occurs sometime.
4.	Headache is common.	Headache may or may not be present.
5.	Loss of apetite is very common.	Loss of apetite occurs sometime.
6.	Shortness of breath is not so casual.	Shortness of breath is most common symptom for Covid-19
7.	Respiratory issues may present sometime.	Respiratory issues are common.

Diagnosis of infection

Novel corona virus is highly contagious or transmittable than SARS-CoV because it has higher effective reproductive number which is 2.9 than SARS-CoV which have effective reproductive number of 1.77. Therefore it becomes very necessary to diagnose the Covid-19 infection as early as possible **(Adhikari *et al.*, 2020).** For patients who are suspects real time polymerase chain reaction (RT-PCR) is performed to detect the presence of novel corona virus in swab, sputum, and lower respiratory tract secretions **(Woo *et al.*, 2005),(Shen *et al.*, 2020).**

Examination by CT imaging

Reports may vary with age, immune power, pathological condition and drug intervention. Five stages of the diseases are demonstrated by CT imaging based on the onset time and immunity of person which are shown in given table: **(Jin *et al.*, 2020)**

S.No.	Stage	Important features
1.	Ultra-early stage	Clinical manifestations are not seen in this stage, but after being exposed to environment contaminated by virus throat swab tests positive within 1-2 weeks.
2.	Early stage	This stage comes after 1-3 days of clinical manifestations appearance. Single or multiple scattered ground-glass opacities are main pathological features of this stage.
3.	Rapid progression stage	It comes after 3-7 days of clinical manifestations appearance. Cellular rich exudates in alveoli are primary pathological features of this stage.
4.	Consolidation stage	This stage comes after 7-14 days of clinical manifestations appearance. Fibrous exudation are the main pathological features of this stage.

5.	Dissipation stage	It comes after 2-3 weeks of clinical manifestations appearance. Patchy consolidation and strip like opacity are shown by CT imaging.

Apart from the techniques described above there are some other laboratory tests also.

1. Hematology examination
2. Detection of virus in respiratory tract
    - Respiratory virus nucleic acid
    - Flu antigens
    - Covid-19 nucleic acid detection
    - Other laboratory test including blood gas analysis, liver and kidney function, erythrocyte sedimentation rate, coagulation image, urine routine test, anti-acid staining, etc.

Prevention of Covid-19

Till now there is no specific treatment for Covid-19. Self care and social distancing is the best option to prevent the spread of deadly infection. Following are some preventive measures which need to be taken care off when symptoms are visible:

1. Wash your hands frequently with sanitizer.
2. Drink water or take more liquid.
3. Take hot shower to relieve the pain of throat.
4. Keep yourself warm.
5. Take rest and have proper sleep.
6. Have food which boosts up your immunity or the food having high vitamin C content.

Apart from these preventive measures if symptoms still persists then immediately call for medical help without any delay **(American Nurses Association, 2020).**

Immunostimulant essential oils

Some of the essential oils which boost up immunity are as follows:

1. Lemon essential oil: Lemon essential oil is isolated from the plant *Citrus limon* which belongs to family Rutaceae. Lemon is a very good source of zinc and vitamin C, which are essential components for immune system as it improves the natural killer cells function (These are very crucial and active to eradicate infection or to kill microorganisms). Vitamin

C improves the function of body's helper cells like lymphocytes and thus helps the body to resist infections. In research study it has been found that 1gm of vitamin C and 30mg of zinc taken on daily basis helps in improving conditions like common cold, respiratory infections, malaria, diarrhoea (in children) and pneumonia etc **(Sheean *et al.*, 2008)**.

2. Cinnamon essential oil: Cinnamon essential oil is isolated from the bark of the plant *Cinnamomum zeylanicum* which comes under family Lamiaceae. It is commonly used for its antidiabetic, antifungal and antibacterial properties. Apart from this it is believed that cinnamon is potent immune booster and in combination with honey it makes immune system strong. The low dose i.e 10mg/kg of cinnamon increases serum immunoglobulin levels, while at high doses i.e 100mg/kg, it increased serum immunoglobulin levels and neutrophil adhesion **(Niphade, Asad, Chandrakala, Toppo, & Deshmukh, 2009).**

3. Clove oil: Biological source of clove oil is *Eugenia caryophyllata* which belongs to Myrtaceae family. It is used as food flavour and also used to treat dental and respiratory diseases, sore throat and headache. Clove essential oil also have antifungal, antibacterial, anti-inflammatory, antiviral and cytotoxic properties. Clove oil affects macrophage cytokine release in a dose dependent manner **(Dibazar, Fateh, & Daneshmandi, 2015).**

4. Lavender essential oil: It is isolated from the flowers of *Lavendula augustifolia* belonging to the family Lamiaceae. In pregnant women massage with 2% lavender essential oil shows significant increase in salivary IgA concentration which is an indication of immunostimulant action **(Peterfalvi *et al.*, 2019),(Giovannini *et al.*, 2016).**

5. Eucalyptus essential oil: It is isolated by steam distillation from the leaves of plant *Eucalyptus globulus* belonging to family Myrtaceae. Eucalyptus essential oil treatment for 15 days has shown increase in monocytes concentration as well as phagocytic ativity of monocytes is also increased **(Serafino *et al.*, 2008).**

6. Rosemary essential oil: Rosemary essential oil is obtained from the plant *Rosemarinus officinalis* which belongs to Lamiaceae family. Main components present in rosemary essential oil are α-pinene, camphor, 1,8-cineole and many more which are responsible for its anti-inflammatory, antiseptic, anaesthetis, antimicrobial, analgesic, antifungal and antiviral

properties. From various studies it is also found that aromatherapy massage with rosemary essential oil can boost up humoral immunity in broilers **(Rostami *et al.*, 2018).**

Apart from these there are some essential oils which can be used to formulate sanitizer and listed here: **(Valeriano *et al.*, 2012),(Musterman & Placeholder, 2017)**

1. Peppermint oil
2. Lemongrass oil
3. Lavender oil
4. Jasmine oil
5. Frankincense oil
6. Thyme oil

Results and Discussion

The reviewed literature provides significant insights into the biological features, transmission mechanisms, and clinical implications of SARS-CoV-2 infection, along with the potential therapeutic relevance of plant-derived bioactive compounds. SARS-CoV-2 is an enveloped positive-sense single-stranded RNA virus belonging to the β-corona virus group. The viral genome is relatively large, consisting of approximately 30 kb, which encodes multiple structural and non-structural proteins required for viral replication and pathogenicity. Viral entry into host cells primarily occurs through the interaction between the spike glycoprotein of the virus and the angiotensin-converting enzyme-2 (ACE-2) receptor located on host cell membranes. This interaction facilitates membrane fusion and subsequent release of viral RNA into the host cytoplasm, initiating the replication cycle. Once inside the host cell, the viral RNA undergoes translation to produce poly-proteins that are further cleaved by viral proteases to generate functional replication complexes. These complexes synthesize viral RNA through transcription and replication processes, leading to the production of structural proteins and assembly of new virions in the endoplasmic reticulum–Golgi intermediate compartment. The newly formed viral particles are then transported in vesicles and released from the infected cells, contributing to viral propagation and disease progression. The transmission dynamics of SARS-CoV2 demonstrate a high degree of infectivity compared to previously identified corona viruses such as SARS-CoV. The primary route of transmission is

through respiratory droplets and close contact with infected individuals or contaminated surfaces. Clinical manifestations of COVID-19 commonly include fever, dry cough, fatigue, and shortness of breath, although severe cases may progress to acute respiratory distress syndrome and multi-organ complications. Early diagnosis using molecular diagnostic techniques such as real-time polymerase chain reaction (RT-PCR) and imaging approaches including computed tomography (CT) scanning plays an essential role in identifying infection and monitoring disease progression. In addition to understanding viral pathogenesis, recent research has explored the role of natural products and plant-derived compounds in enhancing host immune responses and potentially supporting the management of viral infections. Essential oils obtained from medicinal plants have gained considerable attention due to their diverse pharmacological properties, including antiviral, antimicrobial, antioxidant, and immunomodulatory activities. Lemon essential oil, derived from *Citrus limon*, is a rich source of vitamin C and micronutrients such as zinc, both of which are important for maintaining immune function. Vitamin C has been widely reported to support immune cell activity, particularly by improving the function of lymphocytes and natural killer cells, thereby enhancing the body's resistance to infectious agents. Similarly, essential oil extracted from the bark of *Cinnamomum zeylanicum* (cinnamon) has demonstrated immunomodulatory properties. Experimental studies have indicated that cinnamon extracts may enhance serum immunoglobulin levels and improve immune cell responses, suggesting potential benefits in strengthening immune defense mechanisms. Clove oil obtained from *Eugenia caryophyllata* contains eugenol as a major active component, which possesses antiviral, antibacterial, and anti-inflammatory properties. Studies have reported that clove constituents can influence macrophage-mediated immune responses and modulate cytokine production, thereby contributing to immune regulation. Likewise, lavender oil from *Lavandula angustifolia* has been associated with enhanced immune responses, including increased levels of salivary immunoglobulin A (IgA), which plays a critical role in mucosal immunity. Another plant-derived essential oil with potential immunostimulatory effects is eucalyptus oil obtained from *Eucalyptus globulus*. Experimental findings suggest that this oil may stimulate innate immune responses by enhancing the phagocytic activity of immune cells such as monocytes. Rosemary essential oil from *Rosmarinus officinalis* also contains several bioactive compounds including α-pinene, camphor, and 1,8-cineole that contribute to its antimicrobial, antioxidant, and anti-inflammatory activities. In addition to these medicinal plants, other essential oils such as peppermint, lemongrass, thyme, jasmine, and frankincense have demonstrated antimicrobial activity and may be incorporated into disinfectant or sanitizer

formulations to reduce microbial contamination. Although these natural compounds cannot directly replace antiviral drugs or vaccines, they may offer supportive benefits by enhancing immune responses and reducing microbial exposure. Overall, the available literature suggests that plant-based bioactive compounds possess promising pharmacological properties that may contribute to improved immune function and infection control. However, most of the existing evidence is derived from in vitro studies, animal experiments, or preliminary clinical observations. Therefore, extensive clinical trials and pharmacological investigations are required to establish their efficacy, safety, and therapeutic relevance in the management of COVID-19 and other viral infections.

Conclusion

The emergence of SARS-CoV-2 has created an unprecedented global health challenge, highlighting the urgent need for effective therapeutic strategies and preventive measures. Understanding the biological characteristics, transmission patterns, and clinical manifestations of the virus is essential for controlling the spread of the disease and improving patient outcomes. Plant-derived bioactive compounds and essential oils have shown considerable potential as supportive agents due to their immunomodulatory, antimicrobial, and anti-inflammatory properties. Natural products obtained from medicinal plants such as lemon, cinnamon, clove, lavender, eucalyptus, and rosemary contain various phytochemicals capable of enhancing immune responses and contributing to overall health maintenance. These compounds may serve as complementary approaches in infection prevention and immune system support. Nevertheless, despite encouraging preliminary findings, the therapeutic use of plant-based compounds against COVID-19 requires further scientific validation. Well-designed clinical studies are necessary to determine their pharmacological mechanisms, optimal dosage, safety profile, and potential interactions with conventional therapies. Future research focusing on phytochemical isolation, drug formulation, and clinical evaluation may facilitate the development of plant-based pharmaceutical agents that can contribute to the management of viral infections. In summary, medicinal plants represent a valuable source of bioactive compounds with potential applications in strengthening immune responses and supporting disease prevention strategies. Continued research in phytopharmaceutical science may lead to the discovery of novel therapeutic agents that complement existing antiviral treatments and enhance global preparedness for future viral outbreaks.

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