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Curcumin- A Immunomodulators against COVID-19

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ABSTRACT

The whole world is suffering from the coronavirus, a global pandemic, which has captured world attention to the immune system. As the world scrambles to find a cure for Covid-19, health experts have suggested boosting the body's immunity. Immune system defense against bacteria, viruses, and other organisms may help minimize the effects and hasten the recovery from the disease. Covid-19 still has a troublingly high mortality rate. A person with a strong immune system and good body health should be able to recover from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection without any complications because the immune system producing antibodies. Immunity will be "our saviour" against the virus. The idea is that if you don't have a potent weapon to combat the enemy, a strong and effective shield is the best bet to protect yourself. There are still millions of people in the world at risk due to old age, weak immune system, and pre-existing medical issues. Turmeric (Curcuma longa; active constituent curcumin) plays a major role to boost the immune system and a potent immunomodulatory agent that can help the population to prevent the COVID-19 infection.

1. INTRODUCTION

The outbreak of the new coronavirus (SARS-CoV-2) infection is spreading to every continent; Hailing from a large family of viruses, Coronaviruses can cause respiratory illnesses. As per the statistics, geriatric peoples are more susceptible to the COVID-19 infection because of their low immunity against pathogens & various underlying diseases. [1] Covid19 is a newly identified infectious disease. In 2019, December the new Coronavirus was found in Wuhan, China with several cases of pneumonia patients. Corona Viruses are big groups classified in Nidovirales order; by use of a nested set of mRNAs virus get replicated ("Nido-" for "nest"). [1][2] There are four genera of Coronavirus subfamily: alpha, beta, gamma, and delta coronaviruses. [3] Two genera of the human coronaviruses (HCoVs): alpha coronaviruses (HCoV-229E and HCoV-NL63) and beta coronaviruses (HCoV-HKU1, HCoV-OC43, Middle East respiratory syndrome coronavirus [MERS-CoV], and the severe acute respiratory syndrome coronavirus [SARS-CoV). [1][2]

2. COVID-19 AND IMMUNITY:

2.1 Transmission of COVID-19 (SARS-COV-2)

This virus is transferred from one individual to another by airborne droplets to the nasal mucosa. In cells of the ciliated epithelium virus get replicate and then inflammation, cell damage is caused. [4]

The virus Covid-19 is transmitted in humans by contact routes and respiratory droplets.

By Droplets: There are different sizes of droplets by which infections of respiratory transfer-

•Respiratory droplets - >5-10 micrometer in diameter [5]

The person who is sneezing or coughing is in one-meter close contact with another person who can transmit the infection through the respiratory droplet.

•Airborne droplet transmission- ≤5 micrometers in diameter

It transfers in population from one person to another in more than 1-meter distance also.

By Contact:

•Indirect contact with the material, surface which is used by Covid-19 suffering patient.

•Direct contact with Covid-19 infected person.[5]

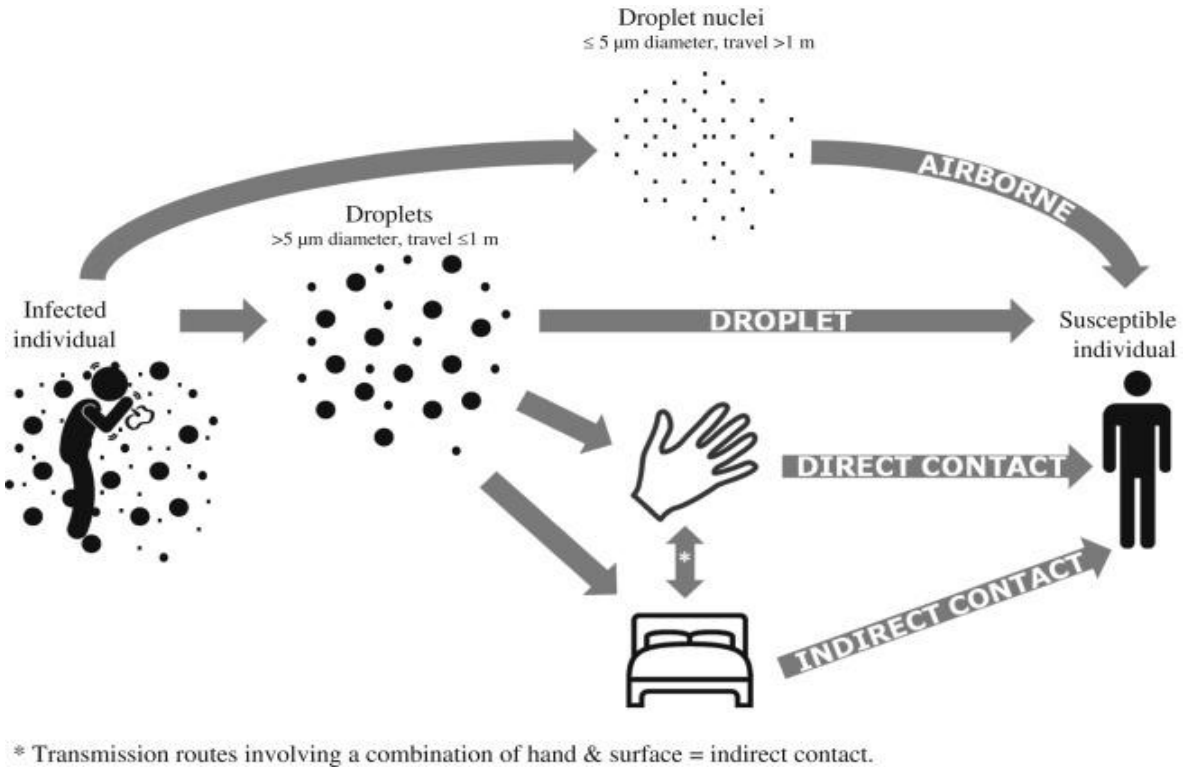

Figure No. 2.1: Transmission of COVID-19 [6]

2.2 Spread of COVID-19

In 2019, the Centres for Disease Control and Prevention (CDC) started monitoring the outbreak of the new coronavirus (SARS-CoV-2) infection is spreading to every continent. [7]

Covid-19 start from China and now this virus spread all over the nation. Some countries like the USA, Italy, Spain, Iran are the most suffered countries with Covid-19 as of 19 April 2020.[8]

2.3 Structure of COVID-19

Coronaviruses are medium-sized, spherical, or pleomorphic enveloped, non-segmented (single-stranded) positive sense RNA Viruses associated with a nucleoprotein within a capsid comprised of matrix protein in Nidovirales Order. The envelope bears spikes like projection on the surface which is made up of glycoproteins which give the virus a characteristic crown-like appearance. [4]

There are 6 ORFs in the genome of COV. sgRNAs of COVs work as a translator of every accessory and structural proteins. ORFs 10, 11 present close by 3′-Terminals, on the genome of one-third it encoded 4 major structural proteins. In pathogenesis phenotypic and genetic structure of SARS-COV-2 is necessary.[9]

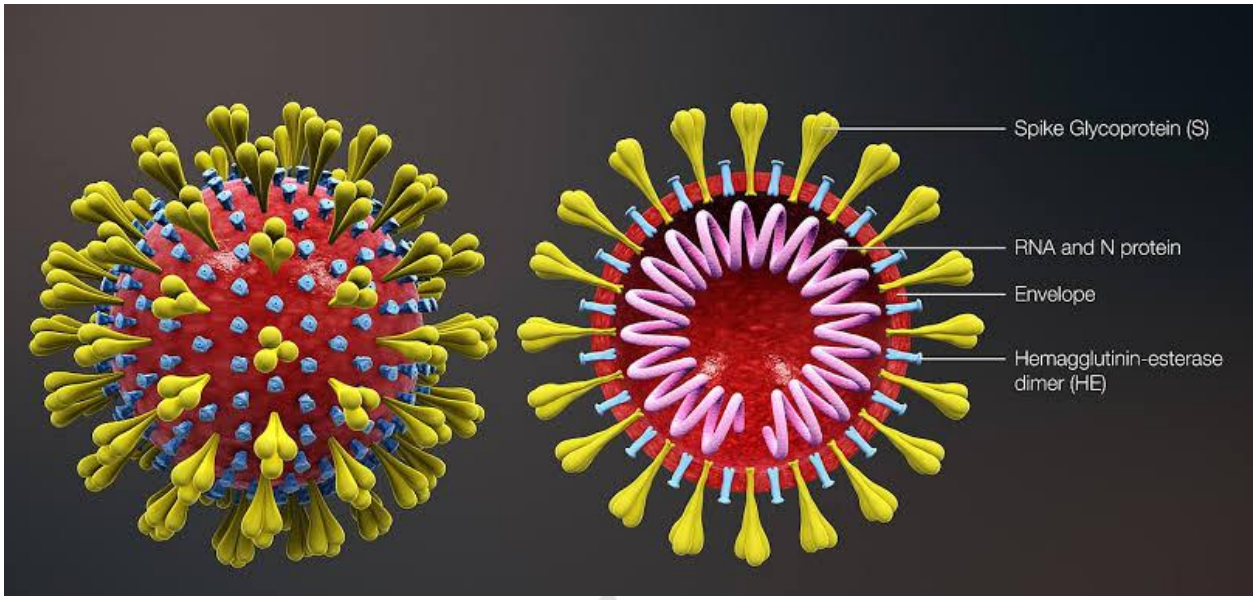

Figure No. 2.3: Structure of SARS-COV-2[10]

3. Role of immunity in COVID-19

A report in Lancet shows that acute respiratory distress syndrome (ARDS), a common immunopathological event for SARS-CoV-2, SARS-CoV, and MERS-CoV infections is the main death cause of COVID-19, and one of the main mechanisms for ARDS is the cytokine storm. The occurrence and development of SARS-CoV-2 depend on the interaction between the virus and the individual's immune system. Viral factors include virus type, mutation, viral load, viral titer, and viability of the virus in vitro. The individual's immune system factors include genetics (such as HLA genes), age, gender, nutritional status, neuroendocrine-immune regulation, and physical status. These factors all contribute to whether an individual is infected with the virus, the duration and severity of the disease, and the reinfection. In the early stages of the epidemic, an accurate diagnosis helps control the spread of the disease. [11]

3.1 Treatment

Clinical trials are ongoing but specific vaccines or treatment are not available and approved for SARS-COV-2. Some drugs are tried.[12]

In the case of immune-mediated diseases 2 generic drugs are given by doctors which are widely used, these are antimalarial drugs hydroxychloroquine, chloroquine shows antiviral action against COVID19 in some invitro cases and poorly controlled clinical studies. In some cases, hydroxychloroquine show side effects.[13]

A nucleotide Analogue prodrug that is remdesivir shows in vitro action against COVID-19 by inhibiting viral RNA polymerase. Improvement in 36 patients was observed out of 53 by giving drug remdesivir in cohort of patients hospitalized due to SARS-COV-2.[14]

Scientists, Government, Doctors spearhead for fighting against Covid19. Number of Researchers are trying to found a vaccine for SARS-COV-2, Firstly doctors objective is to relieve the patient from different symptoms like pneumonia than find a complete cure. Vital Organs like the heart, lungs, intestine, blood vessels are the main attack place for COVID19. Scientists, Researchers try to find antibodies against proteins of the COVID-19 virus. German Enterprise, Cure Vac try to design RNA based vaccine to treat the COVID-19 virus. Scientists aim to code viral proteins and introduce them in the body than the body produces an antibody which works out for the attack of the virus.[15]

As yet, effective treatment is unavailable**,** social distancing &boosting the body's immune system may prevent the disease from spreading. [16][17]

3.2 Immune System

Our immune system consists of a complex collection of cells, processes, and chemicals that constantly defends our body against invading pathogens, including viruses, toxins, and bacteria. [16][17]

After an incubation period, the invading COVID-19 virus causes non-severe symptoms and elicits protective immune responses. The successful elimination of the infection relies on the health status and the HLA haplotype of the infected individual. In this period, strategies to boost immune response can be applied. If the general health status and the HLA haplotype of

the infected individual do not eliminate the virus, the patient then enters the severe stage, when the strong damaging inflammatory response occurs, especially in the lungs. [18]

It seems that when the body is unable to produce an adequate adaptive response against the virus, the persistent innate-induced inflammation can then lead to a cytokine storm, ARDS, and diffuse organ involvement. With aging, the population of naïve T-cells shrinks while antigen-experienced, memory T-cells comprise an important portion of the T-cells population. [19]

4. Who infected more?

The National Institutes of Health (NIH) suggest that several groups of people have the highest risk of developing complications due to COVID-19. These groups include Young children, According to WHO People aged 65 years or older get infected more because of weak immunity & According to CDC due to physiologic and immunologic changes Pregnant Women are more susceptible to viral respiratory infections, including Covid19. [20]The people more infected by Covid19 are who suffers from diseases like Chronic Respiratory disease, diabetes, Cancer, Cardiac problem. [21]

The population is generally susceptible to SARS-CoV-2, the median age was 47.0 years (IQR, 35.0 to 58.0), 87% case-patients were 30 to 79 years of age, and 3% were age 80 years or older, and the number of female patients was 41.9%. Most cases were diagnosed in Hubei Province, China (75%). 81% of cases were classified as mild, 14% of cases were severe, and 5% were critical. The overall case-fatality rate (CFR) was 2.3%, but cases in those aged 70 to 79 years had an 8.0% CFR and cases in those aged 80 years and older had more chance to suffer from COVID19. [22]

Anti-tumor necrosis factor (TNF) antibodies have been identified in disease tissues of patients with COVID-19. Also, there is sufficient evidence to support clinical trials of anti-TNF therapy in patients with COVID-19. [23]

Except in children and adolescents, this virus infects the age group evenly and it is reported in a survey of 1000 patients in Wuhan, China. Near 15% of cases, progress to severe phases, and 65% have a big chance to progress to the severe phase. [24]

5. Immunity work

Immunity solitary breaks the chain of transmission by the starved pathogen of host infect, breaking chain of transmission help to protect the health of humans. [25]

The division of two-phase is played an important role: the first immune defense-based protective phase and the second inflammation-driven damaging phase. Doctors should try to increase immune responses throughout the first phase and put down it in the second phase. [15][24] To conclude, in populations at risk (elderly, associated comorbidities, immunosuppressed), when the activation of the innate immune system fails to produce an adequate adaptive response (i.e., virus-specific CD8+ T-cells), it seems that persistent self-induced inflammation can then cause mortality. Thus, mounting an early adaptive immune response may save the lives of humans. [19]

6. CURCUMIN AND IMMUNITY

6.1 Turmeric

Curcumin is the main active compound in turmeric. It has powerful anti-inflammatory properties, and animal studies indicate that it may help improve immune function. [26]

6.2 Curcumin as Immunity Boosters

Hot milk is given with turmeric because it helps the respiratory system to stay healthy.[27] Curcumin has positive effects on numerous disease conditions in patients and animal systems. The terminal stage of viral diseases is often the onset of a cytokine storm, the massive overproduction of cytokines by the body's immune system. The suppression of cytokine release by curcumin correlates with clinical improvement in experimental models of disease conditions where a cytokine storm plays a significant role in mortality. [28]

Curcumin regulates inflammatory cytokines such as IL-1 beta, IL-6, IL-12, TNF-alpha, and IFN gamma and associated JAK-STAT, AP-1, and NF-kappaB signaling pathways in the immune system.[29]

As curcumin (diferuloylmethane), a component of turmeric (Curcuma longa) can block TNF-α action and production in in-vitro models, in animal models, and humans. [30] Curcumin was shown inhibitory properties for SARS-CoV in the range of 3–10 μm.[31] A study

showed significant decreases in all markers of inflammation (soluble CD40 ligand(sCD40L), interleukin 1 beta (IL-1β), interleukin 6 (IL-6), soluble vascular cell adhesion molecule 1 (sVCAM-1), and erythrocyte sedimentation rate (ESR) comparing baseline to follow-up, while the control group did not. [32]

A molecular docking study to examine several medicinal plant-derived compounds that may be used to inhibit the COVID-19 infection pathway found the curcumin molecule have a good affinity, and low binding energy with low inhibition constant, this study also concludes that demethoxycurcumin, curcumin's related compound, have stronger affinity than the curcumin molecule.[33]

Therefore, we suggested that demethoxycurcumin and curcumin are few of the most recommended compounds found in medicinal plants that may act as potential inhibitors of COVID-19. [33]

7. DOSE OF CURCUMIN

Dose study of Curcumin shows that Curcumin does not show any toxic effect if consume 12g/day over 3 months. [34]According to other studies' doses of 1,200–2100 mg of curcumin per day for 2–6 weeks there is no toxic or adverse effect occurs. [35][36]

8. SUMMARY

The whole world is in great trouble nowadays due to the pandemic of COVID-19, which is a highly contagious viral infection causing severe respiratory discomfort & even death in some cases. Significantly high blood plasma levels of inflammatory cytokines such as IL-1 beta, IL-6, IL-12, TNF-alpha etc. were found in patients with COVID-19 infection. The severity of this coronavirus infection was found to be too high in peoples of old age and/or of immune-compromised once. In this review, we suggest that the boosting of the immune system may found helpful in the prevention of COVID-19 infection. We also present curcumin, a turmeric phytochemical, as a potent immune-booster as well as an anti-inflammatory agent, which also proved its affinity in a molecular docking study.

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