

SARS-CoV-2 and TCYTE Syrup

The Novel Coronavirus, SARS-CoV-2 (causing COVID-19) is an enveloped positive-strand RNA virus that infects vertebrates. Mutation rates of RNA viruses are greater than DNA viruses, suggesting a more efficient adaptation process for survival of the virus.

Scientists and clinicians have learned much of COVID-19, and its pathogenesis [1]: not all people exposed to SARS-CoV-2 are infected and not all infected patients develop severe respiratory illness [1]. Accordingly, SARS-CoV-2 infection can be roughly divided into three stages: **stage I**, an asymptomatic incubation period with or without detectable virus; **stage II**, non-severe symptomatic period with the presence of virus; **stage III**, severe respiratory symptomatic stage with high viral load [2].

Up to 81% of infected people experienced mild to moderate infection and around 14% with severe infections and around 5% critical cases, half of whom die! [3]. One of the biggest unanswered questions is why some develop severe disease, whilst others do not [1].

Two-phase immune responses induced by COVID-19 infection

Clinically, the immune responses induced by SARS-CoV-2 infection are two phased [1]. During the incubation and non-severe stages, a specific adaptive immune response is required to eliminate the virus and to preclude disease progression to severe stages [1]. For the development of an endogenous protective immune response at the incubation and non-severe stages, the host should be in good general health and an appropriate genetic background (e.g. HLA) that elicits specific antiviral immunity [1].

However, when a protective immune response is impaired, virus will propagate and massive destruction of the affected tissues will occur, especially in organs that have high ACE2 expression, such as intestine and kidney. The damaged cells induce innate inflammation in the lungs that is largely mediated by pro-inflammatory macrophages and granulocytes. Lung inflammation is the main cause of life-threatening respiratory disorders at the severe stage [4].

The two-phase division is very important: the first immune defense-based protective phase and the second inflammation-driven damaging phase [1]. Doctors should try to boost immune responses during the first, while suppressing it in the second phase [1]. Since Vitamin B3 (Niacinamide) is highly lung protective, it should be used as soon as coughing begins [1].

Most of deadly cases in elderly and weak individuals, with co-morbidities, can be explained that the innate and adaptive arms of their immune system are sub-optimal. This favours COVID-19 to replicate more aggressively and to spread to lower parts of the respiratory system

reaching to alveoli and causing pneumonia [5]. It was observed that most of the damage to lung tissue in severe cases is due to severe inflammation rather than a direct damaging effect of the virus itself [5]. In other words, it is the exaggerated immune response, or the immunopathogenic response, which is responsible for severe pneumonia and consequently respiratory failure [5].

The virus didn't cause the second stage at all, but by patients' runaway immune systems. For 2 reasons that still aren't clear, some people, especially the old and sick, weren't able to turn off their inflammatory response, leading immune cells and inflammation-inducing molecules known as cytokines to flood into the lungs. This is so-called "cytokine storm" [6].

From the context of the underlying knowledge of COVID-19 and host immune system interaction, the possible explanation of the course of COVID-19 infections is as follows: First, the healthy adults, unlike elderly and weakened individuals, have intact innate immunity along with competent humeral and cell-mediated immunity; the net result is that their immune system can limit the infection from progression and set out recovery within 2-3 weeks from the beginning of symptoms. This is enough to prevent the virus from reaching alveoli in huge numbers like in deadly critical cases. Therefore, these patients recover from mild-moderate infection. Second, elderly patients and/or with co morbidities and compromised immunity do not have the same fit innate and adaptive humeral immune response as healthy adults; therefore, COVID-19 keeps getting lower, in huge numbers, until reaching alveoli beyond which blood circulation is strictly guarded by alveolar lymphocytes and macrophages [5].

This eventually results in severe hypoxia and respiratory failure and may be collateral damage in downstream organs like liver and kidney [5]. Accordingly, the shortcomings of innate and humeral immunity in these patients make cell-mediated immunity to mount a vigorous attack at very dangerous area, the alveoli. Here's where the catastrophe occurs [5].

The 80% of the people who contracted the virus and recovered without any major incident, had immune system strong enough to thwart the infection. Macrophages are the first line of defense and constitute important participants in the bi-directional interaction between innate and specific immunity. Macrophages are in a quiescent form and are activated when given a stimulus [7].

Modulation of immune functions using phytochemicals as a possible therapeutic measure has become an accepted therapeutic approach [8]. It is now being recognized that immunomodulation of immune response could provide an alternative to conventional, for a variety of disease conditions, especially when the host's defense mechanism has to be activated under conditions of impaired immune responsiveness [8].

One of the good examples of an important phytopharmaceutical is *Carica papaya* leaf extract, being used extensively as a therapeutic in many ailments. Phytochemical analysis of the leaf extract [9] reveals the presence of flavonoids, alkaloids, carbohydrates, saponins, glycosides, phytosterols, phenolics, terpenoids and tannins. It mainly consists of seven phenolic compounds namely quercetin, protocatechuic acid, p-coumaric acid, caffeic acid, chlorogenic acid, kaempferol, and 5,7- dimethoxycoumarin. Previous report [10] states that the administration of aqueous leaf extracts of *Carica papaya* exhibits potential anti-dengue activity as indicated by the increased platelet count from $55 \times 10^3/\mu\text{L}$ to $168 \times 10^3/\mu\text{L}$, White blood cells from $3.7 \times 10^3/\mu\text{L}$ to $7.7 \times 10^3/\mu\text{L}$ and neutrophils from 46% to 78% in patients with dengue fever.

Quercetin scavenges nitrogen and reactive oxygen species (ROS), targets noticeable pro-inflammatory signaling pathways including MAPK, NF- κ B and STAT1, and inhibits replication of many types of viruses and infectivity of target cells (Boots et al., 2008). It increases excellent immunomodulatory effects.

TCYTE syrup, a brand trusted by clinicians across India, has *Carica papaya* leaf extract as one of the prime actives in it. Besides which a well balanced, precisely formulated combination of various active phytopharmaceuticals with defined activities complimenting each other. Some of which are:

Centella asiatica (Mandukaparni): Stimulates both non-specific cellular & humoral immunity; offers anticoagulant, cardio-protective, and antihypertensive properties [11-12].

Tinospora cordifolia (Giloy): Giloy's immunity boosting benefit is well documented and currently being advocated by the Department of Ayush, Government of India. It activates macrophages & increases their phagocytosis action. Hence strengthens innate immunity, which acts as the 1st line of defense [13].

Boerhaavia diffusa (Punarnava): Active ingredient Punarnavine, offers immunomodulatory activity [14].

Ocimum sanctum (Tulsi): Stimulates T & B Lymphocytes, which provides strength to adaptive immunity [15].

T-foenum graecum (Fenugreek-Danamethi): Elevates humoral immunity & strengthens infection fighting capacity [16]. Fenugreek also offers anticoagulant activity [17].

Aloe vera: increases cell viability and count of macrophages, functions effectively in the first line of defense against pathogens [18]. *Aloe vera* reduces pro-inflammatory cytokines [19]. This can tone down the cytokine storm in patients with severe symptoms (Phase II).

Terminalia chebula (Haritaki): Offers antioxidant and anti-inflammatory action [20].

Phyllanthus emblica (Amla): besides its well known antipyretic effect has excellent anticoagulant & anti-inflammatory properties and a rich source of vitamin C too [21].

Trikatu: a blend of equal parts of the fruits of Black Pepper (*Piper nigrum*), Long Pepper (*Piper longum*) and the rhizomes of Ginger (*Zingiber officinale*) used to treat inflammatory disorders. Trikatu suppresses the cell mediated and humoral immune response, decreases the macrophage phagocytic index and most significantly Trikatu maintains the cytokine homeostasis [22].

Some of the major complications:

SARS-CoV-2 virus primarily affects the respiratory tract. Numerous studies have published that more patients in the death groups had complications such as ARDS, acute cardiac injury, acute kidney injury, shock, and DIC [23]:

DIC (Disseminated Intravascular Coagulation)

In COVID positive patients it was observed that 71.4% of non-survivors and 0.6% survivors met the criteria of DIC during their hospital stay [24]. Due to these developments, many studies and doctors support the use of LMWH for managing COVID positive patients with elevated D-dimer levels [25].

Thrombocytopenia

It was seen that 72.5% of patients developed thrombocytopenia during admission [26]. Additionally, hampered platelet production, increased platelet destruction & increased consumption of platelets from the circulation have been known to further contribute to development and progression of thrombocytopenia in COVID-19 patients. These complications firmly contribute to prognosis of COVID-19 and its mortality rate.

TCYTE works at 2 levels

TCYTE provides balanced stimulus to immunity with 10 proven herbal ingredients that create stronger, healthier immunity in patients.

Offers balanced therapeutic actions like increased thrombocyte production – anticoagulant effects, antiviral, antipyretic, antioxidant, and anti-inflammatory effects and thus prevents complications.

Conclusion:

In managing COVID-19 patients it is important to consider both the stages of the symptoms (Mild to moderate symptoms & severe symptoms). While currently it is difficult to find a solution in managing these patients suffering from COVID-19, **TCYTE** could effectively be your answer in this crisis. **TCYTE** plays a vital role in boosting and maintaining stronger immunity. Upto 85% of the people infected with SARS-CoV2 could recover without major incidents because of their effective immune system.

In the event of severe symptoms in a COVID-19 patient, along with the blood thinners; **TCYTE** can complement as it works on both, increasing platelet count and anticoagulation benefits. The reason being that the main etiological factor - cytokine storm needs an anti-inflammatory effect to tone down pro-inflammatory cytokines and their cascade of cardio-vascular effects.

To boost immunity:

**(Adults and Children over
12 years of age)**

TCYTE syrup - 10ml twice a day

Children below

12 years of age

TCYTE syrup - 5ml twice a day

For 5 Days

(Repeat same course after every 3 to 4 weeks)

Managing Complications:

**(Adults and Children over
12 years of age)**

TCYTE syrup - 10ml 3-times / day

Children below

12 years of age

TCYTE syrup - 5ml 3-times a day

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