

Virus or Visha? Anti-Toxins/Detoxification Solution of SARS-CoV-2

Divya Kajaria^{1*} and Tanuja Nesari²

¹Department of Kayachikitsa (Internal Medicine), All India Institute of Ayurveda, New Delhi, India

²Department of Dravyaguna (Modern Pharmacology), All India Institute of Ayurveda, New Delhi, India

Abstract

The article explores the concept of developing pathogenesis specific medicines for the management of SARS-CoV-2. This is high time to shift the paradigm from pathogen specific (vaccine) treatment to pathogenesis specific treatment for the permanent solution of such pandemics. The article gives an empherical outlook about the fact that immune system gives a sequential response to any invading matter and augmenting the immune response at first step prevents the development of disease. During evolution, immune responses for invading proteins are specified and categorize based on their lethality. Those proteins which are encounter during envenomation are recognized by the immune cell as toxin. The core concept that the human body has stored memory for venomous protein response conclude possibility that envelop proteins of coronavirus belongs to venom group of protein. The article introduces the concept that human immune system recognizes novel coronavirus envelop protein and nucleocapsid as toxin and therefore giving hyper-immune response like cytokines storm. Potential of this concept and its utility in the management of COVID-19 is discussed under two headings (1) Use of anti-toxin herbs and (2) Detoxification therapies. Herbs described as Anti-toxin can be extracted and use as natural source of neutralizing antibodies for passive immunity. The article gives the details of natural ways described in Ayurveda for creating HERD immunity and also explains the concept of cosmic immunity, its role in the outbreak of epidemics and utility in prevention of spread of disease. Novel concept of neuro-endocrine-immune response (using thought modulation as immune-stimulant) and the possibility of pseudo-illness due to infodemic is also converse in the article. The Ayurvedic measures described in the article can be used for asymptomatic patients, quarantine people and high risk health workers. These are simple, safe measures that can be easily followed to maintain physical as well as mental health during pandemic.

Keywords: Envenomation • Latent carriers • Neuro-endocrine-immune response • Neutralizing antibodies • Anti-toxin herbs

Abbreviations: COVID-19: Corona Virus Disease 2019 • SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus-2 • SIR: Sequential Immune Response • MHC: Major Histocompatibility Complex • NEI: Neuroendocrine Immune Response • ACTH: Adrenocorticotrophic Hormone • JDh: Janpadodhwansa • Th1: T helper type 1 • Th2: T Helper Type 2 (gene) • PAMPs: Pathogen Associated Molecular Patterns • STAT1: Signal Transducer And Activator Of Transcription 1 • STAT2: Signal Transducer And Activator Of Transcription 2 • ISGs: IFN-Stimulated Genes • TNF: Tumor Necrosis Factor • IL: Interleukin • DPPH : 2,2-Diphenyl-1-Picrylhydrazyl • NO: Nitric Oxide • NDV: Newcastle Disease Virus • PBMCs: Peripheral Blood Mononuclear Cells • VC : Vital Capacity • TV : Tidal Volume • ERV: Expiratory Reserve Volume • BHT: Breath Holding Time • PEFR: Peak Expiratory Flow Rate • EC: Endurance Capacity • HST: Harvard Step Test • G-CSF: Granulocyte-Colony Stimulating Factor • IP-10: Interferon-Inducible Protein 10 • MCP-1: Monocyte Chemoattractant Protein 1 • MIP-1A: Macrophage Inflammatory Protein-1 Alpha • ISRE: IFN-Stimulated Response Element • CRS: Cytokine Release Syndrome

Introduction

In December 2019, a case of pneumonia of unknown origin was reported in the Wuhan city of Hubei province, China and officially this was the first case of novel corona virus infection [1]. World Health Organization (WHO) declared it as pandemic on 11 March 2020 as it spread to over 200 countries and territories across the globe [2]. As of now 7th June 2020, there are 6,750,521 laboratory-confirmed cases of coronavirus disease 2019 (COVID-19) infection globally, with 395,779 reported deaths [3]. The World most powerful country is affected worst with >1.96 million confirmed cases and >1 lakh death reported. India reported 247,000 confirmed cases and 6929 deaths till now (7th June 2020;

***Address for Correspondence:** Divya Kajaria, Assistant Professor, Department of Kayachikitsa (Internal Medicine), All India Institute of Ayurveda, New Delhi, India, Tel: +8826167515; E-mail: divyakajaria@gmail.com

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6.45 PM) [4]. SARS-CoV-2 is a new strain of coronavirus that has not been previously identified in humans. Facts related to the origin or original source of virus is much conflicting. Mode of transmission is air droplets and human-to human via direct as well as indirect medium [5]. The COVID-19 pandemic is one of the major infectious threats of the century. It is rapidly progressing worldwide and a substantial number of patients get severe COVID-19 related pneumonia that requires mechanical ventilation and admission to the intensive care unit. The acute respiratory distress syndrome is associated with a substantial mortality and morbidity partly as a consequence of uncontrolled lung and systemic inflammation [6]. At this time, there are no specific vaccines or treatment for COVID-19 is available. Scientist, pharmaceutical companies and physician from all over world are working day and night to search cure of COVID-19. Earlier China claimed that Traditional Chinese Medicines are useful in the management of COVID-19. Indian Traditional System of Medicine, Ayurveda hold the treasure of herbs and dictum for longevity and conquering diseases should also be search for the management of COVID-19.

Literature Review

Ayurveda enwrapped the secret of healthy living based on acquaintance of natural law abiding with its unique holistic approach of treatment. Ayurveda

consider imbalance of three humors (disturbance of homeostasis) is the root cause for all diseases. The clinical sign of this imbalance is reflected in the loss of strength (both physical as well as mental); the capacity to cope with the stress, external as well as internal and in terms of medical science it is defined as loss of immunity. As Ayurveda is an absolute clinical science where every entity related to the patient is given objectivity to assess its magnitude for planning the treatment including dose of medicine that exclusively decided for individual. Enduring this golden rule, immunity is also quantified in terms of Bala (strength). There are three types of Bala viz. Sahaja (genetic/ innate immunity), Kalaja (cosmic immunity) and Yuktikrita (acquired immunity). It is important to mention here that besides considering natural immunity and acquired immunity, Ayurveda also consider cosmic immunity. This is very important concept that has to be explored in term of immunotherapy. Bala is also related to Oja which is defined as vitality. Good immunity improves vitality. This is very basic introduction about the fundamental concepts of Ayurveda which is necessary to enumerate before discussing the treatment modality for COVID-19 through Ayurveda. It is written in Ayurveda that naming of the disease is not always possible and gives the liberty to plan treatment by understanding the pathogenesis of the disease i.e., its origin, its mode of spread, the target organ or site of inoculation of pathogen, nature of disease causing agent, etc. Therefore, it is necessary to understand its pathophysiology before formulating treatment protocol. On the basis of symptoms, nature of virus and considering its fatality the COVID-19 related illness can be correlated with Jangam Visha (zootoxin) janya vyadhi. Based on symptoms it can also be correlated with Vishama Sannipataja Jwara (Vata predominated depleted Kapha Sannipataja Jwara). There may be different opinion regarding its correlation in Ayurveda, therefore treatment should be plan according to patho-physiology of the disease. As per Ayurveda, Visha causes immediate loss of life and its fatality depends upon its size; smaller the size, fatal is the Visha. Visha has unique property that it disseminates immediately in the whole body causing instant loss of life. On the basis of origin there are two types of Visha viz. Sthavara (plant toxins) and Jangama (animal toxins). The most interesting fact is that animal toxin can cure plant toxin and vice-versa. The scientific explanation for this concept is that the toxic proteins of different origin (plant and animal) act as natural neutralizing antibody for each other. Thus, they can be used as passive immunity. This can be understood with an example – snake venom which is highly modified saliva having zootoxins containing more than 20 different compounds, mostly proteins and enzymes. Venom proteins mainly belongs to at least eight families: metalloproteinase, disintegrin, serine proteinase, phospholipase A (2), etc. on the other instant plant toxin includes ribosome- inactivating protein, lectins, protease inhibitors, antimicrobial peptides, etc. [7,8]. Encountering both groups of polypeptides nullifies each other lethal biological effect. This is very clear that toxins are capable of producing the lethal biological effect because of its ability to digest and immobilize its prey which signifies that these polypeptides have natural ability of cellular adherence and cell penetration without getting trapped in innate immune cells of the host. This natural capacity of toxins is non-specific to the type of host cell i.e., snake venom is as poisonous for human being as it is lethal for cattle. This ability of toxins is attributed to its cytotoxic enzymes like phospholipase that transforms the phospholipid molecule into a lysophospholipid. Lysophospholipid gets attached with fat molecule causing rupture of cell membrane. This ability of toxins to get access of any cell can be used for the medicinal benefit but to the limited extent. There are 24 types of treatment for poison described in Ayurveda. Among these, few remedies are entirely for the management of snake venom while other can be used as general measure to treat any type of exogenous toxin. Treatment is based on the manifestation suggesting the level of immunity is infringed. The aim is to wipe-out the toxins as soon as possible or neutralize it so that its biological effect can be nullified. Some relevant concept of Ayurveda in the regard of immunity has to be understood before discussing pharmacological and non-pharmacological interventions for the management of COVID-19.

Targeted response (Self vs. Non-self or Harmful vs. Non-harmful)

The concept of pathogenesis based medicine emerges from the fact that body immune system opt a sequential immune response. In this sequential

response, no step can be pass over neither any step can be replaced irrespective of the diversity of pathogen. The very first step in immune response is identification of invading particle/ substance as self-versus non-self or harmful versus non-harmful. This ability to distinguish what is foreign from what is self is a fundamental feature of adaptive immunity. Failure to proper identification leads to destruction of host's own molecule causing autoimmune disorders. And erroneous identification of non-harmful as harmful leads to allergic reaction or even anaphylactic reaction. Identification of pathogen (any substance having ability to produce disease) and its classification for recruiting most effective form of adaptive immune response for their destruction/expulsion is exclusive work of Innate immunity. The innate immune cells having Pattern Recognition Receptors (PRPs) identify two classes of molecules (1) pathogen-associated molecular pattern which are associated with microbial pathogen and (2) Damage-Associated Molecular Patterns (DAMPs). Thus, the innate immune cell can recognize particular types of molecule (proteins) that are common to many pathogen but absent in host cell. These pathogen associated molecules stimulate two types of responses- inflammatory responses and phagocytosis. The innate immune cell through PRPs can recognize various pathogen associated immunostimulants (PAIs). These PAIs may be specific like peptide containing formylmethionine at the N-terminus must be of bacterial origin or it be generally composed of any molecule that do not occur in multicellular host cell. Once the foreign matter is identified only then the further response is tailored. Thus, at first step the immune response is much generalized and is divided into two category (1) antigen (non-self & harmful) and (2) toxin (non-self & every harmful). Depending upon this initial screening the next level of immune response is decided. Thus, beyond diversity of pathogens, body immune response is customized as anti-allergic or anti-toxin response. Therefore, it is postulated that irrespective of the causative organism the anti-toxin or anti-allergic treatment can be given to augment the primary immune response.

Understanding the concept of poison/ toxin mitigating it with virus

Toxin is defined as a poison of plant or animal origin, especially one produced by or derived from microorganisms and acting as an antigen in the body. Virus produces a wide range of structural as well as biochemical changes in the host cell that eventually causes its death. All these effect of virus on host cell are termed as cytopathic effects including cell lysis, alterations to the cell membrane and apoptosis. Proteins of virus have distinctive function in altering cellular signaling that results in cessation of normal activities and finally death of cell. Thus, virus has toxic effect on host cell or in other words virus is taken as antigen by host cell. Therefore as soon as the virus gets entry into the cell the body immunity starts targeting to destroy it. According to Ayurveda there are seven layers of immunity that are breaches by the toxins to finally cause death of organism. At each layer there are specific manifestations and also specific treatment. There is an emerging concept of Sequential Immune Responses (SIR) that describes the sequential response of immunity in higher animals [9]. It is new in sense that it projects how the component of immune system get activated in stepwise manner to counter the existing threat rather than merely describing the initiation of immune response. According to this model, the first step involves activation of enzymes like NADPH oxidase etc., present in host cells. Step 2 involves activation of immune cells like macrophages, next step involves more advanced cell to recognize pathogens like dendritic cell or neutrophils. Step 5 involves presenting antigen to T lymphocyte through Major Histocompatibility Complex (MHC). Step 6 includes synthesis of antibodies by B lymphocytes and Step 7 is final lysis of host cell with destruction of antigen. Accepting this concept necessitate the sequential management plan for the treatment of disease.

Concept of vishakanya in ayurveda

The visionary Acharyas of Ayurveda know the fatality of diseases caused by Visha or toxins and therefore there is one complete section devoted for the description of types of poison, their origin, manifestation, etc. While describing the methods by which the toxins can be transmitted to the human (especially the King or influential persons), there is description of human to human sexual mode of transmission by Vishakanya (poison damsel). This is very interesting

concept in which young girl were raised on increasing dose of poison until she become poisonous. This is an excellent example of concept of adaptability. Giving small dose of poison regularly develops the antibodies/cellular proteins that inhibit the entry of toxins into the cell. As the toxin does not get access into the cell the host cell remains unaffected and therefore no symptoms of toxin infestation appears. On the other hand despite of oral ingestion of toxin, it remains in the circulation as well as in body fluid without getting metabolized or phagocytosed and above all its concentration in bodily fluid as well as in circulation is directly proportional to the amount of oral intake. As the toxin remains in the bodily fluid as well as in circulation it is possible that there is formation of neutralizing antibodies that defends the cell by neutralizing the biological effects of toxin. As per definition, neutralizing antibodies are part of the humoral response of the adaptive immune system that defend host cell against virus, bacteria and bacterial toxins [10]. These neutralizing antibodies bind specifically to the surface structure of toxin molecule and prevent it from interacting with the host cell and inhibit its entry into the cell. Neutralizing antibodies are most efficient in combating intracellular parasite like viruses that require host cell for replication but is not effective in preventing the extracellular replication of pathogen. Neutralizing antibodies are different from binding antibodies that bind the antigen and assist the recruitment of immune cells for their complete destruction. The concept of Vishakanya signifies the role of latent carrier in the spreading of disease. This is useful concept for the management of COVID-19. In condition where *in-vitro* harvesting of IgG is not possible to develop passive immunity, toxin polypeptides can be use as neutralizing antibodies [10].

Concept of shanka visha (neuroendocrine-immune response)

This is also an evolutionary concept of Ayurveda suggesting the neuro-hormonal immune relation. As per Acharya Charaka, mere suspicion of poison without real encounter of any toxic substance can also provoke the symptoms of poisoning. The message is very clear: the body gives the alarming symptoms without original encounter of the threat. The thoughts of poisoning stimulate the memory of poisoning (based on previous exposure or knowledge gained through external sources / social information viz. hearing, watching or reading) which in turn stimulate acute stress response activating all the immune cell and giving the symptoms of poisoning. Here it is important to mention that one is able to give the symptoms of poisoning either because he has stored memory of such reaction (learned reaction) or the immunological cascade that has to be functional after encounter of any such toxins in already stored in genes i.e., during evolution while the human being subject to various types of exotoxins the replica for each type of response based on the reading of proteins in toxin is stored in genes memory. This principle can be utilized both in good as well as bad sense. Its negative aspect is that the excessive awareness of the disease originally create disease because at subconscious level the thoughts are processed and stored in memory as neural memory track encoded with particular set of neurotransmitters that are again selected based on the external information and genetic coding thereby unconsciously disease is developed in the mind. There are lots of research showing the relation between level of cortisol and IgE level, cortisol and high blood pressure, cortisol and insulin level, etc. suggesting the direct link between stress and manifestation of disease. The positive aspect of this principle is that the body can be prepared for possible threat prior to the original encounter of threat similar to injecting low virulence bacteria for synthesis of antibodies in the body without developing disease. Idiopathic anaphylaxis reaction is an example of Sanka Visha (NEI) in which rapid allergic reactions starts that often causes death. Without any known or obvious reason the immunological reactions starts with the binding of IgE to the undefined antigen causing disruption of mast cells and release of inflammatory mediators that subsequently increases the contraction of bronchial smooth muscles, trigger vasodilation, increase the leakage of fluid from the blood vessel and reduces heart muscles contractions. This unknown antigen if taken as stress which triggers a neural response in hypothalamus followed by stimulation of pituitary gland and secretion of Adrenocorticotrophic Hormone (ACTH). ACTH stimulates adrenal gland via the sympathetic nervous system releasing the hormone epinephrine. Epinephrine results in the production of the hormone cortisol. Cortisol in turn activates IgE

producing allergic response. During this neurohormonal-immune response, the intensity of emotion that is brought on by the stimulus will also determine the nature and intensity of the allergic response.

Above two concepts make us understand that immunity is regulated with great precision in human beings [11].

Concept of Janpadodvansa (epidemics) in Ayurveda

Mass destruction of population at a particular time is known as Janpadodhwansa (JD) and is well described in all Ayurvedic Samhitas (Charaka Samhita-Vimana sthana-3rd Chapter, Sushruta Samhita while discussing Ritucharya under the title Maraka-Sutra sthana- 6th chapter and Ashtangas angraha, described under Viruddhanna Vijnaniyam chapter 9th of Sutra sthan). The concept of epidemics and pandemics are well known to the great Indian physicians and they have also documented its management. Before discussing the management of epidemics as per Ayurveda, it is important to understand its pathophysiology. According to Acharya Charak (the great Indian physician), changes in the celestial movement or direction causes vitiation of season which in turn vitiates the land (soil) and produces epidemics. As we know today, that season on earth occurs because the axis of rotation of earth in its orbit remains tilted in one direction (about 23½ degree). Season changes because the orientation of earth axis changes over time. This is called Precession. Spinning of earth on its axis not only determined the season but also determined the electromagnetic field on the earth. Change in the intensity of magnetic field influences the movement of ionic charge (ionosphere). These changes influence the living system also. They changes the blood flow, especially in capillaries, affect blood pressure and boost adrenaline. Thus, astronomical changes are linked with seasonal disturbance which in turn causes disturbance in the ecosystem and changes the flora; spoiling the soil, water and air. Even slight change in the milieu extern disturbs the homeostasis of milieu interne. These changes results in excessive production of free radicals and Reactive Oxygen Species (ROS) which in turn impair the cellular signalling and ultimately causes cellular damage. The description relates the energy imbalance of environment with the outbreaks of disease at a particular time. Thus, as per Ayurveda the reason for such outbreaks is impaired immunity this also points out one more interesting concept of cosmic immunity (Kaalaja Bala) which is exclusively defined by Ayurveda and yet unknown to the modern science [12].

Oupasargika roga (communicable diseases)

Ayurveda describes communicable diseases under the heading of "Oupasargika roga" as-Oupasargika roga samsarga jatah i.e., these diseases occurs due to contact with affected person. The different modes of disease transmission from one person to another are mentioned in Ayurveda including human-to human transmission like Prasangath (sexual transmission), Gatra samsarsath (direct physical contact includes hand shaking, kissing, hugging etc.), Nishwasath (respiratory droplets and aerosols), Sahabhojanath (sharing food with infected person), Sahasayayasanath (sitting and sleeping with infected person- indirect contacts including touching contaminated surfaces, objects), Vastramalyanu lepanath (using the clothes, cosmetics and ornaments of infected person). Acharya Sushruta mentioned that diseases like Kushta (leprosy and other skin diseases), Jwara (fevers of epidemic origin like swine flu, SARS-CoV-2, etc.), Sosha (pulmonary tuberculosis), Netrabhishyanda (conjunctivitis) etc., are example of communicable diseases. The only way to prevent oupasargika roga is to avoid direct or indirect contact with infected person as much as possible [13].

Concept of cosmic immunity & its relation with circadian cycle and outbreaks of pandemic

According to Ayurveda there are three types of Bala (immunity) viz. Sahaja (innate immunity), Yuktikrita (adaptive immunity) and Kaalaja (cosmic immunity). Kaalaja Bala depends upon season. Whole year is divided into two sections Aadan Kaal (Uttarayan or Northern solstice) and Visarga Kaala (Dakshinayaan or Southern solstice). The strength of individual or Kaalaja Bala is naturally diminished during aadan kala which includes late winter, spring and summer seasons. The factor responsible for reducing strength is Sun. Scorching sun rays produces excessive heat that absorbs fluid and

vitiated wind (Vata) and results in loss or reduction of strength whereas during Visharga Kala moon is more powerful giving coolness and strength to the individuals. Thus, as per Ayurveda the immunity of an individual depends upon cosmic rays and when this immunity diminished, epidemics occurs (JDh). In current scenario, the outbreak of corona virus starts in late winter (December 2019) trapping the whole world till the midst of March and assume to continue upto June-July i.e., aadana kala disease during which the cosmic immunity is naturally diminished. "Cytokines storm" or imbalance in the Th1/Th2 immunological response and delayed innate immune cell response in recognizing the virus protein by pathogen-associated molecular patterns (PAMPs), high-levels of pro-inflammatory cytokines, delayed in interferon-(INF1) related immunological cascade including activation of JAK-STAT pathway, stimulating phosphorylation of STAT1 and STAT2, transcription of IFN-stimulated genes (ISGs), etc. is responsible for easy viral entry and faster viral replication. Viral entry is an energy consuming process and mounting of immunological response instantly to combat viral replication also require huge energy. Now it has to be understood that how the body energy is related to the cosmic energy and what is its role in diminishing immunity at a particular instant of time? A recent research study published on Jan, 2020 in Cell Reports, by Cincinnati children's hospital medical center tells that fat cell can sense sunlight. The study concluded that sunlight is required for normal energy metabolism. Sunlight exposure stimulates light-sensing genes –opsins which in turn stimulate white fat cells to release fatty acids into the bloodstream, which is further utilize by different cells in the body for liberation of energy. Authors postulate the possibility that photons may penetrate the deeper tissues of skin and affect the cell behavior. It is difficult to depict the clear relation between immunity and sunlight and outbreak of epidemics without any direct evidence but it is very clear that sunlight exposure will definitely have a protective as well as curative role in immune disorders [14].

Detoxification

Using anti-toxin medicines and detoxification therapy like Panchakarma helps in neutralizing and eliminating the endotoxins. Here, toxin refers to anything that causes harm or has deteriorating effect on health including both

mental as well as physical health. The mode of action of herbs describe in Ayurveda as anti-toxin is detailed based on available *in-vitro*, *in-vivo* as well as clinical research studies search on electronic media (Pub Med, Scopus, Elsevier, Science Direct, Google Scholar, etc.). Anti-toxin herbs in Ayurveda is described in Table 1.

Anti-toxin therapies in ayurveda (Panchakarma)

Detoxification or biopurification term can be used to explain the meaning of Panchakarma in border sense to non-Ayurvedic personals. As per Acharya Charaka, Rasayana and Sodhana (Panchakarma) are two treatment modalities for epidemics. Panchakarma including five procedures is not applicable to all individuals at a time because physician has to determine individual's eligibility (that depends upon his strength and severity of disease) for it. Moreover the classical Panchakarma procedures takes longer time for proper execution as it is given in sequential manner viz. at first step Deepana-Pachana is given for 3 to 5 days followed by snehapana (oral intake of medicated ghrita) for 5-7 days followed by external massage (Abhyanga) and sudation (Swedana) for 2 days after which Vamana or Virechana is given followed by Samsarjana Krama for 3-7 days. Thus, overall it takes around 15-21 days for completion of procedures. Beside this, these procedures should be carried out under strict observation and close supervision of physician better should be carried out in indoor patients to avoid any complications. Though it is also very true that these procedures if performed perfectly as per the dictum then they have capacity to cure the autoimmune diseases and potential to rejuvenate each and every cell. Considering the importance of Panchakarma and making it more practicable for the use of common man during this pandemic a non-classical form of Panchakarma procedure is brief here:

Sadhya Virechana: This can be applicable to asymptomatic COVID-19 patients, patients in quarantine for easy expulsion of toxins. Following is the module for the same:

- **Step 1:** Deepana- Pachana- with Panchkola* and Nagarmotha powder (*Cyperus rotundus* root powder) given in equal quantity (3g each) twice in a day with luke warm water for two-three days.

Table 1. Anti-toxin Herbs in Ayurveda and its pharmacodynamics activities.

Name of the Herb	Pharmacodynamics activities
Haridra (<i>Curcuma longa</i> Linn) [15-22]	1. Immune-stimulatory Anti-inflammatory activity Antioxidant activity
	2. Inhibits IL-12 production in macrophages leading to the inhibition of Th1 cytokine profile in CD4+ T cells
	3. Down regulate the expression of various pro-inflammatory cytokines including TNF, IL-1, IL-2, IL-6, IL-8, IL-12, and chemokines, most likely through inactivation of the transcription factor NF-kappa B.
	4. Acts as anti-toxin and increases the level of IgG and IgM
	5. Having antiviral, antibacterial and antifungal activity.
	Curcumin diferuloyl methane or 1,7-bis (4-hydroxy-3-methoxy-phenyl) hepta-1, 6-diene-3, 5-dione) are main chemical constituent.
Manjistha (<i>Rubia cordifolia</i> Linn) [23-28]	• Mostly <i>in-vitro</i> studies evaluate the pharmacodynamics properties
	• Potent immune modulator- Works on both humoral and cell mediated immunity
	1. Reduces oxidative stress induces kidney damage and immuno-suppression due to its antioxidant property
	2. Its immuno- modulating activity is comparable to Vit E. It significantly improves the humoral and cell mediated immune-suppression caused by polluted air.
	3. Inhibits IgE production from B cell on exposure of allergen (in non-toxic manner).
	4. Having cardio protective activity due to various antioxidant compounds.
Nishotha (<i>Operculina turpethum</i> Linn) [29-31]	5. Aqueous extract of leaves and stem have antiviral property; inhibits rotavirus multiplication by promoting virus-induced apoptosis in MA-104 cells.
	6. Reported for having antimicrobial properties also.
	Anthraquinones, especially in the roots, Rubicoumaric acid and rubifolic acid
	Xanthopurpurin and Vanillic Acid and an antitumor bicyclic hexapeptide RA-XVII are main chemical constituents.
	• <i>In-vitro</i> studies and clinical studies based evidences.
	• Potent antioxidant Prevent kidney & cardiac damage due to oxidative stress
Nishotha (<i>Operculina turpethum</i> Linn) [29-31]	1. Reported to have stimulatory effect on RBCs production in dose dependent manner.
	2. Having antioxidant properties that protect the malignant growth due to oxidative stress.
	3. Antibacterial and anti-inflammatory activity.
	α- and β-turpethin, turpethinic acids (A, B, C, D and E), coumarins, cycloartenol, lanosta-5-ene, 24-methylene-δ-5-lanosterol, α- and β-rhamnose, β-sitosterol, lupeol, scopoletin, betulin, acrylamide, stigma-5,22dien-3-O-β-D-glucopyranoside, β-sitosterol-β-D-glucoside (H-1), 22,23-dihydro-α-spinosterol-β-D-glucoside (H-2), and salicylic acid (CH-2) are important chemical constituents.
• <i>In-vitro</i> studies based evidence for RBCs production enhancer (not evidenced in clinical studies)	

Ela (<i>Elettaria cardamomum</i>) [32,33]	<ol style="list-style-type: none"> 1. Aqueous extracts significantly enhance splenocyte proliferation in a dose-dependent, synergistic fashion. 2. Enhance T helper (Th)1 cytokine release by splenocytes and suppress Th2 cytokine release by splenocytes. 3. Significantly enhance the cytotoxic activity of natural killer cells. 4. Exhibits bronchodilatory effect mediated through Ca⁺⁺ antagonist mechanism. 5. Having anti-inflammatory, antifungal, antiviral and gastroprotective activities. <p>Essential oil of cardamom have predominantly monoterpene constituents, such as 1,8-cineole, α-pinene, α-terpineol, linalool, linalyl acetate and nerolidol and the ester constituent like α-terpinyl acetate.</p> <ul style="list-style-type: none"> • <i>In-vitro</i> studies based evidences. • Potent immune modulator works mainly on cell mediated immunity • Having Bronchodilator activity
Chandana (<i>Santalum album</i>) [34,35]	<ol style="list-style-type: none"> 1. Anti-inflammatory and immunosuppressive activity. Flavonoids extracted from the leaves of <i>Santalum album</i> (SA), demonstrated a significant decrease in proliferation, nitric oxide (NO) production and CD14 surface marker, after 48 hours of treatment. In addition it is found to reduce production of many cytokines and pro-inflammatory mediators. It inhibits cyclooxygenase and thereby mediating its anti-inflammatory effects. 2. Anti-microbial and anti-proliferative properties. 3. Anti-oxidant activity: The essential oil inhibits the oxidative enzyme 5-lipoxygenase and has DPPH radical scavenging activity and, <i>in vivo</i>, oil found to have protective effect on livers damage from oxidative stress and the formation of reactive oxygen species. 4. Immunopharmacological activity of aqueous root extract of SA against Hepatitis B Surface Antigen (HBsAg) and Newcastle Disease Virus (NDV) on human Peripheral Blood Mononuclear Cells (PsBMCs). 5. Aqueous extract of SA possess both anti-inflammatory and anti-viral activity. The main constituents of volatile oil are santalol, isovaleric aldehyde, santanone, santalone and tannic acid. <ul style="list-style-type: none"> • <i>In-vitro</i> studies based evidences for pharmacodynamic activities. • Clinical trials based evidences showing its efficacy in the treatment of acne, psoriasis, eczema, common warts, and <i>Molluscum contagiosum</i>.
Katak (<i>Strychnos potatorum</i>) [36-39]	<ol style="list-style-type: none"> 1. Antianaphylactic and mast cell stabilization activity 2. Antioxidant activity is also reported. 3. Antimicrobial activities shown by the alkaloid fraction of <i>S potatorum</i> against gram positive as well as gram negative bacteria and acid-fast bacteria and fungi. 4. Having wide range of therapeutic uses such as anti-diabetic, anti-inflammatory, anti-ulcerogenic, hepato-protective, anti-arthritis, etc. <p>Diabolone (major alkaloid) and its acetate like brucine, loganin, mannose, sucrose, arachidonic, lignoceric, linoleic, oleic, palmitic, and stearic acids are main chemical constituents. On saponification of the oil: β-sitosterol, stigmaterol, oleanolic acid and its 3β acetate, saponins containing acid oleanic, galactose etc. are also present.</p> <ul style="list-style-type: none"> • <i>In-vitro</i> studies based evidences. • Anti-anaphylactic and anti-allergic are important pharmacodynamics properties to be considering in particular context.
Shirisha (<i>Albizia lebbek</i>) [40-44]	<ol style="list-style-type: none"> 1. Antiviral activity: Ethanolic extract of <i>A. procera</i> bark showed good anti-HIV-1 IN activity whereas ethyl acetate fraction exhibited the most potent activity followed by water fraction by using the multiplate integration assay and molecular docking <i>in-vitro</i> studies. 2. Anti-allergic & anti-inflammatory- Using Catechin as a phytomarker it is observed that AL has potent mast cell stabilizing property. Catechin is found to modulate histamine release and cytokine expression of antigen -IgE activated mast cells in host cell. 3. Antimicrobial activity: The antibacterial activity assess against selective human pathogens viz., <i>Escherichia coli</i>, <i>Salmonella typhi</i>, <i>Pseudomonas aeruginosa</i>, <i>Klebsiella pneumonia</i>, <i>Proteus mirabilis</i> and <i>Shigella spp</i> showed significant antimicrobial activity. 4. Antioxidant activity: Shirisha is said to be the best antioxidant drug in Ayurveda this property is attributed to its free radical scavenging activity by virtue of which it inhibits excitotoxicity produced by the toxins especially neurotoxins. <p>A. Lebbek contains 3',5 Dihydroxy 4', 7 dimethoxy flavone and N Benzoyl L phenyl alaninol. The plant also contains saponins, phenolic glycosides and flavonols. It also possess significant amount of essential amino acids.</p> <ul style="list-style-type: none"> • Experimental as well as clinical studies based evidences.
Nirgundi (<i>Vitex negundo</i>) [45-48]	<ol style="list-style-type: none"> 1. Having antioxidant and anti-inflammatory properties. 2. Anti-Viral activity is reported against chikungunya virus. 3. Having cytotoxic, thrombolytic, membrane stabilizing and antimicrobial activity. 4. <i>V. negundo</i> possess potent snake venom neutralizing capacity. Its methanolic extract significantly antagonized the <i>Vipera russellii</i> and <i>Naja kaouthia</i> venom induced lethal activity both in <i>in-vitro</i> and <i>in vivo</i> studies. <i>V. russellii</i> venom-induced haemorrhage, coagulant, defibrinogenating and inflammatory activity was significantly neutralized by plant extract. <p>Phytochemical investigation shows the presence of flavonoids, essential oils, flavonoid glycosides, terpenes, lignans, stilbene derivative and irridoid glycosides.</p> <ul style="list-style-type: none"> • <i>In-vitro</i> as well as <i>in-vivo</i> studies based evidence for pharmacodynamics properties. • Anti-snake venom (anti-toxin) activity is distinguished property in particular context.
Sleshmatak (<i>Cordia dichotoma</i>) [49-53]	<ol style="list-style-type: none"> 1. Antioxidant activity. 2. Anti-inflammatory, antimicrobial and antifungal activities are also reported. 3. Having anti-proliferative and apoptosis inducing activity. <p>Arabinoglucon, Apigenin, Allontoin, β sitosterol, β sitosterol glycosides, Betulin Kaempferol, Chlorogenic acid, etc. are the main chemical constituents.</p> <ul style="list-style-type: none"> • Mostly <i>in-vitro</i> studies based evidences.

- **Step 2:** Snehapana: Intake of medicated ghrita (Panchatikta ghrita guggulu/ Mahatikta ghrita/ Tiktaka ghrita)** in increasing dose. Starting with 60 mL then 120 mL, 180 mL and if individual is able to drink he/she can take 200/220 mL on 3rd day.

- **Step 3:** External massage with sesame oil or any medicated oil properly and then wrap any blanket and take sun bath for at least 30-45 mins for profuse sweating. This maneuver is followed by bath with luke warm water. Individual take normal diet on that day.

- **Step 4:** The next day of external massage the individual take medicine for Virechana-Trivita avleha- 20 g mixed with Kutaki churna 10 g drink with the decoction of Triphala powder 50 mL. After 3-4 hours purgation starts and it may have <8 to >15 bouts of stool of watery to semi-solid consistency in a day, which stops itself without aid of any medicine. Only individual has to take luke warm water intermittently and at night thin gruel can be taken if feel hunger.
- **Step 5:** After Virechana, diet restriction has to be followed for three days so that the gut flora can be rehabilitated and assimilation resume properly.

Diet plan during virechana krama

Deepan-Pachana: Regular diet with Dhanyaka- Sunthi Jala (water processed with Coriander and zinger powder).

Snehapana: The below food items should be taken only when patient feel excessive hunger.

- Luke warm water whole day as and when required.
- Moong dal soup (soup of green gram).
- Roti (bread) + boiled green vegetables with spices. Whenever required.

Abhyanga- Svedana (External massage and sudation):

- **Khichadi (Polenta):** Prepared by moong dal (green gram) + rice + ginger powder + turmeric powder + Saindhavalavan (rock salt).
- **Moong dal soup:** Soup of green gram with spices- Pepper, ginger etc.
- Roti + boiled green vegetables with spices.
- **During Virechana:** Virechana should be given empty stomach and during purgation hot water is allowed to drink. After completion of Virechana diet is planned according to the number of Vega (number of stool pass).
- **After Virechana:** Protocol of diet after Virechana is very specifically defined in Ayurveda and termed as Samsarjana Krama. This dietary regulation advocates the restoration of normal diet in sequential manner starting from very light liquid diet to normal solid diet. The dietary module given after Virechana is as followed- (Table 2) [15-50].

Mental detoxification techniques

- **Yoga, Meditation & Aachara Rasayana:** Fear and insecurity is so pronounced related to this pandemic that mental unrest is very natural
- **Yoga:** Yoga including Pranayama and Surya-Namaskara is beneficial for every age group even for elderly. Yoga helps to remain active during home stay and improves lung and cardiac functions. Healthy and active body pacifies toxic thoughts through autoregression. These forms of exercise can be easily performed staying at home. Research studies showed that Yoga produces significant improvement in Vital Capacity (VC), Tidal Volume (TV), Expiratory Reserve Volume (ERV), Breath Holding Time (BHT), and Peak Expiratory Flow Rate [56]. As per research study, doing Nadisuddhi, Kapalbhathi, Bhastrika and Bramhari Yoga only for 5 mins for 2 months helps to improve the respiratory and circulatory functions significantly [57]. Yoga practice for 3 months showed a significant improvement in diastolic function with minimal or no change in systolic functions. It is found to be more effective than walking in improving cardiac function in elderly with high Pulse Pressure. On the basis of endurance capacity (EC) measured by Harvard Step Test (HST) before and after aerobic training and asanas with pranayama showed that there is no significant differences in endurance capacity between aerobic exercise and yoga therapy [58]. Yoga helps in improving glycemic control, reduction of blood pressure and improvement in quality of life.
- **Surya-Namaskara (Sun salutation):** In its traditional forms consist of 12 asana, each of the asana (postures) is accompanied by a mantra (chanting religious phrases). It is believe that these mantras represent

expected consequence. Social stigma, discriminative phrases, loss of relatives, loss of jobs, economical setback, scarcity of essential things, etc., create much mental perplexity that have to be manage properly and timely to prevent crime and mental disorders. A cross-sectional study assessing the mental health problems related to social media exposure among Chinese citizen during COVID-19 pandemic (Jan 31 to Feb 2, 2020) showed positive association of mental problems like depression and anxiety with frequent social media exposure [51-54]. The authors suggested that proper measure should be taken to manage the "infodemic" during such pandemics. This study and other such studies point up the fact that pandemic of COVID-19 cause high level of psychological distress and evidences suggested that negative coping styles related to subsequent mental illness [55]. Negative thoughts related to COVID-19 cumulate to disturb mental harmony and produces pseudo-illness. In such condition thought modulation is required to replace the negative or toxic thoughts with positive one or implementation of early psychological interventions to general population for training them about positive coping style and management skills. Yoga, meditation and Aachara Rasayana (behavioral conduct regimen) are simple and useful techniques for maintaining good mental health.

Table 2. Showing dietary module given after Virechana.

Day	Annakala (Timing)		Pravara Shudhi	Madhyama Shudhi	Avara or Hina Shudhi
I	1st	M			
		E	Shali Peya (Thin gruel)	Shali Peya (thin gruel)	Shali Peya (Thin gruel)
II	2nd	M	Shali Peya	Shali Peya	Shali Vilepi(Thick gruel)
		E	Shali Peya	Shali Vilepi	Krita/Akrita Yusha (Green gram soup)
III	4th	M	Shali Vilepi (thick gruel)	Shali Vilepi (thick gruel)	Krita/Akrita Mamsa rasa (Processed/unprocessed meat soup)
		E	Shali Vilepi	Akrita Yusha	Normal diet
IV	6th	M	Shali Vilepi	Krita Yusha	
		E	Akrita Yusha	Akrita Mamsarasa	
V	8th	M	Krita Yusha	Krita Mamsarasa	
		E	Krita Yusha	Normal diet	
VI	10th	M	Akrita Mamsarasa		
		E	Krita Mamsarasa		
VII	12th	M	Krita Mamsarasa		
		E	Normal diet		

*M: Morning; E: Evening; Pravara Shuddhi: No. Of stool >20; Madhyam Shuddhi: No. of stool >10; Avara Shuddhi: No. of stool <10

Table 3. Use of simple herbal medicines and symptoms of COVID-19.

Symptoms	Management
Asymptomatic/ mild symptoms quarantine	<ul style="list-style-type: none"> Sadhya Virechana followed by Rasayana therapy (Shirishavleha)
Fever	<ul style="list-style-type: none"> Drinking water processed with Tulsi (<i>Ocimum sanctum</i> Linn) leaves (30 in numbers) mixed with Bilva (<i>Aegle marmelos</i> L.) leaves (100 in numbers) boil in 1litre of water till it remains one fourth after every 4 hours for two days. OR Take fresh Neem (<i>Azadirachta indica</i>) leaves -10-15 in number and Lahsuna (<i>Allium sativum</i>), 6-8 in number make paste and add mustard oil 1 TSF, given twice in a day for two days. Decoction of Neem (<i>Azadirachta indica</i>), Triphala* and Giloy (<i>Tinospora cordifolia</i>) powder -1/2 TSF each boiled in 500ml of water till it remains one fourth [61].
Respiratory Distress	<ul style="list-style-type: none"> Steam inhalation of Camphor and Eucalyptus oil for 10-15 minutes, twice or thrice in a day. Nebulization with Tulsi aerosol⁶² every 8 hourly. Haritaki churna (<i>Terminalia chebula</i> Retz)- 1 TSF mixed with castor oil-1 TSF taken at bed time with luke warm water.
Blood diathesis	<ul style="list-style-type: none"> Mahamanjsthadhi Kwath** - 40 mL twice in a day Triphala Guggulu*** - 2 tab twice in a day
Prevention	<ul style="list-style-type: none"> Herbal Tea: Tea fortified with five herbs for their putative immunoenhancing effect namely Aswagandha (<i>Withania somnifera</i>), Madhuyasti (<i>Glycyrrhiza glabra</i>), Sunthi (<i>Zingiber officinale</i>), Tulsi (<i>Ocimum sanctum</i>) and Ela (<i>Elettaria cardamomum</i>) all taken in equal parts and added in place of regular tea. Chyvanprashavleha- 10 g daily with milk [63]. Following dietary, seasonal and behavioral regimen as per Ayurveda.

*Triphala: Equal parts of three herbs *Emblica officinalis* (Amalaki), *Terminalia bellerica* (Bibhitaki) and *Terminalia chebula* (Haritaki).

**Mahamanjsthadhi Kwath (ingredients): <https://www.ayurmedinfo.com/2012/02/15/maha-manjsthadhi-kashayam-benefits-dose-side-effects-ingredients-reference/>

***Triphala Guggulu(ingredients): <https://www.ayurtimes.com/triphala-guggulu-triphala-guggulu/>

the 12 zodiac signs and supply energy to the body. It is supposed that in completing these 12 asanas in sequence is equivalent to about performing 288 powerful yoga postures. These asana activates the Manipura (Solar plexus) Chakra, which is located in the navel area also known as second brain. These especially designed body posture in Surya Namaskar helpful in stretching each and every muscles of the body and expose the whole body surface for definite duration of time. As we discussed above that sunlight exposure is beneficial for improving cosmic immunity, a Yogic technique of exercise can be practice daily for 15-30 minutes. These are very simple, easily applicable, and free of cost measures to prevent oxidative stress.

- Aachara Rasayana:** This is good conduct dictum or behavioral regimen that has to followed by every individual in his daily life to maintain mental health. It holds simple practicing techniques like-Being truthful, free from anger (keep away from anger by practicing meditation), avoid alcohol and maintain celibacy, avoid violence, avoid exhaustion, excessive thinking, indulge in creative activities, be cheerful, spread happiness by using pleasing words, chant any religious phrase, keep patience and have courage, indulge in the work of charity, avoid impolite behavior, respect God, elders and teachers, etc. The best way to teach this mental attitude is to display good conduct guidelines on social media and electronic media.

Discussion

COVID-19 is first reported in the Wuhan province of China in December 2019 and it spread all over world within duration less than three months. Despite of the fact that it belongs to the corona virus group in the genus Betacoronavirus, its genomic composition differs markedly from SARS-CoV (2002-2003) and MERS-CoV (2011). It is highly contagious having human to human transmission (infecting >5 million population worldwide as of now). The virus disturbs the immune homeostasis by altering the immune regulatory network. There is bizarre immune response including cytokines storm (high-levels of pro-inflammatory cytokines including IL-2, IL-7, IL-10, G-CSF, IP-10, MCP-1, MIP-1A, and TNF α) initiating sepsis and multiorgan failure [59]. Increased total neutrophils (38%), reduced total lymphocytes (35%), increased serum IL-6 (52%) and increased c-reactive protein (84%) also correlate with disease severity and death. Delayed innate immune response in recognizing the pathogen-associated molecular patterns (PAMPs) and secretion of interferons-1 (IFN-1) which in turn activates the downstream signaling cascade, i.e., NF- κ B and IRF3, accompanied by their nuclear translocation,

activation of the JAK-STAT pathway for the phosphorylation of STAT1 and STAT2 that form a complex with IRF9, and together they move into the nucleus to initiate the transcription of IFN- Stimulated Genes (ISGs) under the control of IFN-stimulated response element (ISRE) containing promoters [60]. Thus, it is very clear that there is a dysregulated/exuberant innate response in SARS-CoV-2 pathology. Previously in case of SARS-CoV, it is proposed that a strong neutralizing antibody response generated against the Spike (S) glycoprotein of SARS-CoV is completely protective in the susceptible host. But it was found that neutralizing antibody titers and the memory B cell response were short lived in SARS-recovered patients. Thus, it is very clear that the pathological hallmark for SARS-CoV-2 is dysregulated innate immune response i.e., immune cells recognize it as harmful toxin rather than antigen and therefore the immune response is much augmented and is mediated as Cytokine Release Syndrome (CRS) characterized by increased IL-2, IL-7, granulocyte colony stimulating factor, IFN-gamma and TNF-alpha. Therefore, anti-toxin or detoxification treatment modality is useful in treating SARS-CoV-2 [61-63].

Now there is reporting of large number of asymptomatic COVID positive cases. Asymptomatic means that body immunity develops the neutralizing antibodies. This is just visualizing the concept of Vishakanya in Ayurveda. As in Vishakanya toxin are in the circulation and body fluid of the girl which can kill anyone who comes in close contact with her but she herself remains asymptomatic. This phenomenon causes SARS-CoV-2 to become highly contagious as the virus spread rapidly via asymptomatic individuals. This signifies that toxins are in circulation but virus is not able to invade the host cell, thus it needs only to eliminate the toxins from the circulation but the question is how? Virechana (medicated purgation as described above) is the simplest and easiest way to move toxins from the circulation. Virechana removes endotoxins regulate trafficking of plasma contents including cytokines, immunoglobulin, carrier proteins, hormones etc. Therefore, it is suggested that asymptomatic patients should be given Sadhya Virechana. This helps in detoxifying the asymptomatic patients as well as prevents them from spreading infection to others. Use of anti-toxin herbs like Shirisha (*Albizia lebbak*) in the form of decoction or proprietary Ayurvedic formulation like Shirishavleha or Shirishasava can be given to symptomatic patients having respiratory distress. Santalum album oil (sandalwood oil) in the dose of 2-5 drops mixed with 10 mL of water taken empty stomach is highly beneficial in inflammatory lung and renal diseases therefore it can be used in the progressive disease involving kidney along with conventional medicines. Similarly, Haridra (turmeric) powder in the dose of half teaspoon can be taken with milk for prophylaxis. Besides these anti-toxin herbs, other simple herbal medicines can be used to combat symptoms of COVID-19 (Table 3).

Conclusion

We hope that the simple herbal remedies described in the article with scientific justification and logistic explanation will prove beneficial to all readers globally especially for those who are working as frontline warriors, asymptomatic patients and those who are in home quarantine. Misconception is the most lethal believable truth particularly when all argument for disclosing the reality is brutally macerated. In this direction, this article is an effort to give the best from the Ayurvedic science for serving humanity.

Authors' Contributions

Concept and collection of information for compilation of article is done by Dr. Divya Kajaria, Editing and finalization of article is done by Prof (Dr.) Tanuja Nesari.

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Consent for Publication

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