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Traditional Indian Medicine

A broad perspective on COVID-19: a global pandemic and a focus on preventive medicine

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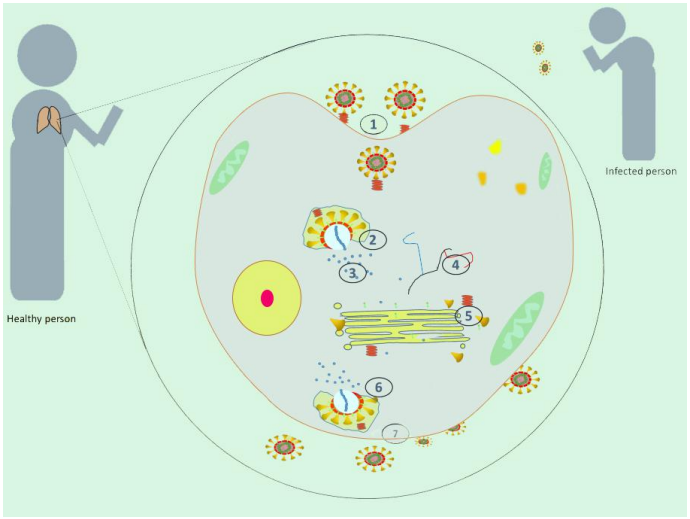
Highlights

The present review suggests certain traditional herbs and complementary and alternative medicine as a supporting public healthcare measure to boost the immune system and also that may provide some lead to treat and prevent this infection.

Tradition

In India and China, the traditional system of medicine comprising Ayurveda, Siddha, Unani, Homeopathy and Yoga & naturopathy and traditional Chinese medicine remains the most prehistoric yet existing customs. Many traditional herbs have been reported to possess potent anti-viral properties. The Kabasura kudineer chooranam (preparation) is a traditional Siddha medicine having literature source from Agasthiyar Mani 4000 (in the form of poetry written by Siddhar Agathiar around 1200 B.C.E.). Ten phytocompounds from the Kabasura kudineer preparation exhibited promising activity against glycoprotein spike COVID. They serve as ligands to attach with viral proteins to prevent host receptor binding. Currently, the traditional herbs and complementary and alternative medicine can be integrated with Western medicine to improve the immune system and to combat the severity of disease in COVID infected patients.



Abstract

Coronavirus 2019 has become a highly infectious disease caused by severe acute respiratory syndrome coronavirus-2, a strain of novel coronavirus, which challenges millions of global healthcare facilities. Coronavirus are sub-microscopic, single stranded positive sense RNA viruses that leads to multi organ dysfunction syndrome, severe acute and chronic respiratory distress syndrome and pneumonia. The spike glycoprotein structure of the virus causes the viral protein to bind with the receptors on the lung and gut through angiotensin-converting enzyme 2. In some cases, the infected patients become hyper to the immune system because of the uncontrolled production of cytokines resulting in "cytokine storm", a devastating consequence of coronavirus disease 2019. Due to the rapid mutant strain and infective nature of severe acute respiratory syndrome coronavirus-2, discovering a drug or developing a vaccine remains a global challenge. However, some anti-viral agents, certain protease inhibitor drugs, non-steroidal inflammatory drugs and convalescent plasma treatment were suggested. The containment and social distancing measures only aim at reducing the rate of new infections. In this view, we suggest certain traditional herbs and complementary and alternative medicine as a supporting public healthcare measure to boost the immune system and also may provide some lead to treat and prevent this infection.

Keywords: Complementary and alternative medicine, Cytokine storm, Immune system, SARS-CoV-2, Spike glycoprotein

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***Abbreviations*:**

ACE2, angiotensin-converting enzyme-2; WHO, World Health Organization; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2; MERS, Middle East Respiratory Syndrome; 2019-nCoV, 2019 novel coronavirus; COVID-19, coronavirus disease 2019; RT-PCR, reverse transcription-polymerase chain reaction; NSAIDs, non-steroidal anti-inflammatory drugs; COX, cyclooxygenase; IL-6, interleukin-6; MSCs, mesenchymal stem cells; RdRp, RNA-dependent RNA polymerase; HIV, human immunodeficiency virus; CAM, complementary and alternative medicine.

***Competing interests*:**

The authors declare that there is no conflict of interest.

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Background

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), a recent emergence of an epidemic strain was designated by the World Health Organization (WHO) as novel coronavirus (2019-nCoV). The first outbreak of this contagion with severe pneumonia was reported in the city of Wuhan, Hubei Province, China, on December, 2019 [1]. As of 20th 11 2020, WHO has recorded 55.6 million cases and nearly 1.34 million fatalities of coronavirus disease 2019 (COVID-19) worldwide and the outbreak was stated a public health emergency of international concern by the WHO on 30 January 2020 [2, 3]. Coronaviruses are zoonotic and later it became anthroponoses [4]. There were also seven human coronavirus strains, first recognized in the middle of the 1960s; including 229E, OC43, NL63, HKU1, SARS-CoV, Middle East Respiratory Syndrome (MERS)-CoV and SARS-CoV-2. Each strain caused lower and upper respiratory tract infection, common cold, pneumonia, bronchiolitis, rhinitis, pharyngitis, sinusitis, diarrhoea [5]. Among these strains, MERS-CoV, SARS-CoV and 2019-nCoV have been associated with more serious and life-threatening diseases [6]. Genetically COVID-19 is less comparable to MERS-CoV by about 50% and SARS-CoV (about 79%) [7]. Clinical studies on SARS-CoV-2 infected patients showed a high concentration of chemokines and cytokines in human plasma, indicating that cytokine storm was related with multi-organ failure and mortality. In certain cases of death and severe illness, co-morbidities have been recorded [8]. These observations in COVID-19 patients are more likely related to SARS-CoV syndrome. Hence, COVID-19 (genera: β-*coronavirus*) may share a sequence similarity with the severe acute respiratory syndrome-related coronaviruses. The virus uses the host cell receptor angiotensin-converting enzyme-2 (ACE2) for an infection as like SARS-CoV [9]. COVID-19 virus has a characteristic structure of spike glycoprotein that plays a critical role in the infection course [10, 11]. The novel coronavirus offers a global risk of tasks and trials both in primary and secondary prevention to treat the infected patients [12].

To date, there are no specific treatment and preventive vaccinations for corona virus infection. Moreover, many viruses remain without effective immunization, there is a growing need to explore more efficient novel antiviral vaccines or prophylaxis that must ensure safety and be cost-effective for controlling and managing viral diseases. The time period between the production of vaccines and mass casualties could cause a major risk to human health. In the light of that, complementary and alternative medicine (CAM) affords a wide range prospects to mitigate the negative impacts in affected individuals [13].

Herbal medicines and natural products have a broad array of biological activities and provides a great source for the production of novel antiviral drugs [14]. Complementary and alternative medications have been commonly used for centuries to treat numerous illnesses, including viral infections. Several scientific validations have shown that herbal extracts have been proven effective for preventing and treating respiratory viral infections [15]. The AYUSH ministry, government of India, has recently recommended the use of Kadha (decoction), an important Ayurvedic method for enrichment of active pharmacological agents from herbs which boosts the immune system and reduces inflammation and disease-severity in the infected individuals during COVID-19 crisis [16]. In this view, we suggest certain traditional herbs and CAM as a supporting public healthcare measure to boost the immune system and also may provide some lead to treat and prevent this infection.

Molecular evolution of SARS-CoV-2 and the mechanism of entry into human cells

SARS-CoV-2, a member of coronavirus belongs to the family Coronaviridae, is an enveloped virus which retain extremely large single-stranded positive sense RNA genome with a length of 26 to 32 kilobases [17]. Its genome sequence displays close similarity of 85% with the two coronaviruses namely bat-SL-CoVZXC21 and bat-SL-CoVZC45, emanated from bats. However, phylogenetic investigation discloses that SARS-CoV-2 is genetically diverse from MERS-CoV and SARS-CoV. Nonetheless, comparative modelling of protein shows that SARS-CoV-2 and SARS-CoV have identical binding domain receptor in spite of amino acid variant at specific residues. The virus has genetic material inside which contains information to make more copies. The genetic material RNA is protected by a hard protein shell. An external envelope made of lipids permits the virus to contaminate host tissue by integrating via the outer cell membrane. There are projections on the envelope called the spikes made up of protein molecules. This virus uses these spikes like as a way to invade into the target host [18] (Figure 1).

The spike protein does two key functions that help host infection; it enables the fusion of virus with the cell surface receptors of host and helps to integrate viral and host cell membranes into host surface membrane. Another protein that attaches to the coronavirus RNA gene is the n-protein (structural nucleocapsid protein), which forms a capsid or shell round the encapsulated nucleic acid. N-protein interfaces the viral assembly through interaction with the viral membrane protein and by facilitating the synthesis of RNA and protein folding, thereby has a key role in virus budding and influences the response

of host cells throughout the cell cycle process and translation of the cells. The ACE2 is an endogenous protein membrane. Upon infection, ACE2's extracellular peptidase domain fixes to the spike glycoprotein receptor domain. Usually, coronaviruses use a trimeric spike glycoprotein consisting of a subunit S1 (that mediates cell interaction, existing from four central domains S1A through S1D and a subunit S2 (viral and cell membrane fusion) in each spike glycoprotein monomer on the envelope to attach with the target cells. This binding triggers a string of events leading to the integration of the viral and host cell membrane, which paves a way for entry into the host genome [19] (Figure 2).

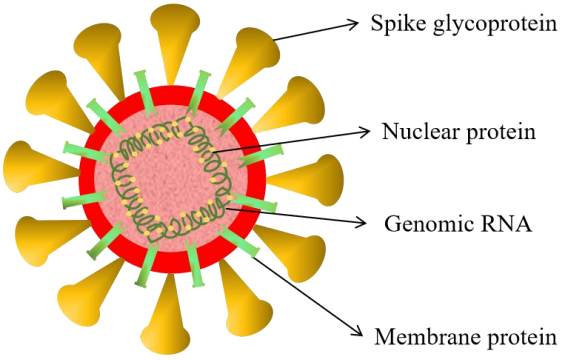

Figure 1 Structure of COVID-19. COVID-19, coronavirus disease 2019.

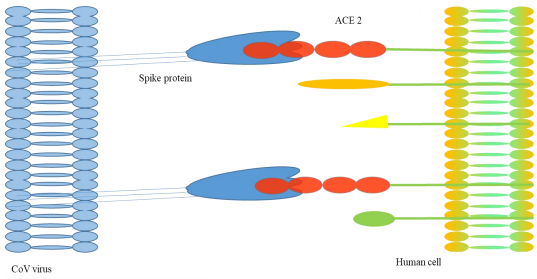

Figure 2 Attachment of coronavirus to the host

Prior cryo-electron microscopic investigations about the SARS-CoV spike protein and the ability to interact with ACE2 cell receptor has demonstrated that the ligand-binding triggers separation of S1 with ACE2, inciting the shipment of S2 to a progressively steady post-fusion stage from metastable pre-fusion stage, which is crucial for the fusion of membranes. Accordingly, ACE2 receptor binding is crucial for SARS-CoV to drive into target cells. Once the protein specifically binds with the receptor, conformational change of the S protein occurs which enables the viral envelope via the endosomal pathway to interact with the plasma membrane. SARS-CoV-2 then releases RNA into host cell. Viral replicase polyproteins 1ab and pp1a are translated from genomic RNA which is then cleaved by viral proteinases into small products. The polymerase enzyme generates a sequence of subgenomic mRNAs by discrete transcription and are eventually converted into specific viral proteins. In Golgi apparatus and endoplasmic reticulum, genome RNA and viral proteins are progressively compiled into virions and afterwards exported through vesicles and expelled out of the host membrane [20] (Figure 3).

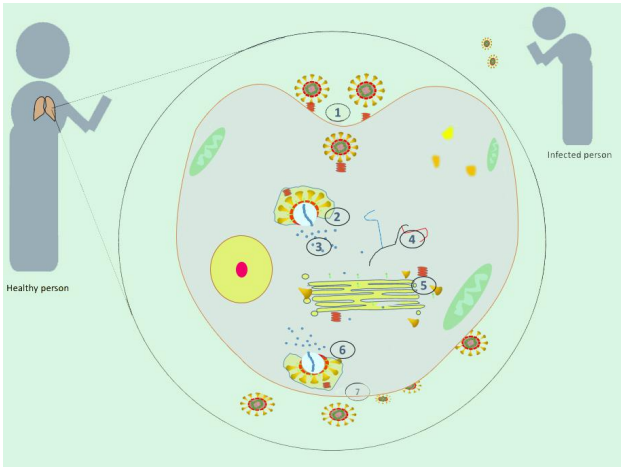

Figure 3 Molecular mechanism of COVID-2019. ① Attachment of coronavirus with the human receptor ACE2 via the spike proteins. ② Coronavirus binds with the host, constitutes a fusion. ③ Discharge of viral RNA into the cytoplasmic membrane of host. ④ After translation, RNA virus produces unglycosylated proteins. ⑤ Proteins were glycosylated at Golgi apparatus. ⑥ Viral capsid contains viral RNA and n-protein. ⑦ Release of coronavirus virions into the lumen. COVID-19, coronavirus disease 2019; ACE2, angiotensin-converting enzyme-2.

Challenges in vaccine production

Understanding more about the molecular evolution of the new coronavirus is important for the development of vaccines. A vaccine must excite the exact parts of the immune system to be effective, and protection is foremost. Good animal models for immunization advancement are not accessible for the new coronavirus. Researchers everywhere throughout the world are endeavouring hard for developing a vaccine for SARS-CoV-2 to spare mankind. There are no accessible immunization against SARS-CoV-2, while past vaccinations or methods used to build up SARS-CoV vaccine can be helpful and effective [21].

Transmission of infection

COVID-19 can be a highly transmittable and pathogenic viral disease triggered by severe acute respiratory illness. The risk of animal-to-human transmission is regulated by numerous factors, for instance, the nature of infection within the host, degree of infection contact, and hence the vulnerability of human population. All these variables are mostly

summed up into three important stages that represent the means of virus transmission [22]. The first stage defines the pathogen strain on human host, the second stage specifies the probability of viral exposure and thus the last stage is influenced by genetics, the probability and extent of infection are regulated by the physiological structure and immunological grade of the human host alongside the second stage factors [23].

SARS virus spreads by coughing or sneezing from an infected individual, leaving tiny droplets within the air. The safe one who inhales these droplets or touches the infected surfaces that get infected as well. Droplet transmission is that the presence of microbes within droplet nuclei, which are usually called particles < 5 μm in diameter and arise from the evaporation of larger droplets or occurs within dust particles. They can stay in the air for long periods of time and be spread over distances of more than 1 m to others [24]. In recent works, live SARS-CoV-2 has been recognized in the stool of patients demonstrating the subsistence of SARS-CoV in the food channel mitigating gastrointestinal signs, likely recurrence, and transmission of the infection through faecal-oral course [25].

Symptoms of COVID-19 infection

The maturation time of the virus must be assessed from 2 to 14 days. The clinical spectrum of COVID-19 differs based on the age and immune system of affected patient [26]. The common signs of COVID-19 infection include dry cough, fever and sore throat [27]. Less common symptoms were reported as aches, cough, diarrhoea, conjunctivitis and tiredness, with phlegm production and the serious infection causes shortness of breath, chest pain and shows respiratory frequency rate of ≥ 30/min, oxygen saturation of blood is ≤ 93%, about < 300 of oxygen supply, coughing up blood and lymphocytopenia [8, 28].

Diagnosis

Depends upon signs and symptoms, an oral swab test is done followed by like real time reverse transcription-polymerase chain reaction (RT-PCR) to confirm the virus infection. RT-PCR measures the viral count and helps to find optimized condition of treatment. After 10 days of infection, RT-PCR is used to conclude the time for downturn of sickness [29, 30]. Typical chest CT-imaging may be strongly recommended to test the abnormalities in asymptomatic patients. The CT-image provides information about the shape, quantity and density of the scathe, distribution of the lesions. Other molecular techniques like reverse transcription-loop-mediated isothermal amplification and reverse transcription-recombinase polymerase amplfication were used to diagnose the coronavirus, which are required for the confirmation of the diseases [31, 32]. On the other hand, another robust method is the detection of RNA by the reverse transcription-loop-mediated isothermal amplification, which has a pH indicator used to readout the amplification based on the colour change [33]. Serological test includes microarrays, a recombinant spike immune fluorescent assay, indirect enzyme-linked immunosorbent assay, micro neutralization, immune chromatographic assay and spike pseudo particle neutralization methods are also done for the diagnosis of coronavirus [34–39]. Early diagnosis also possible with the electron microscope technology and next generation sequencing which analyses the mutation pattern of pathogen [40].

Pharmacological/conventional treatment currently in use for COVID-19

Antiviral drugs

Remdesivir is tested to be a potential drug for the treatment of COVID-19. The drug remdesivir is a C-nucleoside adenosine and it also acts as a phosphoramidate prodrug. This has a wide range of antiviral, prophylactic and therapeutic action against the families of viruses including filoviruses (Ebola), coronaviruses (SARS-CoV) and MERS-CoV [41]. Research showed that remdesivir can help efficiently minimize MERS-CoV-infected mice in the lung tissue, restoring lung function and alleviating lung tissue pathological damage [42]. Remdesivir, a nucleotide analog prodrug, effectively inhibits polymerases of viral RNA. Chloroquine is an antiviral drug that can prevent entry of SARS-CoV by inquisitive with the glycosylation of the ACE2 receptor and its spike protein binding, indicating that chloroquine treatment may be more successful at the early stage of COVID-19 infection and decreasing the expression and function of ACE2 [28].

Protease-inhibiting drugs hamper viral proteases that are responsible for proteolytic cleavage of huge polyproteins, encoded by the viral genome necessary for the expression and replication of viral genes. In an open label, discreetly randomized controlled trial, lopinavir was examined in which COVID-19 patients received either 400mg/100mg lopinavir-ritonavir orally twice daily along with the standard care alone. Treatment with lopinavir and ritonavir causes diarrhoea, nausea, and asthenia so patients getting lopinavir-ritonavir-based treatment have been detected as no benefit [43].

Non-steroidal anti-inflammatory drugs (NSAIDs)

The most widely used, NSAIDs have a wide range of applications. NSAIDs incorporate inhibitors of cyclooxygenase (COX) and COX2 such as ibuprofen, aspirin, diclofenac, naproxen, celecoxib, rofecoxib,

etoricoxib, lumiracoxib and valdecoxib. COVID-19 patients with severe respiratory viral infection are treated with NSAIDs, which produces an extended chance of adverse influences [44]. Use of NSAIDs for urological diseases should still be followed with recognized suggestions, mainly for all patients lacking fever or symptoms of COVID-19, but with greater care. Specific specialities have also issued NSAIDs guidelines addressing conditions for which chronic anti-inflammatory drugs are approved. Conversely, surgeons should routinely test for signs of COVID-19 and illuminate patients before recommending some medication [45]. Type I angiotensin II receptor blockers and ACE inhibitors are prescribed for infections and lead to ACE2 up regulation. It was hypothesized that ACE2-stimulating medicinal products would proliferate the danger of producing lethal COVID-19. NSAIDs may also develop ACE2 due to their pharmacological movement [46].

Convalescent plasma treatment

Convalescent plasma transfusion, a common adaptive immunotherapy is exploited to relieve severe patients. Current studies have shown that one dosage (200 mL) of convalescent plasma has suffered well and could substantially increase or conserve the deactivating antibodies at an elevated level, prompting vanishing the presence of viruses in the blood within 7 days, and the clinical and para clinical standards to improve rapidly within 3 days [47]. Previous study displays that convalescent plasma from COVID-19 patients who have suffered from viral infections can be used for a treatment without serious adverse events occurring. It might therefore be useful to test the treatment and effectiveness of convalescent plasma transfusion in patients affected with SARS-CoV [48]. Immunoglobulin-derived antibodies like plasma-inferred monoclonal antibodies and convalescent plasma are used for the passive immunization therapy that showed some effectiveness in the first two decades of the 2000s. It also acts as a neutralizer against altered corona pandemics such as SARS and MERS. Convalescent plasma-derived antibodies can neutralize a virus by preventing replication (e.g., by complement activation or phagocytosis) or by binding without interfering with replication [49].

Anticoagulants

Hypercoagulable disorder causing vascular thrombosis in COVID-19 is a foremost focus. In a cohort study of COVID-19 patients, distributed intravascular coagulation and increased d-dimer levels were recognized as predictors of poorer outcomes [50]. Heparin has anti-inflammatory activity and can also help to limit virus attachment through conformational modifications to the SARS-CoV-2 surface receptor [51]. Low molecular weight heparin was associated with lower serum interleukin-6 (IL-6) concentrations in patients hospitalized with COVID-19, advising that there could be an additional mechanism besides thrombosis prevention and management [52]. Heparin was associated with COVID-19 spike proteins and IL-6 down regulation, which was found to be complex in COVID-19 patients [53].

Therapeutic targets and methods reported for vaccine development

Monoclonal antibodies

Monoclonal antibodies are monovalent antibody which bind to an equivalent epitope and are derived from one B-lymphocyte clone. Monoclonal antibodies are regularly utilized as diagnostic exams like enzyme-connected immunofluorescence assay, western blot and immunosorbent assays [26]. Monoclonal antibodies based on susceptible viral floor protein websites are increasingly regarded as a useful class of anti-infectious disease medicines and feature demonstrated therapeutic potential for virus sort. Coronavirus-neutralizing antibodies attack the prominent part of the spikes specifically on the interactive portion that mediates entry into the host cell. Powerful neutralizing antibodies also target receptor interactions in the spikes-1 subunit, disabling interactions between receptors [54]. Blocking monoclonal antibodies, because of their tremendous antigen specificity, are perhaps the only applicants for neutralizing virus contamination. Therefore, distinguishing and cloning blocking off monoclonal antibodies that allows you to specifically goal surface viral proteins to restrict the viral passage to host cells may additionally be a completely alluring approach for stopping and treating COVID-19, specifically when powerful vaccines and therapeutics are unavailable inside the origin of the COVID-19 pandemic [55].

Stem cells

Mesenchymal stem cells (MSCs) exhibit self-renewal and multi-differential capabilities that is easily available and flexible in vitro with exceptional genomic integrity and very few ethical issues, indicating their importance in cell therapy, regenerative medicine and tissue regeneration and repair. In stem cells, the immunomodulatory actions are caused by the stimulation of toll-like protein [56]. Research has shown that patients declared positive for SARS-CoV-2 macromolecule have reported promising results using MSCs. When using its reparative and immunomodulatory properties properly, these are also an effective therapeutic approach [57]. MSCs produce antimicrobial effect indirectly by extending the phagocytic function of the microbiota; and specifically, by promoting the secretion of antimicrobial peptides and proteins, and thus by production of substances like interleukin-17 and indoleamine 2,3-dioxygenase.

antimicrobial peptide-mediated arrest of cells occurs through destruction of membrane integrity, inhibition of DNA, RNA or protein synthesis, and association with other endothelial targets. Therefore, stem cells help to suppress the infectious agent [58]. MSCs treatment restrains the overstated reaction of the safe framework and advances, recovers and revives the microenvironment. Treatment with MSCs restrains the system's overestimated reaction and encourages, regenerates and revives the microenvironment. MSCs penetrate the lung parenchyma by entering the bloodstream and exercise the function by improving the micro alveolar pulmonary structure and pulmonary activity that further prevents pulmonary fibrosis. During the management of MSCs, pro-inflammatory cytokines and chemokines are decreased and dendritic cells are regulated in the repaired tissue due to their immunosuppressive capacity. The increase in the rate of interleukin-10 and vascular endothelial growth factor encouraged respiratory parenchymal repair and rejuvenation, which enabled patients with severe COVID-19 pneumonia to recover both clinically and functionally [59].

As a therapeutic option for people affected by 2019-nCoV, mesenchymal stem cells can help improve lung compliance, curb pneumonia and, thus, the factor that causes disease [60]. Duct mesenchymal stem cells being allogeneic and with limited supply, the choice of autologous bone marrow mesenchymal stem cells and adipose-based mesenchymal stem cells may be readily available in greater amounts, even as autologous in nature may help to regenerate the pulmonary micro-alveolar epithelium. It lowers morbidity and mortality, and improves the beneficial standard of living of affected people [20].

Immunosuppressants

People with chronic immune diseases are advised to continue with the immunosuppressive medications with an aim to scale back the danger of greater number of patients become infected with COVID-19 [61]. Cyclosporine A can be a chemical compound related to part of the cyclophilin family. Cyclophillin is involved in folding and hence the inhibitor leads to calcineurin inhibition and the nuclear component of activated T-cells [62]. Mycophenolate mofetil is an FDA-approved opiate blocker, an anti-competitive, specific and reversible inhibitor of inosine monophosphate dehydrogenase, contributing to lymphocyte proliferation activation and the development of antibodies [63]. Glucocorticoids result in a reduced expression of proinflammatory cytokines such as interleukin-1, IL-6, prostaglandins, tumor necrosis factor and leukotrienes, resulting in the growth of anti-inflammatory cytokines and the reduction of inflammatory cytokines [64]. Azathioprine can be a moderately potent immunosuppressant agent, suppressing function of T-cells and generating B-cell antibody [65].

Rituximab is an antibody of glycoprotein-G1 that targets the CD20 antigen, a protein located on the surface of most B-lymphocytes that can induce depletion of B-cells [66]. Methotrexate can be an inhibitor of dihydrofolate reductase which stimulates DNA synthesis, resulting in hepatoprotective and anti-inflammatory activity [67]. During the immune response to virus, interferon binds to its receptor causes Janus kinase activation which activates the signal transducers and activators of transcription components in order to upregulate antiviral immunity [68].

Probiotics

Probiotics have shown useful effects on treatment and prevention of viral infections which proven immunomodulatory activity and skill to stimulate interferon production [69]. Probiotic strains like *Lactobacillus plantarum*, *Lactobacillus casei*, *Bifidobacterium animalis*, *Bacillus coagulans*, *Streptococcus salivarius*, and *Enterococcus faecium* have inhibitory effects on proinflammatory interleukins. Moreover, several conventional probiotics (*Lactobacillus gasseri*, *Lactobacillus rhamnosus*, *Bifidobacterium longum*) potentially increase the extent of antibodies [70]. The antiviral effectiveness of probiotics is elucidated by certain mechanisms. The high-single dose endoscopic administration of appropriate and reliable *Bifidobacterium infantis*, a possible probiotic in patients with gastrointestinal symptoms may result in additional therapeutic effects in coronavirus-infected patients [71]. *Bifidobacterium animalis* theoretically can repress the replication of corona viruses by lessening endoplasmic reticulum stress-related autophagy, particularly the inositol-requiring enzyme 1 pathway, over its anti-interleukin-17 effect. the most pathogenic mechanism that creates viral infection-induced pneumonia seems to be a "cytokine storm"; IL-6 is that the main proinflammatory marker [72]. *Lactococcus lactis* JCM5805 can activate human plasmacytoid dendritic cells in vitro; plasmacytoid dendritic cells play a significant role in anti-viral resistance as a competent type interferon producing cells and an individual development of immunoglobulin A mucosal T-cells. Interferons derived from plasmacytoid dendritic cells type I can indirectly inhibit and propagate viral replication [73]. The probiotics may function as an efficient prevention or treatment decision of viral-based infectious diseases ad quite 20 strains improved the anti-inflammatory interleukins and antibody production against viruses. The utilization of probiotics is an adjunctive option in COVID-19 pandemic [74].

Complementary and alternative medicines

CAMs are diverse healthcare medical practices, gaining much attention World-wide to alleviate the human diseases. India has rich knowledge of traditional medicines to emphasize the human health care system. India has unique structure of AYUSH (Ayurveda, Yoga, Unani, Siddha, Homeopathy) system of medicine which can be used as a supportive medicine during the emergence of new or mutated strains of the virus [75].

Unlike Western medicine, traditional Indian and Chinese medicine have multi-therapeutic benefits and the advantage lies in the effective curative properties and reduce the toxic side effects, improves quality of life, boosts immunity and prolongs survival time [76].

Siddha medicine

Siddha medicine is the ancient medical method commonly practiced in southern India, enhanced with cultural medical expertise and a native of Western Ghats rich biodiversity region. Siddha system treats person and environment as a closed network community [77]. The individual consists of five elements, in multiple combinations such as, Neer (fluid), Vayu (gas), Munn (solid), Akasam (ether) and Ahee (radiance). Such five elements are present in each material but are present in many proportions [78].

Within the body, the biochemical process is regulated by three humours Vatham, Pitham and Kapam (three vital life forces that form the individual body constitution based on Siddha system of traditional medicine). The three humours are responsible for the occurrence of a disease. Those three humours coexist in each and every cell of the body, and work harmoniously. The purpose of the treatment is to restore equilibrium to the mind-body system. Dietary habits have a major role to play not only through preserving health but also in preventing disease [79].

Kabasura kudineer choornam. The Kabasura kudineer (Kabam-cold; suram-fever) chooranam (preparation) is a traditional Siddha medicine having literature source from Agasthiyar Mani 4000 (in the form of poetry written by Siddhar Agathiar around 1200 B.C.E.) and the preparation contains 15 natural ingredients (Table 1). Usually used to treat fever even without an infection in the respiratory tract, which was prescribed mostly during swine influenza outbreak [80, 81].

Table 1 Components of Kabasura kudineer (Kabam-cold; suram-fever) choornam (preparation)

No.	Components	Parts	Character of the herbs
1	*Adathoda vasica*	Leaf	Bitter in taste and helps in Kapha disorders (disease related to fluids and organs).
2	*Anacyclus pyrethrum*	Root	Pungent taste; used as adjuvant in Ayurveda.
3	*Androgra phis paniculate*	Whole plant	Bitter taste and hot helps disaster mitigation interventions.
4	*Cissampelos pareira*	Root	Bitter astringent, carminative; known as short circuit in Ayurveda and highlighted for its efficiency to treat fever, cough and bronchitis etc.
5	*Clerodendron serratum*	Root	Bitter, acrid, thermogenic and lessens expectoration.
6	*Coleus ambonicus*	Leaf	Considered as a diuretic herbal agent and have a pungent taste and odour.
7	*Cyperus rotandus*	Rhizome	As health supplement in Ayurveda and considered best in causing astringent effect.
8	*Hygrophilla auriculate*	Root	Herbaceous used as diuretic and spasmolytic.
9	*Piper longum*	Fruit	Prime rejuvenator drug in Ayurveda used especially for respiratory disorders.
10	*Saussurea lappa* root	Root	Hot in potency, pungent and bitter in taste manages the Vata (energy of movement) and Pitta (energy of digestion and metabolism).
11	*Syzygium aromaticum*	Bark, bud	Sweet, warm-spicy taste; used from ancient time as it maintains the heat system in human body.
12	*Terminalia chebula*	Fruit	In Ayurveda, it supports Vata (energy of movement) and acts as health-harmonizer by cleansing the body system.
13	*Tinospora cardifolia*	Stem	Bitter taste eliminates Kapha disorders (disease related to fluids and organs).
14	*Tragia involucrate*	Root	Small annual herb, forms the basis of an external application and acts as blood purifier.
15	*Zingiber officinale*	Rhizome	Acts as antiemetic, stomachic, expectorant, anti-inflammatory, aphrodisiac etc.

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A docking study reported that 10 phytocompounds from the Kabasura kudineer preparation exhibited promising activity against glycoprotein spike COVID. This research showed 10 phytocompounds, that serve as ligands to attach with viral proteins to prevent host receptor binding. Of these, cucurbitacin B, cardiofoliolide, apigenin and pyrethrin were found to be more efficient with less binding energies needed to bind to spike proteins to prevent viral replication of the fusion lead. Since Kabasura kudineer comprises more active phyto-components, the increased activity was observed. The study showed that Kabasura kudineer could be a prospective Siddha medicine for COVID-19 provided further preclinical and clinical confirmatory studies [81].

Another study showed that Kabasura kudineer plant metabolites may serve as potential anti-SARS-CoV-2 lead molecules for further optimisation and drug development processes to counter COVID-19 and possible viral pandemics [82]. Kabasura kudineer, an official formulation of Siddha described in Siddha's manuscript, is used for phlegmatic fevers, hemorrhagic fever, and is a reliable prescription for fever. In silico studies of plant compounds in Kabasura kudineer against SARS-CoV2 spike protein that supports and increases the reach of these medicinal products in drug reprocessing areas [83]. These studies provide supportive evidence for the therapeutical effect of Kabasura kudineer in COVID-19.

Traditional herbs for the management of novel coronavirus

Herbal remedies were commonly used to prevent and treat various ailments including respiratory viruses. Several antiviral agents have been derived from phytocompounds of medicinal herbs. Some traditional herbs and medicines that are potent against flu viruses are discussed, which may be used to tackle the COVID-19. Since, the traditional medicinal plants ensure more safety and provides immunity, it could help save the lives of individuals with cytokine storm syndrome and reduces the mortality and morbidity rate of the patients infected with coronavirus [84]. There is a vast number of literatures published and still progressing with natural compounds both in India and China after the SARS epidemic about traditional Chinese medicine and CAM treatments for SARS-CoV2.

***Alpinia galanga* L.** *Alpinia galanga* L. has its historical reference as a traditional herbal medicine texted in classical book of *The Materia Medica in Ayurveda*, written by Vaidya Bhagwan Dash and *Bhavapraksha Samhita* (*Emotion Code*) written by Bhavamishra (a treatise, 16 C.E.) [85]. *Alpinia galanga* are of more global value due to its enormous medicinal properties in root oil, *Alpinia galanga* root, root oleoresin and its other volatile oil [86]. *Alpinia galanga* contains specific active flavonoids like kaempferide, alpinin, galangin and 3-dioxy-4-methoxy. The phytoconstituents are known to possess various biological activities include antiviral, antimicrobial, gastroprotective and anticancer activities [87]. Studies shown that 1'S-1'-acetoxychavicol acetate from *Alpinia galanga* rhizomes inhibited the replication of human immunodeficiency virus type 1 by hindering reverse transcription leading to a blockage of human immunodeficiency virus (HIV)-1 replication in peripheral mononuclear blood cells by around > 80 percent. *Alpinia galanga* also has inhibitory function towards human cytomegalovirus and serves as an effective source of platelet-activating factor antagonists [88].

In COVID-19, the ACE2 and the protease inhibitors are the suitable candidates for drug target to halt the life cycle of pathogen. In silico studies of phenylpropanoid compounds from *Alpinia galanga* against 3 target proteins: receptor binding domain-S, protein domain-ACE2, and SARS-CoV-2 protease demonstrated galangin, a phenylpropane from *Alpinia galanga*, bind to these three receptors with lower energy of docking scores −9.94, −6.05 and −6.16 compared to the reference standard compounds. Therefore, the phenylpropanoid compounds of *Alpinia galanga* possessing inhibitory effect to these receptors suggests the protective mechanism from viral infection [89]. Further *in vitro*, *in vivo* and clinical research can be done to prove the anti-COVID effect of these phytocompounds.

Vitex negundo. *Vitex negundo* hold great therapeutic values in Ayurveda and is referred to as the remedy for all diseases. *Siddha Yoga* by Vrinda around 9th century C.E., various Ayurvedic classics and *Nighantus* (lexicons, traditional collection of words, grouped into thematic categories; 10–17 C.E.) refer its medicinal value [90]. The active chemical constituents such as vitedoin A, vitedoamine A, vitedoin B, vitexoside, negundin A, negundin B have been showed to possess various medicinal properties. The *Vitex negundo* has peripheral and central analgesic effect and possesses anti eosinophilic activity. It exhibits strong antipyretic activity in yeast induced hyperpyrexia model and also the phytoconstituents can be used as adjuvant with standard drugs [91, 92]. *Vitex negundo* and its flavonoid contents are effective in targeting the reverse transcriptase activity of HIV, thus acting as anti-viral agent [93]. *Vitex negundo* have been known to hit the RNA-dependent RNA polymerase (RdRp) entangled in dengue virus and chikungunya virus, thereby inhibits the protein expression and replication of the virus. In COVID-19, RdRp is a core enzyme involved in synthesis of positive and negative-strand of RNA which offers a potential target for drug design. As *Vitex negundo* targets the essential enzymes of viral infection, it can also be tested for action against SARS-CoV-2 [94].

Adhatoda vasica. *Adhatoda vasica* has been used in

indigenous medicinal system for over 2,000 years, indicated in the classical book of *Bhavapraksa* (lexicon of medicinal plants used in Ayurveda and covers etymology by Shri Bhava Mishra (16th century C.E.) [95]. *Adhatoda vasica* has powerful inhibitory activity on retro pepsin (HIV-protease) by diminishing the life cycle of HIV at the active site. Studies disclosed that the leaves of this plant contain medicinally purposeful quinazoline alkaloids such as vasicine, vasicinone, vasicoline, anisotine and deoxy vasicine. Vasicine is an important compound and the studies showed that it suppresses the antigen-induced mast cell degranulation and proved to have bronchodilatory effect [96]. A commercial drug called Wintry, contains both vasicine and vasicinone for bronchial asthma treatment and the Bisolvon, an intravenous drug was developed from vasicine helped to clear airways by lessening the excretion of mucus and opening air passages. Moreover, this alkaloid rich plant owns respiratory stimulant activity through its action on breathing centre and partially on peripheral olfactory fibers [97]. These phytocompounds act as an active anti-herpes simplex virus 1 and anti-herpes simplex virus 2 mediator by disturbing the early stage of viral infection [98]. Currently, in silico studies on vasicoline and anisotine has been proved to be effective than hydroxychloroquine and pemriolast (clinically proved drugs) against SARS-CoV-2 by targeting both protease and RdRp [99]. Thus, these two compounds could be a very promising lead for the COVID drug development.

Curcuma longa. *Curcuma longa* L. has been well documented in Ayurvedic pharmacopoeias which includes *Sushruta Samhita* (treatise, systematic compilation of knowledge; 1500 B.C.E. –600 C.E.), *Nighantus* (lexicons, traditional collection of words, grouped into thematic categories; 10–17 C.E.), *Chikitsagrantha* (compendia of Ayurveda by Chakrapanidatta; 11th century C.E.) and *Rasashastra* (compendia related to alchemy by Shrimad Govind Bhagvatapad; 7th century C.E.) [100]. Turmeric extract and curcumin acts against virus by suppressing the reverse transcription activity and also offers a wide range of biological benefits [101]. Studies have shown that curcumin and its derivative comprising boron are effective against HIV 1 protease [102]. As the compounds from *Curcuma longa* are completely capable of reducing the viral load in the host which helps to slows down the progression of HIV virus, it may be studied for SARS-CoV-2 infection. Molecular docking of curcuminoids and the major compounds of *Curcuma*. Desmethylcurcumin and bisdesmethylcurcumin showed better interaction with the ACE2 receptor, receptor binding domain and SARS protease, thereby believed to contribute for the care and prevention of COVID-19 [103].

Glycyrrhiza glabra. *Glycyrrhiza glabra* (liquorice), a classical medicinal plant has been in use since ancient times (atleast since 500 B.C.E.) in folk medicine and has been referred to as “the grandfather of herbs” [104]. Historically, its use in medicine was found in *Code Humnubari* (complete written legal words and a collection of 282 rules proclaimed by Babylonian king Hammurabi; 2100 B.C.E.) [105]. Traditional Siddha system of medicine and Hippocrates also mentioned its use as a remedial agent [106]. Glycyrrhizic acid was confirmed for its anti-allergic, hepatoprotective and anti-inflammatory properties and also employed for the treatment of viral hepatitis, HIV and acquired immunodeficiency syndrome [107]. Flavonoids, isoflavonoids, glycyrrhizin, glycyrrhetinic acid and chalcones are some of its active compounds. Glycyrrhizic acid, glycyrrhizin, glycyrrhetinic and liguiritigenin (a flavonoid) restricts the production of immunoglobulin-E stimulating cytokines in asthma and also the compounds attenuate the pulmonary inflammation and mucus production by dropping the cytokine production and by repressing the mRNA expression of interleukin-1β and tumor necrosis factor-α [108]. Cytotoxic studies show that glycyrrhizin acts as a powerful blocker of SARS-associated coronavirus replication than Ribavirin (antiviral drug) in Vero cells with a selectivity index of 67. Besides inhibiting the replication of viruses, glycyrrhizin also restricts the adsorption and perforation of the viral antigen thus, blocks the premature phase of infection and may be used to neutralize SARS-CoV-2 [109].

Tinospora cordifolia. In Ayurveda, *Tinospora cordifolia* (Guduchi) was mentioned in the ancient texts by Rishi Sushruta of *Sushurta Samhita* (ancient text on medicine and surgery; 1907) flourished around 6th century B.C.E. and *Ashtang Hridaya* (heart or essence of all the eight branches of Ayurveda by Vagbhata, 1996; around 7th century (500 C.E.)) [110, 111]. It is extensively used in the traditional Ayurveda for its anti-inflammatory, immuno-modulatory and anti-pyretic activity. Syringen, cardiol, berberine, cordifolisides A to E, tinosporone are some of the active compounds isolated from *Tinospora cordifolia*. It is used as a soothing agent in bruised mucous membranes by increasing the production of mucin. *Tinospora cordifolia* has potent effect in HIV infection and also helpful in treating other viral diseases and plasmodium attacks. Studies have shown that the *Tinospora cordifolia* crude extract provides a natural mode of immunity in mice by inducing polyclonal B cell mitogen response [112]. *Tinospora cordifolia* acts as an immunostimulant and possess immunomodulatory effect by increasing the level of cytokines and the active components reported to have a role in immunotherapy [113]. Thus, with these efficacy reports, *Tinospora cordifolia* may be suggested for novel corona virus infection due to its virtue in natural course of the defense against infections and its immunotherapy effects.

Withania somnifera. *Withania somnifera* largely referred to as Ashwagandha is a vital medicine in Unani and Ayurveda system of medicine, which can be traced back to 6000 B.C.E. [114]. Ancient literatures *Astanga Nighantu* (knowledge of branches of a science by Vahatacharya; 8th century C.E.), *Dhanvantari Nighantu* (lexicon dealing with technical terms of medicinal herbs and plants by author Dhanvantari; 10th–13th century C.E.) and *Bhava Prakasha Nighantu* (Ayurvedic medical substances applicable to drugs; 16th century C.E. by Acharya Bhavamisra), published in 1857 mentioned about the drug *Withania somnifera* [115–117]. Withaferin A, the main constituent of *Withania somnifera* exerts anti-arthritic and anti-inflammatory activities. Some studies showed that administration of *Withania somnifera* significantly increases the red blood count, hemoglobin concentration and platelet count. Withaferin A and withanolide E possess definite immunoregulatory response on B and T lymphocytes (withaferin A attenuates the neuraminidase activity of H1N1, thereby terminating the release of progeny viruses and thus offers protection against the viral infection [118]. Study of molecular docking of an active constituent withanone from *Withania somnifera* has been shown to decrease the electrostatic components of binding free energy between ACE2 receptor and the viral receptor binding domain [119]. Thus, *Withania somnifera* may be an alternative medicine of natural origin in preventing the novel coronavirus entry into the host genome due to its target specific antiviral activity.

Acacia catechu. In ancient Ayurvedic text of *Charaka Samhita Sutra Sthana* (section on fundamental principles of Ayurveda on internal medicine; 3rd century C.E. by Acharya Charaka) described the *Acacia catechu* as a best drug of choice for treating various diseases [120]. *Acacia catechu* Willd., a valuable source of catechin and epicatechin have been in medicinal use for a long term. *Acacia catechu* exerts anti-inflammatory activity by curtaining the transcription of pro-inflammatory cytokine genes [121]. Epicatechin-3-O-gallate, catechin, epicatechin and epigallocatechin-3-O-gallate are predominant catechins present in *Acacia catechu*. It has been reported that the naturally occurring compounds which include sinigrin, aloe-emodin, quercetin, epigallocatechin gallate and gallocatechin gallate were able to attenuate the enzymic activity of SARS 3C-like protease, which might be a promising drug target in COVID infection, thus strongly reduces the viral replication process and prevents the infection of new hosts [122]. *Acacia catechu* has shown itself to be an anti-viral candidate against herpes simplex viruses and HIV-1 infection. This may be due to the HIV1 protease inhibitory effect and also it interferes with the LTR-Tat protein interaction, thus suppressing the transcription of viral load [123]. Since, *Acacia catechu* and its active constituents has multiple mode of action on viral enzyme, it may be suggested as a lead compound for COVID-19 infection.

Andrographis paniculata. In classical literatures of *Nighantu Adarsha* and *Priya Nighantu* (Ayurvedic lexicon by Shri Bapalal Vaidhya and Acharya Priyavrata Sharma), *Andrographis paniculata* was identified as Kalamegha [124]. *Sushruta Samhita* (ancient Sanskrit text on medicine and surgery; 1500 B.C.E. –600 C.E.) by Sushruta also indirectly referred *Andrographis paniculata* as a predominant ingredient in drug formulations [125]. In Ayurveda and Siddha, *Andrographis paniculata* was used for an array of diseases due to its valuable medicinal properties. Paniculide-A, paniculide-B, paniculide-C, neoandrographolide, 14-deoxyandrographolide, andrographolide and 14-deoxy-11,12-di-dehydro-andrographolide are the active compounds in clinical use [126]. Andrographolide was reported to possess anti-inflammatory effects by downregulating the gene expression of inflammatory COX-2 and inducible nitric oxide synthase and is also effective in dealing upper respiratory infection [127]. Andrographolide exhibits efficient activity against the Epstein Barr virus, herpes simplex virus, human immunodeficiency virus, chikungunya virus and influenza virus via different mechanisms [128–131]. Similarly, research studies shown that andrographolide possess viricidal activity against Ebola virus with EC50 activity of 10 µM and against the growth of dengue virus that reduces viral replication by 50% [132]. Andrographolide has been reported to be significantly active against the SARS coronavirus with an EC50 activity of 1.1 µg/mL in the neutral red and cytopathic toxicity and of 1.2 µg/mL in the visual assay. This might be due to its inhibitory action on nuclear factor kappa-B pathway, which may enhance interferon-mediated antiviral activity [133]. Due to its good pharmacokinetics profile and potent benefit in the treatment of broad spectrum of viral diseases, the compound may be suggested to the treatment and control of novel coronavirus.

These various herbs reported for the management of COVID-19 have no direct clinical evidence for SARS-CoV-2. Although, the results of pharmacological studies having an evidence for antiviral and immune-boosting efficacy of these herbs could render a new lead can be identified from these herbs for anti-SARS-CoV-2 drug development.

Advisory from ministry of AYUSH to the outbreak of COVID-19 in India

Ministry of AYUSH has recommended AYUSH system of medicine and certain traditional evidence-based plant extracts as preventive measure of COVID-19, which enhances immunity of the host and helps in improving the respiratory symptoms. The holistic approach to manage the pandemic virus

recommended by AYUSH are comprised in Table 2 [134]. AYUSH ministry has given general advisory measures of using Ayurveda, which is a plant-based science that helps to boost the host immune response [16] (Figure 4).

Table 2 Advisory recommendations by ministry of AYUSH

Systematic approach recommended by AYUSH	Indian traditional system of medicine	Plant extract	Herbal formula character of the formula/herbs in formula	Therapeutic effects and mechanisms	Recommended dosage
Preventive and prophylactic	Ayurveda	Aqueous extract of *Tinospora cordifolia*.	Decoction from *Tinospora cordifolia*.	Bitter in taste; has post-digestive and astringent effect, decreases energy of digestion and metabolism, acts as rejuvenator and immunomodulator.	Five hundred mg; twice a day with warm water for 15 days.
	Siddha	Aqueous extract of *Andrographis paniculata* & others.	Decoction drink comprises of ingredients: *Andrographis paniculata*, *Chrysopogon zizanioides*, *Coleus vettiveroides* root, *Zingiber officinale*, *Piper nigrum*, *Cyperus rotundus*, *Santalum album*, *Oldenlandia corymbose* and *Trichosanthes cucumerina*.	Bitter in taste; used to relieve body fever.	Sixty mL of Nilavembu Kudineer; twice a day for 14 days.
	Unani	Decoction made of three herbs.	Boiling of *Cydonia oblonga* 3 g, 5 *Zizyphus jujube*, 9 *Cordia myxa*.	Effective against fevers and diarrhoea of warm origin; possess neuroprotective and anti-inflammatory activities; improves quality of sleep.	Boil the ingredients in 250 mL water until it reduced to half; twice a day for 14 days.
	Homeopathy	Arsenicum album 30 pellet (made by heating arsenic with distilled water).	Prepared by diluting aqueous arsenic trioxide generally, until there is little or no arsenic remaining in individual doses.	Tasteless; in homeopathy, it is mentioned as a polychrest with a wide field of action; and used for mental and emotional symptoms of patients.	One dose with an empty stomach for three days and repeat after 30 days.
Symptom management of COVID-19 like illnesses		AYUSH-64.	Composed of Ayurvedic herbs: *Alstonia scholaris*, *Picrorhiza kurroa*, *Swertia chirata* and *Caesalpinia crista*.	It is a patent medicine (patent number No.152863 by central council for research in Ayurvedic sciences).	Two tablets; twice a day.
	Ayurveda	Agasthya Hareetaki.	Decocotion made with *Aegle marmelos*, *Oroxylum indicum*, *Stereospermum suaveolens*, *Gmelina arborea*, *Solanum indicum*, *Solanum xanthocarpum*, *Desmodium gangeticum*, *Uraria picta*, *Tribulus terrestris*, *Mucuna pruriens*, *Hedychium spicatum*, *Sida cordifolia*, *Scindapsus officinalis*, *Achyranthes aspera*, *Piper longum*, *Plumbago zeylanica*, *Clerodendrum serratum*, *Inula racemosa*, *Hordeum vulgare*, *Terminalia chebula*. Then separate *Terminalia chebula* Retz. fruits and strain the decoction by rubbing barley properly. Added cow's ghee and sesame oil and cook the *Terminalia chebula* Retz. fruit pulp until it gets brown.	Aromatic and a famous Ayurvedic drug for pneumonia, predominant uncomplicated illness and for immunocompromised conditions.	Five g with warm water; twice a day.
		Anuthaila/sesame oil.	Combination of Multiherbs with sesame oil and goats' milk.	Balances bodily humor; enhances respiratory health and used for headache and diseases related to the five sense organs.	Two drops per day in each nostril.
	Siddha	KabaSura preparation or Nilavembu preparation.	Kabam-cold; suram-fever (ingredients listed in Table 1).	Bitter pungent taste herbal concoction acts as blood purifier and used for flu infections	Sixty mL; twice a day.
		Adathodai Manapagu syrup.	*Justicia adhatoda* juice and palm extract.	Sweet syrup used to treat various types of fever, stomach disorders.	Ten mL; twice a day.

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Table 2 Advisory recommendations by ministry of AYUSH (*Continued*)

Systematic approach recommended by AYUSH	Indian traditional system of medicine	Plant extract	Herbal formula character of the formula/herbs in formula	Therapeutic effects and mechanisms	Recommended dosage
Add on interventions to the conventional care	Ayurveda	AYUSH-64	Same as above.	–	Two tablets; twice a day.
		Agastya Hareetaki Avaleha/sesame oil.	Same as above.	–	Five g with warm water; twice a day.
	Siddha	Vishasura Kudineer.	Decoction made with *Azadirachta indica*, *Indigofera tinctoria*, *Zingiber officinale*, *Hemidesmus indicus*, *Aristolochia bracteata*, *Vetiveria zizanioides*, *Glycyrrhiza glabra*, *Elettaria cardamomum* and *Santalum album*.	Used for viral fever and associated illnesses.	Sixty mL; twice a day after food.
		Kaba Sura Kudineer.	Given in Table 1.	Bitter pungent taste herbal concoction; used as intervention for preventive category (cough, sore throat, breathing problems).	Sixty mL; twice a day.

–, not mentioned.

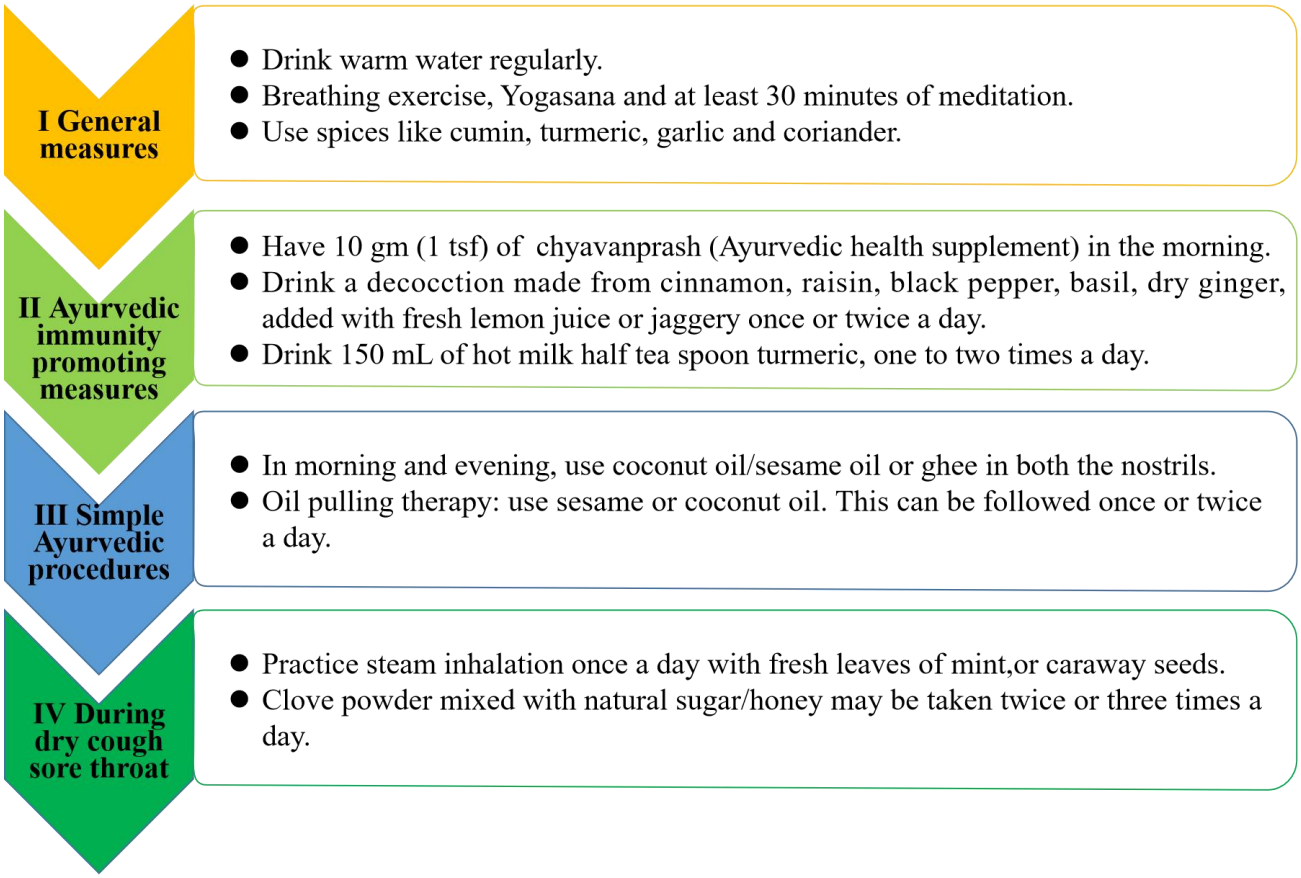

Figure 4 General immunity boosting measures recommended by ministry of AYUSH [16]

Conclusion

COVID-19 is an unprecedented challenge to the global healthcare. Vaccine development and exploring new antiviral drugs for treating corona virus in the mainstream conventional medicine is a great challenge. In silico strategies of some medicinal plants and phytocompounds as antiviral agents offers a lead which should be carried forward for further investigations towards anti-SARS-CoV-2 drug development. It is obvious that several herbal medicines have been exploited to tackle the coronavirus infection. The need of the hour is not only

the development of vaccine, but also to explore the phytocompounds from natural sources to improvise the antiviral efficacy. As a new way ahead in the medication of COVID-19 infection, CAM can be integrated with the conventional system of medicine as a supportive measure to the treatment practice, that may assist to alleviate the symptoms and side effects, ensures healthy life and quicker recovery.

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