Immunity against COVID-19: Potential role of Ayush Kwath

Shankar Gautam a, *, Arun Gautam b, Sahanshila Chhetri c, Urza Bhattarai d

a Ministry of Health and Population, Kathmandu, Nepal
b Ministry of Social Development, Gandaki Province, Nepal
c TU Ayurveda Teaching Hospital, Kirtipur, Nepal
d MCOMS, Pokhara, Nepal

Abstract

SARS-CoV-2 infection associated respiratory disease—COVID-19 has evolved into a pandemic but, being a new form of virus, pathogenesis of disease causation is not fully understood and drugs and vaccines against this virus are still being tested so that no effective drugs or vaccines have been advised by regulatory authority. In this context, the Ministry of AYUSH, Government of India has recommended ‘Ayush Kwath’ to improve the immunity and combat the infection. Our objective of this literature review is to review the role of immunity in pathogenesis of COVID-19 and role of Ayush Kwath against the virus and regulation of immunity. Current review was conducted using a search of available literature on COVID-19 and immunity, VayadhiKshamata, Ayurveda and COVID-19, Rasayana, Coronavirus, SARS-CoV-2, immunomodulatory effects of medicinal plants; Tulsi/Holy Basil/Ocimum sanctum, Dalchini/Cinnamon/Cinnamomum zeylanicum, Sunthi/Ginger/Zingiber officinalis and Marich/Black Pepper/Piper nigrum. Ayurveda, being an ancient science have both medicinal and cultural values and had stimulated our kitchen and influenced what we ate in different seasons and the remedies we used for common ailments. Herbs such as Tulsi, Marich, Sunthi, Dalchini are the most commonly used and easily available drugs in home. Thus, Ayush Kwath due to its immune-modulatory, antiviral, anti-oxidant, anti-inflammatory, anti-platelet, anti-atherosclerotic, hepato-protective, reno-protective properties; seems to be effective in immuno-regulation for controlling viral infections like COVID-19. Further pre-clinical and clinical trials need to be done for the evaluation of safety and efficacy of this polyherbal formulation.

1. Introduction

COVID-19, also known as severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) is an infectious disease believed to be originated from bats and transmitted to human beings [1]. Being a new form of virus, pathogenesis of disease causation is not fully understood and drugs and vaccines against this virus are still being tested so that no effective drugs or vaccines have been advised by regulatory authority. Not only for Coronavirus, many other viruses also lack preventive vaccines and effective antiviral medications. Studies have explored that these viruses can form drug-resistant mutants, which decrease the existing drug’s efficacy. So, these viruses can be a threat to the mankind for long time [2].

High mortality among immune-compromised and those with some underlying pathology implies that the factors that improve immunity can prevent serious manifestations due to COVID-19 infection [3]. Many herbal products are found to have immune-modulatory and antiviral property, so their discovery can be a milestone in the prevention and control of COVID-19 [2]. In this context, the Government of India has recommended to take ‘Ayush Kwath’ in order to boost the immunity. As this is a new formulation, this needs to be validated scientifically. We have made an attempt to review the immune-pathogenesis of COVID-19 and the role of each herb over it.

2. Immunopathogenesis of COVID-19

The ‘S’ protein of coronavirus can bind to host cells through the ACE2 receptor found in the oral and nasal mucosa [1,4]. Other sites where ACE2 receptors are found are lungs, stomach, intestine, bladder, heart, and kidney [5]. Variable presentation of disease in

* Corresponding author.
E-mail: shankar.gautam@mohp.gov.np.
Peer review under responsibility of Transdisciplinary University, Bangalore.

https://doi.org/10.1016/j.jaim.2020.08.003
0975-9476/© 2020 The Authors. Published by Elsevier B.V. on behalf of Institute of Transdisciplinary Health Sciences and Technology and World Ayurveda Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
different age groups, serious manifestations that are seen more commonly in immune-compromised, old aged and in those with underlying pathology, many asymptomatic cases in pediatric age group, and presence of lymphopenia in the majority of the cases; these factors implies that immunity has a vital role in the pathogenesis of COVID-19 [1,6–8]. It is assumed that our immune system has lack of memory against such a virus that gave it an edge over humans [3].

Viruses cause cell destruction mainly in two ways; direct cytotoxic effects of the virus and immune response mediated destruction [9]. COVID-19 cannot lyse the cells directly as the major pathway of cell destruction is due to immune-mediated destruction [10,11]. It has been mentioned that unlike adults, less vigorous cell-mediated immune response in alveoli of children results in being asymptomatic in the majority of the cases [3].

The pathogenesis can be split into two stages: Non-severe and Severe [12].

2.1. Non-severe stage

The virus fuses with the host cell membrane and enters inside the host cell through airway epithelium [13,14]. The virus propagates and multiplies inside the host cell and can reach lower airway and alveoli. In adults with good innate cellular and humoral immunity propagation of virus can be limited and viral load reaching alveoli can be reduced thus recovery can take place within 2–3 weeks with mild symptoms [3].

Humoral immunity prevents the viruses to enter new cells while cell-mediated immunity targets on eradicating virus-infected cells [1,15]. In this stage, a strong immune system can be helpful in preventing the propagation of the virus thus reducing the severity of the disease [12].

2.2. Severe stage

Once the immune system is breached, the virus propagates and reaches the lower respiratory tract and alveoli. Then the virus can penetrate alveoli and reaches systemic circulation causing viremia [3]. The virus binds to multiple organs having ACE2 receptor protein. During this stage, cell-mediated immunity becomes robust and starts releasing various pro-inflammatory cytokines (IFN-α, IFN-γ, IL-1β, IL-6, IL-12, IL-18, IL-33, TNF-α, etc.) and chemokines (CCL2, CCL3, CCL5, CXCL8, CXCL9, CXCL10, etc.) causing damage to multiple organs known as Cytokine storm [16,17]. We may need to suppress the inflammation for improvement during this severe stage [12]. IL-6 receptor antagonist (Tocilizumab), and anti-inflammatory interleukin (IL-10) are proposed to have a therapeutic role in the reduction of severity and mortality of COVID-19 [18,19]. As increased risk of thromboembolic phenomena is also found to be associated with COVID-19, prophylactic antithrombotic medications are advised during this stage [20].

3. Ayurveda purview

3.1. Disease concept

It seems that most early cases had a history of contact with the original market for seafood, but the disease has now advanced to be transmitted through human to human contact [1]. Thus, this disease can be considered as Communicable-both contagious and infectious diseases. In Ayurveda, epidemics are discussed under the term of janapadodhwasma [21]. S.Vi. 3/5–6] by Charakara and Maraka by Sushruta [22, S.S.Soo. 6/17]. The symptoms like fever, cough, breathing difficulty, headache, and vomiting resemble with clinical features of SARS [22, S.S.Soo. 6/19]. Dalhana in his commentary has mentioned that symptoms like anosmia, cough, catarrh will occur after the entry of contaminated air through the nasal opening which is similar to typical clinical features of COVID-19 [22, S.S.Soo. 6/19]. Furthermore, this disease can be classified as Adidaivika Bala Prawritya Vadyadi (ABPV), Sansargaja, Upsargaja, and Aupasargic Raga. ABPV are those diseases arising due to causes that cannot be controlled by human intelligence. Upsargaja Vadyadi are those fever-like diseases that manifest due to close contact with diseased persons [22, S.S.Soo. 24/7] whereas Sansargaja Vadyadi resides with people who are cursed by almighty god i.e. due to influence of invisible forces/forces behind human control [22, S.S.Soo. 24/7]. Aupasargic Vadyadi is defined in two different ways by Sushruta; one as a disease which spreads from one person to another person [22, S.S.Ni. 5/33–34] and another as ‘...Upadravasangya’ i.e. complications or associated diseases that manifest after primary disease [22, S.S.Soo. 35/18]. Susruta mentions the diseases like Jwara, Kushtha (skin diseases), Shoshosa (tuberculosis), Nisradhiyu (conjunctivitis), and other Aupasargika raga (alike communicable diseases) can be spread through Prasanga (intimate relationship), Galra Sansaraphsa (direct contact), Nishwusa (breathing or airborne), Sahahbojana (eating together), Sahashayana (sleeping together), sharing and using of others’ clothes, ornaments, ointments, etc. [22, S.S.Ni. 5/33–34].

Agantuja Vyadhi (diseases of exogenous origin) occurs due to physical/external factors like Bhuta, Visha, Vayu, Agni, and Prahara (trauma), etc. without any involvement of Vataadhi Dosha initially; however, in later stage dosha are involved in the disease process [21, C.S.Soo11/45]. Cakrapanidatta clarifies that Bhuta means Visakrmi or a virulent organism [21, C.S.Sa.1/121]; Krmi may be Sahaja (natural) or Vaikarika (pathogenic) organisms that may be visible (macroscopic) or invisible to the naked eye (microscopic) [21, C.Vi. 7/9,11].

Thus, it is difficult to correlate this disease with specific Ayurveda terminology but, while interpreting the disease on the basis of Samprapti by considering the causative agent and the clinical features like fever (Jwara), cough (Kasa), anorexia (Aruchi), fatigue (Tandra), generalized body ache or myalgia (Angamartha) and Tiredness; it can be contemplated as an Agantuka Vyadhi which later on due to the involvement of dosha develops to Nija Vyadhi as Kapha-Vatolvana Hina Pitta Sannipatjata Jwara (Severe Vata and Kapha with mild Pitta) [21, C.S.Soo. 11/45; C.S.Chi. 3/92]. While talking about the pathogenesis of fever in Ayurveda, Charaka mentioned that when Vataadhi dosha either singly or in Sansristra (two dosha) or in Sannipatjata (all three dosha) got aggravated then it enters Amashaya and mixed with Rasa Dhatu causing obstruction of Rasavaha and Swedavaha Srotas resulting in the destruction of Agni; Agni then spreads out from its Sthana to whole over the body causing the febrile condition [21, C.S.Ni.1/20, 23, 26; C.S.Chi.3/129-132].

3.2. Immunity concept in Ayurveda

Strength, health, lifespan, and vital breath are dependent on the condition of Agni [21, C.S.Soo. 27/342]. Charaka has mentioned the term Vyadhisshamata and states that during certain conditions, or due to certain factors, even unwholesome (unhealthy) food does not produce disease immediately; all unwholesome diet are not equally harmful, all dosha are not equally powerful, all persons are not capable of resisting diseases [21, C.S.Soo. 28/7]. This suggests that the body’s immune system plays a crucial role in disease development. The equilibrium state of Dhatu is called Swasthya [21, C.S.Soo 9/4]. The person who is desirous to be healthy should adopt healthy practices related to diet, conduct, and activities [21, C.S.Soo. 7/60]. Thus, Immunity can be considered in Ayurveda as
Vyadhikshamatwa and Oja; which depends on the condition of Agni, Dosh, and Dhatu.

There are three factors Aahara, Swapna, and Brahmacharya (diet, sound sleep, and celibacy) that support the life with which the body will be endowed with strength, complexion, and development till life span [21, C.S.Soo. 11/35]. Bala (Strength/Immunity) is of three types-congenital, time affected, and acquired. Congenital is that which is developed naturally in the body and mind; time affected is due to seasonal variation and age factor and acquired one is produced by the proper application of diet and exercise [21, C.S.Soo.11/36]. Thus not only diet but also performing yoga or exercises with reduced by the proper application of diet and exercise [21, C.S.Soo.11/36]. The equilibrium state of Kapha promotes strength, that's why normal Kapha is called Oja. [21, C.S.Soo. 17/117]. Normal pure blood promotes strength, complexion, health, and lifespan [21, C.S.Soo. 24/4]. While dealing with Sannipataja Jwara, Susruta in Uttarsthanam mentioned Abhinyasa Jwara, also called as Hataujasa Jwara, indicating the loss or deranged condition of Oja [22, S.S.Utt. 39/39-44].

The word ‘Rasayana (Rasa + ayana)’ refers to nutrition and its transportation in the body for attaining excellent Rasadi Dhatu, which leads to gain longevity, freedom from disorders, optimum strength of physique and sense organs [21, C.S.Chi. 1-1:4-8]. Rasayana promotes nutrition by explicitly enriching the nutritional value of Rasa by enhancing Agni, i.e. digestion, metabolism, and absorption (by Srotashodhana). Consequently, any medication that improves Rasa’s consistency would enhance the health of all body tissues.

4. Role of Ayurveda and traditional medicine

Every society has its own medical system, which is deeply rooted in its culture and guided by its philosophy of life. Being culturally and linguistically diverse countries, there developed several types of traditional medicines (TM) based on practices, skill, traditional knowledge based on beliefs, theories, and experiences indigenous to different cultures. Ayurveda, Traditional Chinese medicine (TCM), Ancient Egyptian medicine, Sowa Rigpa, etc. system of medicine remain the most ancient yet living traditions. Ayurveda and TM have made a significant contribution to the prevention of communicable diseases for thousands of years. A long history of medicinal plants enhance NK cell activity, inhibit activated transcription factor 2 (ATF-2), down-regulate Th17-related cytokines including transcription factor RORc, IL-17A and Th2-related cytokines including IL-5, IL-13, and IL-6, inhibit GATA3, IL-4, IL-6, IL-10, RORyt, IL-17A, TNF-α expression and increase the secretions of IL-10, INF-γ, etc., it shows that natural products have potent immune-modulatory and immune-enhancing effects that may be helpful during the infection course by increasing innate immune response to infections [27,28].

5. Ayush Kwath

Considering the importance of immunity boosting measures in the wake of COVID-19 outbreak, the Ministry of AyUSH, Government of India with the interest of health promotion of the masses, recommends ‘Ayush Kwath’ or ‘Ayush Kadineer’ or ‘Ayush Joshanda’ which comprises of four medicinal herbs (Table 1) [29,30]. The herbs like holy basil, cinnamon, ginger, black pepper are highly available, accessible and widely used in the kitchen and are convenient to educate and train about its use to community health workers, community and even to all public that they can have cost-effective treatment with herbal home remedies. This will help to promote immunity and to lower the gatherings at hospitals and pharmacies in this pandemic. This type of public health measure would eventually promote ‘health for all’ with the theme ‘our health in our own hands’ making responsible to each and every person by active involvement in their own health instead of relying on mass distribution of some medicine. As people leave their homes to earn a living, this herbal decoction will ensure broad access to health care. The WHO SEARO adopted a resolution to revitalize PHC through health systems strengthening to achieve health for all with the emphasis on health promotion and disease prevention [31]. This Kwath is not just a mechanical invention for the COVID-19 pandemic, but it is a revival of health tradition.

Method of preparation and use:

Take all the ingredients in dry form as per standards laid down in Ayurvedic Pharmacopoeia and make coarse powder. Make sachets or tea bags each of 3 g of powder or 500 mg tablet of aqueous extract, to be consumed like tea or hot drink by dissolving in 150 ml of boiled water, once or twice daily. Gud (Jaggery)/Draksha (Resins) and/or Lemon juice can be added while consuming the formulation.

5.1. Tulsi

Many in-vitro, animal and human experimental scientific studies showed that; due to presence of eugenol, phenolic compounds, linoleic acid, etc. compounds Tulsi has antimicrobial (including antibacterial, antiviral, antimalarial), anti-diarrheal, anti-oxidant, anti-inflammatory, hepatoprotective, cardio-protective, reno-protective, analgesic, antipyretic, immunomodulatory properties and is thus recommended as a treatment for a range of diseases including features like cough, fever, asthma, anxiety, diarrhea, gastric, cardiac and genitourinary disorders [32–36]. Due to its anti-inflammatory and antioxidant properties, it
mechanism to assess T-cell-dependent antibody responses i.e. ailments like change in water and food consumption, body weight, and hematological symptoms or CNS and ANS toxicities or death and did not show any

NK cells; phagocytic activity and index with the rise in lymphocyte counter as it enhances immune response by increasing T-helper and improving vital capacity also is an immune-modulator and regulator besides by enhancing immune response boost the defense mechanism.

The compounds such as ursolic acid, carnosol, rosmarinic acid, chavicine, apigenin, eugenol, and cirsimaritin present in aqueous and methanol extract of leaf and seed oil) besides protects against toxic chemical-induced injury, enhance the anti-oxidant enzymes and protect cellular organelles and membranes by clearing damaged free radicals [37].

The compounds such as ursolic acid, carnosol, rosmarinic acid, chavicine, apigenin, eugenol, and cirsimaritin present in O. sanctum increase haemoglobin concentration, enhance SRBC agglutinin titters, decrease cyclo-oxygenase (COX)-2 and lipoxygenase (LOX)-5 enzymes activity, suppress NF-κB classical pathway, up regulation of IL-2, IFN-γ and TNF-α, down regulation of IL-1β and produce of SRBC antigen-specific antibodies, which represent a major defense mechanism to assess T-cell-dependent antibody responses i.e. Tulsi by enhancing immune response boost the defense mechanism against the infection [38–40]. Several studies have shown that Tulsi (aqueous and methanol extract of leaf and seed oil) besides improving vital capacity also is an immune-modulator and regulator as it enhances immune response by increasing T-helper and NK cells; phagocytic activity and index with the rise in lymphocyte count, neutrophil count and antibody titer [35,41].

In an acute toxicity study, it did not produce any hazardous symptoms or CNS and ANS toxicities or death and did not show any change in water and food consumption, body weight, and hematological and biochemical profiles [42].

5.2. Dalchini

It is a potent immune system booster and is used in various ailments like flu, indigestion, edema, cough, etc. [43,44]. Cinnamon bark contains cinnamaldehyde, benzaldehyde, cinnamaldehyde and terpenes [45]. In one study, cinnamon at high dose (100 mg/kg) showed immune-stimulant activity as it significantly increased the phagocytic index, serum immunoglobulin levels and antibody titer and decreased the percentage reductions in neutrophil count. Cinnamon low dose (10 mg/kg) increased serum immunoglobulin levels only. This showed that high dose increases both cell mediated and humoral immunity whereas low dose showed effect only on humoral immunity [44]. The studies also suggest that cinnamaldehyde can act as a strong regulator of monocyte/macrophage-mediated immune responses by inhibition of PI3K, PDK1 and NF-κB activation of signaling components. In addition to this, by the activation of CD29 and CD43, it blocked cell migration cell adhesion induced but not cell-fibronectin adhesion and it was able to suppress both the production of nitric oxide (NO) and up regulation of surface levels of co-stimulatory molecules. It also causes a reduction in the sub-G1
phase, accompanied by an increased ratio of apoptotic cells to necrotic cells [47]. The constituents like cinnamaldehyde, cinna-
morphilin etc are found to be a thromboxane A2 receptor antagonist, anticoagulant, anti-atherosclerotic and thus prevents unnec-
essary clumping of platelets and atherosclerotic CVD [48].

In a systematic review of its adverse events, relatively few self-
limiting adverse effects were reported like allergic reactions and
gastrointestinal disorders on clinical trials, case reports and case
series. The evidence available show that cinnamon is safe for use as
spice in daily diets or as a medication [49]. However, its use for
therapeutic reasons, in high doses or for prolonged periods, can
cause some adverse effects and should be observed clinically.

5.3. Sunthi

An alcohol extract increases the immunological status of mice
with increased phagocytosis by macrophages whereas crude
extract was also shown to increase humoral and cell-mediated
immune responses [27]. The bioactive compounds of ginger such
as nevirapine, ß-sitosterol, 6-gingediol, germacrene, methyl-6-
shogaol, 6-gingerol, s-linalool, 6-shogaol, gingerid, zingeriberene,
etc., are known to inhibit viral replication; among these the most
potent inhibitors of reverse transcriptase (RT) enzyme is ß-sitos-
terol, which is predicted to be used as non-nucleoside reverse
transcriptase (NNRTIs) HIV-1 inhibitors [50,51]. It is reported that
Ginger contains TNF-α which is also known as an anti-influenza
cytokine [52]. The rhizome of Ginger and its main components
like gingerols, shogaols, etc inhibit prostaglandin and leukotriene
biosynthesis, inhibit cyclooxygenase and lipoxygenase activities,
inhibits the synthesis of pro-inflammatory cytokines such as IL-1,
TNF-α, and IL-8 without any significant effect in IL-6 levels;
inhibit the excessive production of NO, PGE (2), TNF-α, and IL-
1beta, reduce the elevated expression of NFkB and TNF-α, down-
regulate inflammatory iNOS and COX-2 gene expression, inhibit
thromboxane synthetase, raise levels of prostacyclin without a
concomitant rise in PGE 2 or PGE 2 alpha, inhibit platelet aggre-
gation, decrease age-related oxidative stress markers and enhance
fibrinolysis [53–58].

The concentration of IgM and eosinophil count in non-smokers
was significantly increased in a comparative study of the effect of
ginger extract among male smokers and non-smokers, whereas the
concentration of hemoglobin and lymphocyte count in smokers
was strongly increased. This indicates that in non-smokers, ginger
results in a stronger antibody response or humoral immunity than
in smokers [59].

According to Ayurveda, it is contraindicated to be used in a few
diseases: Kushtha, Pandu, Mutakriccha, Raktapitta; and in Grishma
(summer) and Sharada (autumn) Ritu. There are few minor adverse
effects recorded that did not need care, such as mild gastrointes-
tinal symptoms, sleepiness, mild diarrhea during prior few days of
reatment. It is also explained that ginger has the ability to induce
heartburn and as a gastric irritant with doses above 6 g [60]. During
pregnancy, ginger did not pose a major risk for side effects or
 adverse events [61].

5.4. Marich

It has been also found to increase bioavailability, thus enhance
the therapeutic efficacy of many drugs, vaccines and nutrients and
have immune-modulatory, anti-oxidant, antiplatelets, antihyper-
tensive, anti-asthmatic, antipyretic, analgesic, anti-carcinogenic,
anti-inflammatory, anti-diarrheal, antipsasmodic, anxiolytic, anti-
depressants, hepatoprotective, anti-ulcer, anti-thyroids, anti-
apoptotic, anti-metastatic, antimitogenic, antibacterial, antifungal
and anti-amoebic properties [62–65]. The extract and its
constituents like piperine, regulate the balance of the cytokines
production of Th1, Th2, Th17, and Treg cells, reduce the accumu-
ation of inflammatory cells, inhibit the expressions of GATA3, IL-4,
IL-6, IL-1β, RORγt, IL-17A and TNF-α, increase INF-γ and IL-10 se-
cretions in BALF (Broncho-alveolar lavage fluid) and increase
macrophage activation and T and B cell proliferation [63,66].

Besides this, Marich possess cytotoxic activity, suppresses the
levels of total IgE, anti-OVA IgE, anti-OVA IgG1 and histamine
release in serum, ameliorates fibrosis and infiltration of inflam-
matory cells, inhibits the allergic responses, inhibitsTh2/Th17 re-
 sponses and mast cells activation, inhibits NF-kB, c-Fos, cAMP
response element-binding (CREB) and activated transcription fac-
tor 2 (ATF-2); suppresses PMA-induced MMP-9 expression, inhibits
PKCζ/extracellular signal-regulated kinase (ERK) 1/2 and reduces
NF-κB/AP-1 activation. In addition, piperine also inhibits the P-
glycoprotein (P-gp) and CYP3A4 functions [67–69]. Piper nigrum is
found to have dose dependent antifertility effects on mice [70].

6. Discussion

According to Ayurveda, therapeutics is of two types: 1. Swas-
thasvarjakāra—which promotes strength (immunity) in the healthy
and 2. Rogasvar-jāra—which alleviates disorders. Both of these groups
perform both of these functions but Rasayana and Vajikara
are mostly used for promotive treatment (C.S.Chi. 1:1/4–8) [21]. Ayush
Kwath has both immune promoting and disease alleviating prop-
erties which can be achieved by various treatment modalities like
Rasayana, Satwawajaya, Yuktiyaprasyaha, Vayadhi Vipartarthakari
chikitsa, etc.

The Katu and Tikta Rasa, Usna Vira and Deepana, Pachana,
Yakrituttejakaya properties of Ayush Kwath help to improve Agni
and Srotosodhana (improves microcirculation and tissue perforation);
thus promotes proper digestion, metabolism, and absorption and
acts as Rasayana for the development of preceding Dhatu and
finally form Oja. Oja itself acts as immunity to prevent disease.
Immunity is dependent on the condition of Agni. Ayush Kwath with
its Agni promoting and Kaphashamaka properties balance Kapha;
and with Raktashodhakha, Hridhya, Krimighna properties purify the
blood. It is already mentioned that natural Kapha and pure blood
promote Oja and Bala respectively. Krimighna is the Prabhava
(special action) of Tulsī and Sunthi which directly acts against
pathogens. The properties like Jwaragāna (esp. Vatashlikhiṃka,
Vishama), Kasahara, Swasahara, Khayanashaka, Shoolaprashamana,
Swothahara, Kaphagahna, Hridayaotejakaya, Yakrituttejaka have direct
role to alleviate various clinical signs, symptoms and complications.

As this disease is considered as Kapha-Vatodvāta the Pitta
Sampraptaja Jwara, the Kapha Vata Shāmakā properties of Ayush
Kwath can play a significant role in balancing the vitiated doshas.
After six days of Jwara, Charaka suggests the decoction of Pachana
drugs in the case of Amodha and Shāmaniya drugs in Niramodha
[21, C.S.Chi. 3/160]. This shows that Yuktiyaprasyaha and Vayadhi-
viparita chikitsa can be done even after the involvement of Doshā in
later stages. Ayush Kwath has potential psycho-neuro-immune
mechanisms via evidence of a reduction in depression, anxiety,
and stress in controlled trials and shows meaning response as it is a
specific remedy for cough and respiratory problems; this shows the
role of Satvawajaya Chikitsa in its management [71].

Immunity plays a key role in the pathogenesis of COVID-19 both
during the early non-severe stage and during the severe stage of
the disease. The early-stage strong immune response may prevent
the propagation and spread of viruses inside the body thus
 reducing the severity of cases and early termination of infection.
While during later stage, strong cell-mediated immunity of the
body against the virus itself can be a factor responsible for grave
consequences due to cytokine storm. The target during the early
stage should be to reduce viral propagation, while at a later stage should be to reduce the inflammatory response of the immune system. Medicinal herbs with immune booster property can be an option during the early non-severe stage while herbs with anti-inflammatory and anti-thrombotic properties can be an option during a later or severe stage. Cytokine storm that is believed as a major factor responsible for complications and death of COVID-19 patients has been found to be reduced with anti-inflammatory drugs like steroids and IL-6 receptor antagonists. Anti-inflammatory interleukins (IL-10) in modern medicine [72]. The role of medicinal herbs with anti-inflammatory property on the cytokine storm is still lacking in research. Like anti-inflammatory interleukins and IL-6 receptor antagonist (Tocilizumab); IL 10 that are proposed in modern medicine to have a therapeutic role in the reduction of severity and mortality of COVID-19. Cinnamon bark that is found to decrease INF-γ and IL-4. Its anti-atherosclerotic, anti-coagulative and anti-platelet activity can be a topic of research to reduce inflammatory and thrombotic complications in COVID-19 patients. Sunthi due to its inhibitory effects on pro-inflammatory cytokines and Marich with its property of reducing the accumulation of inflammatory cells with controlled cytokine production balance can be an option to reduce cytokine storm in COVID-19 patients and need to be researched with the therapeutic trial.

Each herbal constituent of Ayush Kwath is found to have some role in increasing the immune response. On correlating immune-pathogenesis of COVID-19 with immune-modulatory effects of herbs, Ayush Kwath can be an option before infection and during the non-severe stage to enhance immune response, prevent the propagation of COVID-19 virus to lower airways and thus help in early recovery with mild symptoms. Pharmacodynamics and pharmacokinetics of this polyherbal formulation (PHF) is not yet studied, but it is believed that the pharmacological agents or the active principles of PHF may exert potentiating, synergistic, agonistic antagonistic actions resulting maximum therapeutic efficacy with minimal side effects [73,74].

The dose of each herb is mentioned in API (The Ayurvedic Pharmacopoeia of India) as 2–3 g powder of Tulsī leaves, 1–3 g powder of cinnamon bark, 250 mg—1 g powder form of black pepper, and 1–2 g powder of ginger [75].

According to Ayurveda, on the basis of predominance of dosha, each person has their own different constituent, and every season and the place have their identical role over the person’s Prakriti. According to Ayurveda, Tikṣha properties can stimulate the urinary system thus increasing urine, and can cause sweating [30]. As these drugs have Laghu and Tikṣha properties, they can cause Srotoshodhana, thus can increase urination and defection in higher doses. Due to Usna Virya, it can cause Pitta Vriddhajakṣa like hyperacidity, hot or burning sensation, excessive sweating, fatigue, loss of taste and sleep disturbances. Ginger is contraindicated in the hyperacidity, hot or burning sensation, excessive sweating, fatigue, nary system thus increasing urine, and can cause sweating [30]. As according to Ayurveda, draprabhavati every person has their own different constituent, and every season region. Thus, this formulation must be evaluated using scientific methods to understand bioactive compounds responsible, their mechanism of action, and ways to regulate the activity of these compounds on COVID-19 related immunological factors. Toxicological studies and clinical trials must be done before its extensive usage.

7. Conclusion

With various Ayurveda concepts and biomolecular studies, these Ayurveda herbs are seen to have rich sources to fight against the immuno-pathogenesis process of viral diseases, but to date, no study has been found about its effectiveness against COVID-19. Ayush Kwath due to its antiviral, immune-modulatory, antioxidant, anti-inflammatory, anti-platelet, anti-atherosclerotic, hepatoprotective, renoprotective properties; seems to be effective in regulating immunity for the prevention and reduction of viral disease complications. As there is lack of enough evidence to support its specific role against coronavirus, there is a requirement to validate the effectiveness of these formulations with extensive biotechnological, pharmacological, and clinical research.

Source of funding

This work did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of interest

None.

References

[1] Zhou P, Yang X-L, Wang X-G, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature 2020;579:270–3. https://doi.org/10.1038/s41586-020-2012-7.
[2] Lin LT, Hsu WC, Lin CC. Antiviral natural products and herbal medicines. J Trad Compliment Med 2014;4:24–35. https://doi.org/10.4103/2225-4120.144335.
[3] Abdulamir AS, Hafidh RR. The possible immunological pathways for the variable immunopathogenesis of COVID-19 infections among healthy adults, elderly and children. Electr J Gen Med 2020;17:1–4. https://doi.org/10.20533/ ejgm.7850.
[4] Xu H, Zhong L, Deng J, Peng J, Dan H, Zeng X, et al. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. Int J Oral Sci 2020;12:8. https://doi.org/10.1038/s41368-020-0074-x.
[5] Donoghue M, Hsieh F, Baronas E, Godbout K, Gosselin M, Staggiano N, et al. A novel angiotensin-converting enzyme-related carboxypeptidase (ACE2) converts angiotensin I to angiotensin 1-9. Circ Res 2000;87:E1–9. https://doi.org/10.1161/01.res.87.5.e1.
[6] Cruz AT, Zeichner SL. COVID-19 in children: initial characterization of the pediatric disease. Pediatrics 2020. https://doi.org/10.1542/peds.2020-0834.
[7] Li Q, Guan X, Wu P, Wang X, Zhou Z, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med 2020;382:1199–207. https://doi.org/10.1056/NEJMoa2001316.
[8] Liu Y, Gayle AA, Wilder-Smith A, Rocklov J. The reproductive number of COVID-19 is higher compared to SARS coronavirus. J Trav Med 2020.27. https://doi.org/10.1093/jtm/taaa021.
[9] Porter DD. Destruction of virus-infected cells by immunological mechanisms. Annu Rev Microbiol 1971;25:283–90. https://doi.org/10.1146/annurev.mi.25.100171.001435.
[10] Li R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet 2020;395(10224):565–74. https://doi.org/10.1016/S0140-6736(20)30251-8.
[11] Liu K, Fang YY, Deng Y, Liu W, Wang MF, Ma JP, et al. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. Chin Med J (Engl) 2020;133(9):1025–31. https://doi.org/10.1097/ CM9.000000000000744.
[12] Shi Y, Wang Y, Shao C, Huang J, Gan J, Huang X, et al. COVID-19 infection: the perspectives on immune responses. Cell Death Differ 2020;27:1451–4. https://doi.org/10.1038/s41418-020-0530-3.
[13] De Wilde AH, Sniijder EJ, Kikker M, van Hemert MJ. Host factors in coronavirus replication. In: Tripp R, Tompkins S, editors. Roles of host gene and non-coding RNA expression in virus infection. Current topics in microbiology and immunology, vol. 419. Cham: Springer; 2020. Available from: https://link.springer.com/chapter/10.1007/978-3-319-21772-5. [Accessed 2 May 2020].
Prebiotic potential of culinary spices used to support digestion and bio-absorption. Evid Compl Alternative Med: ECAM 2019;2019:8973704. https://doi.org/10.1155/2019/8973704.

A review on therapeutic potential of Piper nigrum L. (Black Pepper): the king of spices. Med Aromat Plants 2014;3. https://doi.org/10.4172/2167-0412.1000161.

Phytochemical evaluation and antioxidant activity of Piper cubeba and Piper nigrum. J Appl Pharmaceut Sci 2011;1:153–7. Available from: https://japsonline.com/admin/php/uploads/231_pdf.pdf. [Accessed 1 May 2020].

Damanhouri ZA. Biological action of Piper nigrum — the king of spices. Eur J Biol Res 2017. https://doi.org/10.5281/zenodo.839039.

Calcio-herbal formulation, Divya-Swasari-Ras, alleviates chronic inflammation and suppresses airway remodelling in mouse model of allergic asthma by modulating pro-inflammatory cytokine response. Biomed Pharmacother 2020;126. https://doi.org/10.1016/j.biopha.2020.110063.

The protective role of Piper nigrum fruit extract in an ovalbumin-induced allergic rhinitis by targeting of NF-κBp65 and STAT3 signalings. Biomed Pharmacother 2019;109:1915–23. https://doi.org/10.1016/j.biopha.2018.11.073.

Bui TT, Piao CH, Hyeon E, Fan Y, Van Nguyen T, Jung SY, et al. Polyherbal formulation concept for synergic action: a review. JDDT [Internet] 2019;9(1-s):453–66. Available from: http://jddtonline.info/index.php/jddt/article/view/2339. [Accessed 7 May 2020].

The ayurvedic pharmacopeia of India part-I and volume-I, II and III. Ministry of Health and Family Welfare, Govt. of India, New Delhi.

Ayurvedic medicine: the principles of traditional practice. Elsevier; 2006. p. 315. Available from: https://books.google.co.in/books?id=hBFyH7Ze54CA&printsec=frontcover&v=onepage&amp;q=amp;f=false. [Accessed 3 July 2020].