

AYUSH Kudineer: An Immune Boosting Herbal Health Drink for COVID-19

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Abstract

In December 2019, there was an outbreak of mysterious pneumonia in Wuhan city, Hubei province, China. On Jan 7, 2020, it was confirmed that a new type of corona virus named SARSCoV-2 (formerly named as 2019-nCoV) had emerged as pandemic disease. The WHO named the Wuhan pneumonia as Corona virus Disease-2019 (COVID-19) on Feb 11, 2020. Unfortunately, specific antiviral drugs or vaccines are currently unavailable. Since ancient times, herbs of Indian origin have been used as a treatment and preventive strategy for several diseases, including respiratory viral infections. The benefit of using herbs in viral respiratory infections is to build immune stimulating and reduce inflammation to overcome the viral injury. Holistic approach of AYUSH systems of medicine gives focus on prevention through lifestyle modification, dietary management, prophylactic interventions for improving the immunity and simple remedies based on presentation of the symptoms. In this current pandemic situation Ministry of AYUSH has taken lots of efforts to control and prevent the fast spread of corona virus infection through AYUSH medicines and preventive procedures. AYUSH Kwath or AYUSH Kudineer or AYUSH Joshanda is one among the immunity boosting health drink recommended by AYUSH ministry which contains Tulsi (*Ocimum sanctum*), Dalchini (*Cinnamomum zeylanicum*), Sunthi (*Zingiber officinale*) and Krishna Marich (*Piper nigrum*). An attempt has been made to review the ingredients of AYUSH Kudineer, pertaining to its Anti-viral, Immunomodulator, Anti-inflammatory and other pharmacological effects which are involved in the prevention of COVID-19 infection from literatures and scientific publications. The review provides supportive scientific evidences towards the antiviral, immunomodulator, and Anti-inflammatory properties of AYUSH Kudineer. This study recommends the usage of AYUSH Kudineer as prophylactic or preventive health drink for COVID-19.

Keywords: *AYUSH Kudineer*, Health drink, COVID-19.

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Introduction

In December 2019, there was an outbreak of unexplainable pneumonia in Wuhan city, Hubei province, China. The WHO has pronounced this novel corona virus pneumonia epidemic to be a Public Health Emergency of International Concern (PHEIC), and named this infectious disease as “COVID-19” [1]. The causative organism was first named as 2019-nCoV and then it was termed as SARS-CoV-2, a new type of virus by Jan 7, 2020 [2]. The World Health Organization (WHO) named the Wuhan pneumonia as Corona virus Disease-2019 (COVID-19) on Feb 11, 2020 [3]. Cough, fever, other respiratory symptoms, fatigue, myalgia, and diarrhea are the symptoms of COVID-19 [4, 5]. The genome sequence of SARS-CoV-2 was related to severe acute respiratory syndrome-related corona virus (SARS-CoV) and their sequence has 79.5% similarity [6, 7]. SARS-CoV-2 has spike protein (S) which binds with angiotensin converting enzyme-2 receptor to enter into human alveolar epithelial cells [6]. COVID-19 can be diagnosed by either chest CT radiography or a laboratory testing.

Unfortunately, specific antiviral drugs or vaccines currently have not been available for the treatment [8]. Since time immemorial, the medicinal herbs have been used for treating respiratory illness, including infectious diseases. The aim of

using the herbs in the respiratory illness is to reduce the inflammation and to enhance the immune system to combat the disease [9]. Siddha system of medicine provide a holistic approach to the patients consisting broad explanation about dietary advice, prevention of the disease, lifestyle modifications, yoga, kaya karpam, particularly as a prophylactic measure during the pandemic. Ministry of AUYSH has recommended many Indian medicinal plants as preventive and prophylactic for COVID -19. In this current pandemic situation Ministry of AYUSH, GOI has taken lot of efforts to control and prevent the fast spreading of corona virus infection through AYUSH system of medicines. AYUSH Kwath or AYUSH Kudineer or AYUSH Joshanda is one among the immunity boosting health drink recommended by AYUSH ministry which contains Tulsi (*Ocimum sanctum*) leaves 4 parts, Dalchini (*Cinnamomum zeylanicum*) stem bark 2 parts, Sunthi (*Zingiber officinale*) rhizome 2 parts and Krishna Marich (*Piper nigrum*) fruit 1 part. This review mainly focuses ingredients of AYUSH Kudineer and their anti viral, immunomodulator, anti inflammatory and other pharmacological effects which are involved in the prevention of COVID -19 infections. The general properties of ingredients in AYUSH Kudineer as per Siddha pharmacology are listed in the Table No.1.

Table 1. Properties of ingredients in AYUSH Kudineer

Scientific Name	Part Used	Taste/Potency	Actions	Medicinal Uses
<i>Ocimum sanctum</i>	Leaves	Acrid/hot	Stimulant Expectorant Diaphoretic	Cough, bronchial asthma, fever.
<i>Cinnamomum zeylanicum</i>	Stem bark	Acrid/hot	Stimulant Carminative	Cough, asthma, diarrhoea, gastric ulcer, abdominal pain
<i>Zingiber officinale</i>	Rhizome	Acrid/hot	Stimulant Stomachic Carminative	Fever, rhinitis, indigestion, cough, asthma, headache, kabasuram
<i>Piper nigrum</i>	Fruit	Acrid/hot	Antipyretic Stimulant Antidote Carminative	Fever with rigor, cough, cold, tastelessness

Tulsi (Ocimum sanctum L):

Medicinal plants are termed to be one of the easiest sources to get antiviral drugs since they have a proven record for antiviral activity. Tribes living worldwide, traditionally, have been using most of the medicinal plants successfully for many decades [11]. *Ocimum sanctum* L. (Tulsi) is a plant which is grown in different parts of the world and is known to have medicinal properties. Tulsi plant has been studied for its antibacterial, antifungal, antihistamine and mast cell stabilizing activity, radio-protective effect, wound healing effect, anti diabetic effect, antioxidant activity, immunologic effects, anticancer properties, contraceptive effects, larvicidal property, Neuro-protective effects and other miscellaneous activities [12].

A wide range of phytochemicals including eugenol, eugenol, carvacrol, ursolic acid, linalool, limonene, methyl chavicol, caryophyllene, antocyanins, sitosterol, apigenin has been reported in this plant.

Molecular docking for H1N1 influenza:

Mohammed I Alhazmi *et al* has screened the most potent drug by conducting in silico techniques like Docking for H1N1 influenza virus. In this study, the effectiveness of the 38 phytochemicals of Tulsi has been studied for its binding energy of hemagglutinin and neuraminase viral proteins in silico techniques. In Tulsi (*Ocimum sanctum*), 8 phytochemicals have more binding energy with active sites of 8

H1N1 viral proteins as compared with positive drugs Oseltamivir and Zanamivir. Out of the 38 Ligands, top five have been selected and they are Oleanolic acid, Vicenin- 2, Apigenin, Stigmasterol, and Ursolic acid. Among them Apigenin had shown good ADMET property as compared with the standards [13].

Anti viral activity against H9N2 virus:

Ghoke *et al* studied the antiviral activity of *Ocimum sanctum* leaves extract in three experimental models for prophylactic, therapeutic and virucidal in embryonated chicken egg against H9N2 virus. Various extracts of *O.sanctum* were estimated for its anti viral activity by RT-qPCR assay. Crude extract, terpenoid and polyphenol showed virucidal activity and decrease in viral genome. Also the crude and terpenoid extracts showed promising therapeutic effect which was maintained for 72 hrs post incubation [14].

Immunomodulatory effect:

Shankar *et al* studied the immunomodulatory effects of ethanolic extract of Tulsi leaves through a double-blinded randomized controlled cross-over trial on healthy volunteers in which the levels of Th1 and Th2 cytokines before and after the intervention. In this study, healthy volunteers were administered with 300 mgm of ethanolic extracts of leaves of Tulsi or placebo and were tested for other immunological parameters such as T-helper

and T-cytotoxic cells, B-cells and NK-cells also were analyzed using Flowcytometry, significant increase in the inflammatory markers were observed and hence the immunomodulatory effect of Tulsi leaves extract was proved [15].

Gupta G. *et al* studied the Antimicrobial and immunomodulatory effects of *Ocimum sanctum* (ShyamaTulsi) against infectious bursal disease virus infection in chickens. The birds were infected with Georgia strain of infectious bursal disease virus (IBDV), after giving dried leaves powder of *Ocimum sanctum* in the dose of 200 mg/bird and essential oil in the dose of 10 µl/bird daily orally over a period of 25 days. A successful decrease in viral replication in the bursa of Fabricius was noted along with immunopotiation in the birds [16].

P.K. Mediratta *et al* investigate the effect of *Ocimum sanctum* seed oil (OSSO) on some immunological parameters in both non-stressed and stressed animals. The animals were pretreated with *O.sanctum* seed oil and found that the Restraint stress (RS) on humoral and cell mediated immune response were enhanced. Co-administration of diazepam (1 mg/kg, sc), a benzodiazepine (BZD), with OSSO (1 ml/kg, ip) enhanced the effect of OSSO on RS-induced changes in both humoral and cell-mediated immune responses. These immunomodulatory effects may be mediated by GABAergic pathways [17]

Dalchini (*Cinnamomum zeylanicum*):

Cinnamon bark has been used worldwide as a main ingredient of south Indian foods, spices, and in tea. It is being used for common cold, cardiovascular disease, and chronic gastrointestinal and gynecological disorders as home remedy. Substantial studies on the pharmacological activities of the cinnamon bark have been conducted, indicating that cinnamon bark is involved in a vast range of pathological and physiological events. For instance, essential oil and water-based extracts from cinnamon have been shown to be efficacious against pathogenic microbes, viruses, and various types of tumor cell lines [18, 19].

Earlier studies have indicated that the major pharmacological activities of cinnamon bark, such as its anti-bacterial, anti-inflammatory, anti-viral, and anticancer effects are derived from essential oils such as cinnamaldehyde^[18].

Immunomodulatory effect:

Beom-Joon Lee *et al* studied the immunomodulatory effect of water extract of cinnamon bark (CWE) in oral dose for 7 days on cytokine secretion and involvement of intracellular signaling molecules in activated T cells. The administration of CWE decreased systemic levels of IFN- γ , but not the levels of IL-4 or IL-2. *In vitro*, CWE inhibited anti-CD3 Ab-stimulated IFN- γ and IL-4 at the mRNA and secreted protein levels, also

reduction in sub-G1 phase, accompanied by an increased ratio of apoptotic cells to necrotic cells. Hence Cinnamon bark was proved for its immunomodulatory effect and it can be administered for inflammatory diseases [20]

Sunthi (*Zingiber officinale*):

Ginger (*Zingiber officinale* Roscoe, Zingiberaceae) is a common spice and a widely used medicinal plant, particularly as a broad spectrum anti-emetic agent. Ginger (*Zingiber officinale*) has been studied for several pharmacologic activities, such as improvement of insulin sensitivity to reduce hyperglycemia and hyperlipemia, anti-thrombotic and anti-inflammatory activities by inhibiting synthesis of prostaglandins and/or cytokines/ chemokines, direct and indirect anti-hypertensive effect, gastrointestinal protective effects against ulceration and emesis, antioxidant and radio-protective effects. Besides, ginger has antimicrobial activities against various bacteria, fungi, and nematodes. Ginger has been proved to be effective on various viruses. Ginger is a common ingredient of Chinese traditional prescriptions for airway infections, such as Ge-Gen-Tang(Kakkon- to; GGT) and Sheng-Ma-Ge-Gen-Tang (SMGGT; Shoma-kakkon-to). GGT (Chang *et al.*, 2012) and SMGGT (Wang *et al.*, 2011) are two different Chinese traditional prescriptions that have been proved to have antiviral activity against HRSV. Hence it has been suggested that ginger could be one of the active constituents of GGT and

SMGGT against HRSV. Fresh ginger was tested in both human upper (HEp-2) and low (A549) respiratory tract cell lines and was found to be effective in to inhibit plaque formation induced by HRSV infection.

Ginger contains many terpenes and their derivatives such as zingiberene, beta-bisabolene, sesquiphellandrene, gingerol, zingerone and shogaols. Black pepper contains terpenoids like alpha-pinene, sabinene, beta caryophyllene, delta-3-carene, limonene and beta pinene. In addition to these, it contains an alkaloid piperine also. These principles are known as nutritional medicines or nutraceuticals that give protection to our body from many diseases. Therefore these and related spices have medicinal potential and they form the common ingredients for the indigenous system of medicines in India, China and elsewhere.

Anti - viral effect:

Jung San Chang *et al* aimed to test the hypothesis that ginger can effectively decrease HRSV-induced plaque formation in respiratory mucosal cell lines. In this study the effect of hot water extracts of fresh and dried gingers on HRSV was tested by plaque reduction assay in both human upper (HEp-2) and low (A549) respiratory tract cell lines. Ginger exhibits the anti-viral cytokines that was evaluated by Enzyme-Linked Immuno Sorbent Assay (ELISA). The result of this study, Fresh ginger dose-

dependently inhibited HRSV-induced plaque formation in both HEp-2 and A549 cell lines (po0.0001). 300 µg/ml fresh Ginger could decrease the plaque counts to 19.7% (A549) and 27.0% (HEp-2) compare to that of the control group. Fresh ginger was more effective when given before viral inoculation ($p < 0.0001$); particularly 300 µg/ml of fresh Ginger could decrease the plaque formation to 12.9% on low (A549) respiratory tract cell lines. Fresh ginger dose-dependently inhibited viral attachment (po0.0001) and internalization (po0.0001). Fresh ginger of higher concentration could stimulate respiratory mucosal cells to secrete IFN- β that possibly significant to counteracting viral infection^[21].

Aboubakr *et al* stated that the aqueous extracts of six raw food materials (flower buds of clove, fenugreek seeds, garlic and onion bulbs, ginger rhizomes, and jalapeno peppers) were tested for antiviral activity against feline calicivirus (FCV) as a surrogate for human norovirus. The antiviral study was performed using different extracts dilution below the maximum nontoxic concentrations to the host cells of FCV, Crandell-Reese feline kidney (CRFK) cells. In this study initially no antiviral effect was seen, when the host cells were pretreated with any of the extracts dilution. However, pretreatment of FCV with non-diluted clove and ginger extracts inhibits 6.0 and 2.7 log of the initial titer of the virus, respectively. Also, it shows

significant dose dependent inactivation of FCV, when host cells were treated with clove and ginger extracts at the time of infection or post infection at concentrations equal to or lower than the maximum nontoxic concentrations. By the source of two-dimensional gas chromatography–mass spectrometry analysis, the major components of clove and ginger extracts Eugenol (29.5%) and R-(-)-1, 2-propanediol (10.7%) were identified respectively. The Eugenol exhibits the antiviral activity similar to that of clove extract, along with Eugenol, are responsible for inactivation of FCV. These results manifest that the aqueous extracts of clove and ginger absolutely prevent the foodborne viral contamination [22].

Krishna Marich (*Piper nigrum*):

Spices are the plant parts which are acquired from exotic or indigenous origin. It is also used as a taste enhancer in food which provides strong taste and is also aromatic. Some spices have antimicrobial property and destroy the food spoilage causing pathogenic bacteria or some have antioxidant property which prevents the rancidity and thereby increase the shelf life of foods. Spices provide protection against some diseases and promote healing as they are rich in phytonutrients and other active ingredients. One of the remarkably used spices is fruits of black pepper (*Piper nigrum*) which has been used to treat asthma, colon toxins, obesity, sinus,

congestion, chronic indigestion, and fever [23]. It produces salivation and numbness of the mouth and having a pungent pepper taste. It is admired for its many medicinal uses to treat digestive tract and respiratory tract related diseases.

Anti-viral effect:

Priya and Saravana Kumari proved the anti-viral effect of chloroform extract of *Piper nigrum* against Vesicular stomatitis virus and human para influenza virus on HeLa cell lines and it showed better activity than methanolic extract [24].

One research study was conducted during outbreak of Chikungunya in Kerala, the authors made a three in one food supplement of black pepper, ginger, and garlic in the ratio of 1:4:16 by weight as a preventive food supplement against Chikungunya. Black pepper was added to the Chinese formula of garlic and ginger in order to increase the antiviral properties of the food complex as per Indian traditional system. The authors advised to consume the three in one food supplement daily to prevent Chikungunya. In this study, 45 students (20M and 25 F) of volunteered were enrolled and advised to make this food supplement at home and consume 5 g of it daily along with 50 ml of boiled milk at the time of breakfast for ten days in order to develop immunoresistance against Chikungunya. Of the above group only one student suffered from chikungunya, ARR is 0.23 and NNT is 5. Mean while 12 students (4 M and 8 F) from

a control of 48 students of the college suffered from Chikungunya. This study concluded that the food supplement worked both prophylactically and curatively against the viral. The authors explained the possible mechanism of action in three different ways; one is the effect of poly sulfides and terpenes which dilate the blood vessels and increase blood circulation and excretion of toxins. Second is to stimulate lymphocytes for immune action against the virus and the third is to counteract the inflammatory actions of prostaglandins by decreasing its synthesis and actions by compounds like ajoene^[25].

Conclusion:

The in- depth review has been made on ingredients of AYUSH Kudineer, and this study reveals that the ingredients have anti viral activity against different viruses particularly respiratory virus. They also work as effective immunomodulators in different mechanisms and evidenced to possess anti inflammatory properties. Based on the evidences available in the literatures, scientific publications and traditional usage of these ingredients it is used in food industry / preparation. The usage of AYUSH kwath / AYUSH Kudineer as prophylactic, immune boosting herbal health drink for the prevention of COVID 19 can be advocated on the basis of scientific evidences.

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