Immunomodulatory Effect and Supportive Role of Traditional Herbs, Spices and Nutrients in Management of COVID- 19

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Abstract

Corona Virus disease 2019 (COVID-19) is a new strain of coronavirus that causes respiratory illnesses with a start of flu like symptoms. This disease is fatal and is spread all over the world. The Scientist are working day and night to find vaccine or a cure. World Health Organisation has declared COVID-19 as pandemic [1]. In the view of the pandemic many treatments are being tried on the patients and various treatment modalities are being followed, the traditional medicine has shown a major role to manage this disease. The traditional medicines include the use of herbs, nutrition and spices that are freely available in Asian countries. These are used in day to day life by Asian population [2]. In this paper we have compiled and reviewed the role of various herbs and spices such as Oregano, Ashwagandha, Ginseng, Basil, Sage, Curcumin, Fenugreek, Ginger and Garlic in building immunity and also in curing pathogenic invasions based on evidence based researches.

As there is no cure available for COVID-19 till now so supportive therapy is playing a major role for the patients to fight with this pandemic. The AYUSH ministry has also promoted the use of above herbs for a patient suffering from this disease. The corona virus is present in respiratory system as shown by different studies and it has different strains. The guidelines laid by the ICMR and WHO shows that use of herbs, spices and nutrients can be helpful to manage this virus by increasing the immunity in patients. Hence we are not claiming any cures but the herbs and spices used in day to day life are very much effective in management of COVID-19. World Health Organisation (WHO) has recognised the use of alternative and traditional medicine in the management of COVID-19 but the herbs should be used in prescribed amounts and overdose of them can be harmful for health [1,3]. Therefore the present article will enlighten the readers about the role of herbs, spices and nutrients in improving the conditions in COVID-19.

Key words – COVID-19, Herbs, Spices, Nutrition, Nutrients, Immunomodulatory

Introduction

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It is important to understand the disease first and it is reported that the people suffering from this disease suffer from pneumonia, shortness of breath, respiratory illness which leads to organ failure and ultimately death [3]. The first line of defence against COVID-19 appears to be body's immune system and there are lot of researches going on to strengthen it. But the Immunity is not built in a day and it requires time. The good part is that a well-balanced diet rich in nutrients and some herbs can work to build immunity. A good health which involves an active physical, mental and social life can be key to strengthen the immunity [4]. Spices and Herbs have many natural ingredients that boosts the immunity and also they have many medicinal properties. India is a land of traditional medicines and according to WHO, about 80% of world's population uses spices and condiments to prevent and manage different ailments. The herbs and spices are important for boosting immunity as shown in many studies [35]

1. ANTIVIRAL PROPERTIES OF HERBS

a) OREGANO

The species of Mexican Oregano, *Lippia graveolens* is found in Central America and Mexico. The Mexican oregano is used as medicinal herb and when its essential oil was extracted, it was found out that it contains a compound named as Carvacrol. Carvacrol is an essential oil which is derived from Mexican oregano [5]. The anti-viral activity was shown with a number of studies. It was found that the human respiratory syncytial virus (HRSV) is the main agent causing bronchitis and pneumonia in children and geriatric population. Treatment against this virus is a drug named as Ribavirin but it cannot be used in children. [6,7]. Plant extracts such as carvacrol seemed effective against the viruses such as HRSV [6].

Carvacrol its compound is operative and role in diseases against RNA and DNA viruses. The carvacrol is an essential oil and it is known to hinder the virus attack [5]. Very interesting is the fact that the carvacrol action was current after virus inoculation [8]. Another study showed that Mexican oregano was effective in hindering the activity if various viruses [5].

In other study, it was found that both Mexican oregano oil and carvacrol inhibited the activity of MNV – Murine Norovirus. This is effective in just fifteen minutes. MNV is a very infectious and is catched easily and it causes stomach flu. Its strain is very much familiar with novovirus which cannot be isolated in laboratory [9].

Therefore Oregano Oil and its compound carvacrol is effectively inhibit the viral activities in humans and animals as well. It is said to be effective for countering against the infections

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caused by simplex virus type-1 (HSV-1),which causes diarrhea in children and infants rotavirus and respiratory syncytial virus (RSV) which causes lungs infection. So Oregano is tajen as tea or the oil can be used in cooking [10]

b) Basil

Basil is called as Tulsi, *Ocimum sanctum* Linn. and is a traditional and religiously important herb. The tulsi plant is being worshipped. It is being proven that Tulsi leaf taken in the morning with empty stomach boosts immunity. Many studies were done by taking out the ethanolic extract and the effects are being observed which shows the efficacy of this holy plant leaves on strengthening Immunity [10].

A study was carried out to find out the efficacy of Tulsi leaves in modulating immunity of human body. The ethanolic extract of Tulsi was taken out and then 300 mgms capsules were made to feed 24 patients who were healthy. The levels of Th1 and Th2 cytokines (interferon-γ and interleukin-4), and Other immunological parameters such as T-helper and T-cytotoxic cells, B-cells and NK-cells also were analysed using Flowcytometry pre and post the study. The results showed a positive and strong immunomodulatory role of Tulsi leaves extract on the subjects [10].

In another study, the Tulsi extracts shows the anti-viral activities. One test-tube study showed that Tulsi extracts were responsible for hindering the activity of herpes viruses, hepatitis B, and enterovirus [11].

Therefore if a person even eats 3-5 Tulsi leaves daily can increase the immunity and also gets the benefits of the anti-viral properties of Tulsi Plant leaves.

3) Ginseng

Ginseng have pharmacological activity to reduce the disease attack in the body by Viruses and Bacterias. Numerous studies have shown the role of Ginseng in preventing Cancers, Immune system disorders and cardiovascular diseases [10, 12, 13, 14, 15]

Respiratory syncytial virus (RSV) is known for causing Respiratory Infections and it also shows flu like symptoms as found in COVID-19. This RSV progressively attacks the respiratory system and causes pneumonia and bronchiolitis. The Kang Laboratory (Georgia State University, GA) carried out the research on Ginseng extract and found that Ginseng has

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antiviral capabilities against RSV [16]. The data indicate that Ginseng has immunomodulatory effect and it protects the host from severe pulmonary inflammation [17,18]

Another deadly virus that causes periodic pandemics and endemics is Influenza virus which is of three types A, B and C. A and B causes respiratory disorders and affect the lungs to large extents. Many studies support the role of Ginseng in building immunity against Influenza virus and also increasing the efficacy of the vaccine as well. The dietary intake of Ginseng has shown effects on the influenza virus A infection and the antiviral activities. [19,20]

Ginseng treatment improved the condition of patients suffering from viral infections such as H1N1 and decreased the formation of free radicals such as reactive oxygen species (ROS). [21].

The Ginseng supplementation is freely available in the market so it can be taken to improve immunity and also the anti-viral properties of the Ginseng extract can save us from pandemic COVID -19.

4. Sage

Sage is a plant in the family of Lamiaceae and is called a Salvia officinalis. This herb is native of Middle East and is very important against many diseases. As oxidative stress is cause of many disorders in the body so the antioxidant property of this herb can protect the body from various diseases like cancer, cardiovascular disorders, diabetes, and neurological diseases. The antioxidant components of Sage are carnosol, rosmarinic acid, and carnosic acid, followed by caffeic acid, rosmanol, rosmadial, genkwanin, and cirsimaritin. *Salvia officinalis* is also rich in flavonoids such as quercetin and rutin. Further this herb Salvia officinalis has antifungal, antiviral and anti-malarial effects. [7]

Salvia officinalis has anti-viral properties are due to safficinolide and sage one compunds which are present in the leaves and stem of the plant. This herb is being claimed in many studies to have an effect on HIV-1 infection and it is found that *Salvia officinalis* hinders the activity of HIV. Sage stops HIV from entering the cells and stopping its growth as well. The aqueous extract of salvia officinalis is beneficial against the infection caused by HIV.[7,35,66].

5. Ashwagandha

Ashwagandha, scientifically known as *Withania somnifera*, has been used in Ayurveda as a potent herb for a variety of conditions. Ashwagandha is a Sanskrit word that translates to “Smell of the Horse”. It is named thus as it is said to possess the strength and the vigour of a

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horse. [22] Ashwagandha is also referred to as the "Indian Ginseng". [23] It belongs to the family named Solanaceae, with its distribution throughout the Indian subcontinent. [24] In the medicine system called Ayurveda, Ashwagandha is widely used in the treatment of inflammation, arthritis, tumours, hypertension and asthma. [23] Ashwagandha is also a known immunomodulator and is used as a dietary supplement in the form of churna. [23, 24] Though it is known to have an anti-inflammatory function, it is also reported to have selectively enhancing properties on T helper immune responses [25] as well as plays a role in increment in the body's cognitive function. [26] Ayurveda lists Ashwagandha as under the category of Rasayana, which means it is used for the promotion of mental and physical health, to prevent against diseases as well as delay ageing. [24,27] The body's stress response can be brought to normal levels using adaptogens, which is a class of plants that Ashwagandha falls into. Such herbs make humans elastic at times of physical and emotional stress and help in restoration of a balanced state. Adaptogens are treated with massive respect in Ayurveda due to them acting as boosters without having stimulating effects. [28]

Research suggests that Ashwagandha causes an increment in the production of antibodies. These antibodies engulf the toxins and then eliminate them from the human frame in the form of excretions like sweat, mucus, faeces and urine. [29] Ashwagandha is also known to increase the production of Nitric Oxide, which in turn is responsible for activation of macrophage actions of the immune system with improved ability of ingestion of invader cells. [30] In the phase of infection, the body naturally increases production of nitric acid. Ashwagandha is also known to promote anti-inflammatory effects in the body by reduction of CRP (C-Reactive Proteins) in the body. [28,31] Following immunomodulatory effects are seen as a result of consuming Ashwagandha: A significant increase in the number of CD4+ T helper cells. A less prominent increase was also observed in CD8+ T Helper cells and B cells. A statistically significant increase in the overall level of activated white blood cell. The highest pronunciation of cell activation was found in the CD56+ cells (Natural Killers). This is pivotal, as these cells play an exigent role in how the body responds to flu, tumours or mumps. [32]

2. Anti- Viral Properties of Spices

The function of spices is not limited to just providing aroma and flavour to food but also have healing and magical qualities. They are used to perform religious rites, preserve the corpse, addition to perfumes and as aphrodiasiacs. Here the nutritional, medicinal and therapeutic uses of the amazing fusion of the spices with the food groups will be discussed [34].

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1. Ginger

Ginger, Zingiber Officinale Roscoe is a spice that is famous for its culinary and medicinal properties in India as well as in other countries. Whenever someone suffers from common cold or flu Ginger Tea or Ginger extract is recommended to get relief from the symptoms [37] This has been proved by many researches as well. Ginger has excellent anti-viral properties and treating respiratory issues because of presence of effective plant compounds[38].

The pungent active compound present in Ginger is Gingerol with other sulphur-containing compounds (allicin, alliin, and ajoene), and enzymes (allinase, peroxidase, and myrosinase). Compunds present in Ginger increases the antioxidant activity i.e. superoxide dismutase and glutathione peroxidase in the body resulting in combating the Viral Infections [35]

A study showed that by means of the hot water extract of fresh ginger against Human Respiratory Syncytial Virus (HSRV).The fresh ginger extract was very effective against HRSV-induced plaque formation on airway epithelium by blocking viral attachment [36]

In another study it was determined that Foodborne Viruses such as human norovirus are dangerous and it is a public health concern. To decontaminate the fresh vegetables the aqueous extracts of six raw food materials (flower buds of clove, fenugreek seeds, garlic and onion bulbs, ginger rhizomes, and jalapeño peppers) were tested against the food borne infection. The results showed the aqueous extract of Ginger and Clove were very effective in prevention of the contamination [37].

Garlic

Garlic or Allium Sativum L. is a traditional spice or a medicinal plant used to cure many therapeutic disorders. The benefits of Garlic are known since ages and it has been proven to have property of maintaining the pace of Immune system. The extracts of garlic have much therapeutic usage such as they are cardio protective and it also prevents inflammation in the cells [38]

The maintenance of immune system is supported by garlic as suggested by studies done. The studies have shown the effect of garlic components on the immunomodulatory role. A study was done on white Leghorn chickens by giving them extracts of garlic and it as found there was increase in anti- BA antibody production. The Garlic compounds i.e. Allicin (diallyl-thiosulphinate) are important for T cell increase and also the rise in B-cell differentiation. The

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natural fructans present in garlic are Fructo-oligosaccharides (FOS). The researches on garlic fructans shows that they are helpful in immunomodulation and also have many other functions. Garlic compounds are anti-pathogenic and anti-parasitic in nature and results in killing various infections. Additional benefits of garlic include the stimulation of T-lymphocyte and CD8+ cells and also delay the sensitivity in the cells and tissues of the body [39,40].

3.Cumin

Cumin got its name from the Latin word 'cuminum'. In various parts throughout India, it is referred to as Jiira, Afedziiraa, Safedjiiraa, zeera. Taxonomically, it belongs to the Apiaceae family under genus Cuminum, whereas the species are Cuminumcyminum.[41] Nutritionally, cumin contains around 10.59g of moisture, 13.91g of protein, 5.36g of ash, 16,64g of fat, 22.62g carbohydrates and 30.35g of fiber. A 100g of cumin provides 1274KJ of energy. [42] The same amount provides substantial amounts of the daily value for protein, fat (especially monounsaturated fat) as well as dietary fiber. Other significant micronutrients provided by cumin in the form of vitamins and minerals include B Vitamins, iron, magnesium, manganese and Vitamin E. Cumin has substantial DV amounts of the aforementioned micronutrients. It has been exhibited in phytochemical analysis that cuminumcuminum contains alkaloid, anthraquinone, glycoside, flavonoids, coumarin, resin, saponin, tannin, protein and steroid [41]

Various health effects of cuminumcyminum have been studied in the past to reveal that it has insecticidal, antimicrobial, analgesic, anti-inflammatory, anticancer, antioxidant, antiplatelet aggregation, antidiabetic, bronchodilatory, hypotensive, contraceptive, immunological, anti-osteoporotic, anti-amyloidogenic, alpha glucosidase, aldose reductase and tyrosinase inhibitory effects among other central nervous and protective effects. [41] Cumin can solve a lot of digestive issues, fortifying the gastrointestinal tract; relieve the feeling of nausea as well as bloating and constipation. Traditionally, cumin has been used to treat jaundice, hoarseness, dyspepsia and diarrhea. The seeds are known for the use of their diuretic, stomachic, stimulant, artringent, carminative and abortifacient properties. Oil of cumin is used as perfumery and as a seasoning. The medicinal part of cumin, i.e. Cumin Oil is extracted from the ripe and dried ripe fruit. Most of the benefits provided by cumin are related to the digestive, circulatory and immune systems in our bodies [43,44] From studies it has been found that oral treatment with cumin had immunomodulatory effect, this effect is seen by the modulation of T lymphocytes both CD4 and CD8 cells along with Th1 cytokines. The effect is seen in both normal and immune-supressed subjects. [45]

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4.Fenugreek

Fenugreek is a widely popular herb used in the Ayurvedic medicine as a natural antioxidant and a means of strengthening the immune system. Fenugreek seeds can also be used to preserve pickles, owing to their rich Vitamin E content [46] Fenugreek belongs to the family Leguminosae, carrying the scientific name *Trigonella foenum-graecu*. Use of fenugreek seeds and green leaves in food as well as medicinal applications date long back in human history. Some medicinal properties of fenugreek seeds include lactation aid, hypocholesterolemic, gastric stimulant, antibacterial, galactogogue, antidiabetic agent, anticancer and hepatoprotective effect. The mentioned beneficial physiological effects of fenugreek owe to the dietary fiber constituent with promising value of nutraceutical nature. [47] Per 100g of the seed, 4.63g is saponin and 43.8g protein content [42] Major bioactive compounds include polypenols such as isovitexin and rhaponticin. Nutraceutical properties include cleansing of blood and as a diaphoretic, as it helps in increasing the sweat production so as to remove toxins from the body. Fenugreek is notably known for lymphatic cleansing through irrigation of cells with nutrients and by removal of toxic wastes, trapped proteins and dead cells from the body. These blockages in the lymphatic system lead to improper circulation of the fluid, pain, fluid retention, disease and energy loss in various parts of the body of the person. Fenugreek has proven useful in relief against colds, influenza, bronchial disorders, catarrh, asthma, sinusitis, constipation, pneumonia, pleurisy, laryngitis, sore throat, emphysema and hay fever tuberculosis. The mucosal conditioning of the body can also be maintained by fenugreek, especially in the lungs with the clearing of congestion. Fenugreek also acts as a mucus solvent and a throat cleanser, also easing the urge to cough. The masses of cellular debris may be softened and dissolved by drinking water in which fenugreek seeds have been previously soaked. [48] The fenugreek is beneficial for increasing immunity and also very powerful to heal the flu like symptoms. [46,47] The similar symptoms are being shown in patients suffering from COVID-19. Therefore the fenugreek in moderate amounts can be beneficial for curing cold and respiratory disorders. Fenugreek can be taken in the form of capsule of 300-500 mg/day to treat symptoms of congestion. [49]

5.Capsaicin

Capsaicin (chilli peppers) is the most important component of hot peppers. It hails from the genus *Capsicum*, belonging to the *Solanaceae* family. Many positive effects have been seen on the gastrointestinal and cardiovascular systems due to Capsaicin. [50] Addressing flu symptoms is another health benefit of cayenne peppers, thanks to Capsaicin, which helps in

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boosting of the immune system. [51] Triglyceride and cholesterol levels can be kept in check by moderated use of cayenne pepper, thus helping in prevention of heart disease and lowering blood pressure and preventing the formation of blood clots. [52] Antioxidants in Cayenne peppers include Vitamin C, Vitamin E, β-carotene, luetin, choline, zeaxanthin and cryptoxanthin (A carotenoid) [53] Antioxidants function by removing free radicals from the body, which in question are toxic substances that can prove harmful if they increase in number in the body. Removal of free radicals helps in the prevention of many health issues, such as heart disease, cancer and neurodegenerative diseases like Alzheimer's. [54] Capsaicin is known to relieve symptoms like stuffy nose, sneezing, postnasal drip and congestion when the causatives aren't either smoking or allergy [55]

The COVID-19 shows symptoms like flu and capsaicin is proved to be effective against cold and flu like symptoms. The intake of capsaicin improves respiratory disorders like cold and congestion and helps in relieving nasal blockage along with nasal hyperactivity. [56]

6.Turmeric

Turmeric is alternatively known as "Indian Saffron" is a bright yellow coloured herb of the ginger family, *Zingiberaceae* and is native but not specific to the Indian subcontinent. Turmeric has over two centuries of scientific history. It has been used as an Ayurvedic remedy as well as a flavoring agent for well over 4000 years. Turmeric, whose usable product comes from ground dried root and contains oils, fats, proteins, carbohydrates, minerals and curcuminoids with moisture.

The immunomodulatory properties of curcumin owe to its interaction with different immunomodulators such as cellular components like dendritic cells, macrophages and B and T lymphocytes. Curcumin is a class of compounds named curcuminoids derived from the root of the turmeric plant, scientifically known as *Curcuma longa*. Curcumin has become the most researched natural therapeutic nutrient. The immune system is thrown off balance by a number of factors, such as lack of sleep, prolonged and chronic stress, vitamin deficiencies and toxin exposure. Chronic stress overstimulates the innate immune cells which in turn suppresses the other components of the immune system which are responsible in protecting against viruses. [57] Monoacetylcurcumin and curcumin both helps in the management of H1N1 influenza infections, H5N1 (highly pathogenic avian influenza) virus, HIV/AIDS, zika, chikungunya, hepatitis B, hepatitis C and dengue virus infections. [58] Curcumin plays a role in enhancing immunity by T helper-1 mediated immune responses, it is done by inhibiting T helper 1

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cytokine profile in the $CD4^+$ T cells by suppressing Interleukin-12 production in the macrophages. [59]

Other factors like limited sleep and deficiency of Vitamin D result in over-activation of innate immune cells. [60,61] Fortunately, various studies have resulted in the findings that suggest the use of curcumin as a supplement for lowering the acute-phase proteins responsible for suppression of the innate immunity. [62] The role Curcumin plays here is of a prebiotic to support gut and immune health. [63] Other notable properties of curcumin are suppression of cortisol production in the body by lowering the production of acute phase proteins, as already discussed. [64] Also, experimental studies have shown that curcumin helps in an increment to the body's ability to produce decosaexanoic acid, or DHA, which is an omega-3 fatty acid essential for human health. [65] Conclusively, it can be said that curcumin has immune balancing properties which can be beneficial for those with disorders involving chronic stress. Furthermore, curcumin helps in the promotion of optimal immune responses, owing to the pre-biotic like properties exhibited by curcumin. Other beneficial properties of curcumin are characterized by boosting omega-3 production and lowering cortisol levels in the body. [66]

Conclusion

The herbs, spices and nutrients are being shown to have immunomodulating effect and Anti-pathogenic roles. The results showed that the herb Oregano Oil and its compound carvacrol are effective to inhibit the viral activities in humans and animals as well. It is also shown that a person who eats 3-5 Tulsi leaves daily can increase the immunity. Further the tulsi leaves exhibit the anti-viral properties. The dietary intake of Ginseng has shown the antiviral activities and has effects on the influenza virus A infection *in vitro* and *in vivo*. Sage is being claimed in many studies to have an effect on HIV-1 infection and it is found that Salvia officinalis hinders the activity of HIV. The Researches suggests that Ashwagandha causes an increment in the production of antibodies. Antibodies are essential in the immune system as they help in the body's fight against viruses, bacteria and multiple other pathogens. The results in many studies showed that the fresh ginger extract was very effective against HRSV-induced plaque formation on airway epithelium by blocking viral attachment and internalization. The benefits of garlic include the stimulation of T-lymphocyte and CD8+ cells and also delay the sensitivity in the cells and tissues of the body. Cumin has beneficial health effects such as anti-inflammatory, cholesterol lowering, weight loss and memory boosting are inceptions. Fenugreek has proven useful in relief against colds, influenza, bronchial disorders, catarrh,

asthma, sinusitis, constipation, pneumonia, pleurisy, laryngitis, sore throat, emphysema and hay fever tuberculosis. The intake of capsaicin improves respiratory disorders as well which is typically symptom of attack of capsaicin. Conclusively, it can be said that curcumin has immune balancing properties which can be beneficial for those with disorders involving chronic stress.

The macro and micro nutrients deficiencies are threatening because it causes the body to be infected easily by pathogens. The balanced diet along with the supportive therapies can help a patient to recover from infections and diseases like COVID-19.

An immunomodulatory effect is one that defines intensification or diminution of immune responses and the agent that brings it about is referred to as an immunomodulator. So in this paper, we have laid down the supportive role of various herbs and spices in boosting our immune system as well as fight back the pathogens. COVID-19 is a pandemic in which an attack of Corona Virus is on our respiratory system. AYUSH Ministry has also proposed a 'KADHA' to be taken during these COVID 19 times; this kadha is prepared from various spices and herbs which are beneficial for health. It is a mixture of Basil, Pepper, Ginger etc. and these are also discussed in this paper with supporting researches. Therefore we strongly recommend the usage of these spices and herbs in daily life but in moderation and they can also be used effectively as supportive therapy for managing COVID-19.

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