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Immunity boosters' herbs and foodstuffs: Need of the hour to prevent COVID-19

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Abstract

Any foodstuffs, Ayurvedic concoctions (mixtures of various plant-based elements) and supplements which strengthen or enhance body's natural defense mechanism are known as immunity boosters. The current global public health crisis, a novel Coronavirus disease (COVID-19) also called as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV-2) is rapidly spreading among human population. Foodstuffs and herbs/plants which strengthen immunity have been reported for their potential antiviral capability against SARS-COV-1 and can be further exploited to prevent COVID-19. In this present review, various medicinal herbs/plants like amla, garlic, ginger, eucalyptus, turmeric, tulsi, chhota gokhru, ashwagandha and giloy are listed and their usage in promoting health, improving immunity and prevention from COVID-19 is justified. Herbs/ plants have reported to possess low toxicity compared to synthetic drugs and have a potential to build and maintain immune system of an individual which can be an effective solution for this contagion. Various plants and its constituents are reported to be active against respiratory diseases such as SARS-CoV-1 and can provide basis for the research work and development of new bioactive drugs or even vaccines.

I. INTRODUCTION

Coronavirus (COVID-19) was announced as a 'pandemic' by World Health Organization (WHO) on 11th March 2020 causing 1,039,406 deaths and 35,347,404 confirmed cases globally as reported till 6th October 2020. Out of which, the most affected population is elderly patients in the age group of 61-70 years and least affected age group is 21-30 years.[1] The name coronavirus was coined by June Almeida and David Tyrrell in 1968 as the virus exhibited crown like appearance. The taxonomical classification of coronavirus consists of Coronaviridae family in the Nidovirates order.[2] SARS-CoV was first seen in Southern China in 2003, which again showed its existence in December 2019 in Wuhan City, Hubei province, China.[3] Nearly about 27 cases were hospitalized with a primary diagnosis of pneumonia of unknown etiology. Wuhan's Huanan seafood wholesale market which trades in fish and variety of live animals like bats, snakes, marmots, etc. are said to be associated with these hospitalized cases. A team of scientists were sent to gather information on the outbreak, by the Chinese Centre for Disease Control and Prevention (CCDC). After collection of nose and throat swab samples from patients, the causative agent was identified as Novel Coronavirus by CCDC on 7th February 2020 and WHO named it as COVID-19.[4] Since then many research scientists of all over the world are working in their laboratories to study in detail the pathogenesis and transmission of the virus, discover full proof diagnostic method to identify presence of the virus and develop best curative treatment against the virus.

Patients with COVID-19 infection experience a wide range of symptoms varying from mild signs, reported among 20% of infected patients which advanced to severe conditions like pneumonia, respiratory failure and even death in some cases. The most common symptoms include fever (98%),

cough (82%), shortness of breath (55%), fatigue (70%), myalgia (44%) and sputum production (33%) while the less common symptoms include headache (13%), diarrhea (10%), nausea and vomiting (10%) and haemoptysis (5%).[5]

Currently, the health crisis due to COVID-19 outbreak is affecting the mankind of entire globe where people with feeble immune system are at highest risk. So, improving body's immune system is of utmost importance to survive in this contagion. As there is no vaccine available in the market yet, boosting the immunity with self-care manifests the key to be safe and healthy.[6] This review article encompasses various medicinal plants, herbs and nutraceuticals which can are beneficial in fighting with COVID-19.

I. Amla

Indian goose berry fruits- *Emblica officinalis* Gaerth (*Phyllanthus emblica* Linn.) generally known as Amla belongs to the family of Euphorbiaceae. Amla is a rich source of Vitamin C which is recommended for boosting immunity during this pandemic.[7]

Constituents: Fruits are abundant nutritive reservoir of vitamin C, along with minerals and amino acids. Tannins- gallic acid, sugars, gums, albumin and crude cellulose are present in the pulpy portion of the fruit. An immature fruit may also contain phyllantidine, phyllantine, R1 and R2 growth inhibitors, four other auxins- A1, A3, A4, and A5 and indoleacetic acid.[7]

Pharmacological activities: Amla has been used as a remedy for symptoms of cold and cough since ancient times. It is rich in vitamin C which plays a major role in boosting immunity. Antioxidants present in amla help in reducing free radical activity which eventually avoids oxidative stress. This lowers the risk of diseases and also helps in repairing the body functions. Chromium present in amla helps in lowering the risk of diabetes which is a major cause of death in COVID-19.[7] 100g of amla contains 600mg of vitamin C, so it is recommended to consume it on a daily basis along with other supplements to meet daily requirement. Vitamin C boosts immunity by encouraging the production of white blood cells like lymphocytes and phagocytes which help to protect the body against cough and flu like infections. Being an antioxidant, it protects the body from free radical damage as growth and survival of the cells is affected due to the oxidative stress produced during free radical damage. Also, it reduces the severity of allergic reactions and helps to fight off infections.[8]

Marketed formulations: Chirayu Pharma (Jeevani malt), Zandu (Triphala churna 200mg), and Dabur (Chyavanprash).

II. Food stuffs rich in Vitamin D

Vitamin D is a group of fat-soluble secosteroid hormone normally produced on exposure of the skin to the sunrays emitting UVB rays. It is reported to contribute in decreasing lung injury and maintaining a balance in renin- angiotensin system. It also decreased the risk of acute respiratory tract infections and inflammatory responses along with improving immunity.[9] A connecting link is shown between the rising numbers of COVID-19 cases, mortality and lower levels of vitamin D. A majority of death cases were recorded in a retrospective cohort study conducted on 780 COVID-19 patients was carried out in Indonesia with the individuals having below normal vitamin D levels.[10] Foodstuffs rich in vitamin D should be consumed to meet the daily requirement, which includes fatty fish, cheese, egg yolks along with supplementation. It contributes in improving immune system and lowering COVID-19 induced cytokine storm by regulating white blood cells and controlling the release of higher number of inflammatory cytokines.[11]

Marketed formulations: Dvion (Cholecalciferol granules), D Drop Injection (Vitamin D3), Nano D3 (Vitamin D3 Supplement).

III. Garlic

Garlic- *Allium sativum* Linn. commonly called as Lasan belongs to the family Liliaceae.[12] It is the popular ingredient in cooking, due to its strong and delicious taste complementing most savory dishes like dals, soups and sauces.

Constituents: It contains Vitamin B6, Vitamin C, manganese, selenium and traces of fibre, Vitamin B1, iron, calcium, copper, potassium and phosphorous. Compounds like sulphur, allicin and

diallyl disulfide and s-allyl cysteine are present in garlic cloves.[12]

Pharmacological activities: Garlic and its bioactive molecules and formulations have been widely used for its anti- inflammatory and immunomodulatory properties. It is reported as a promising treatment for preventing colds and flu. It is extensively used as carminative, aphrodisiac, expectorant, stimulant and in intermittent fevers, respiratory diseases such as chronic bronchitis, bronchial asthma, whooping cough and tuberculosis. Along with this, it is reported to have antiviral, antibacterial, antifungal, antitumor and antidiabetic effects.[13] A research work was performed by Shojai et. al, in which specific pathogen free embryonic egg was used to determine the effect of *Allium sativum* extract on two strains (4/91-Intervet and M41) of infectious bronchitis virus (IBV). IBV is a single-stranded RNA virus, positive sense that belongs to the coronavirus. The outcomes of the study stated that a mixture of garlic extract had better inhibitory effects on non-acute strain as compared to acute strain of IBV. WHO has stated that- Garlic is a healthy food that may have some antimicrobial properties, however, there is no evidence from the current outbreak that eating garlic has protected people from the new coronavirus.[14]

Marketed formulations: Garlic plus, Garlic pearls, Organic garlic in honey, Garlic capsules.

IV. Ginger

Ginger- *Zingiber officinale Roscoe*, dried rhizomes popularly called as Adrak belongs to the family Zingiberaceae.[15] It is a perennial herb growing up to 1m and used regularly in Indian cooking items.

Constituents: A ginger rhizome is reported to contain terpenes such as zingiberene, β-bisabolene, α-farnesene, β-sesquiphellandrene, α-curcumene and phenolic compounds include gingerol, paradols, shogaol.[15]

Pharmacological activities: Ginger can relieve sore throat, hoarseness and loss in voice caused due to contagious infection laryngitis. It is used as an adjunct treatment in cold, cough, asthma and in painful stomach problems. It exhibits anti-inflammatory potential relieving the pain while suffering from sore throat. Being a spicy and pungent herb, it provides heat that body requires during this pandemic. Also, it is used as an antiemetic, positive inotropic, spasmolytic, aromatic stimulant, carminative, condiment and flavoring agent.[15] Wasim Raja et.al, highlighted the antibacterial and anti-cough forming activity of *Zingiber officinale* extract. The disc diffusion assay was performed to monitor the antibacterial activity of different concentrations of plant extract. Antibacterial activity was determined for three microorganisms *Proteus mirabilis, Klebsiella pneumoniae and Streptococcus aureus*. The results obtained after 12 hours showed sensitizing effect of extract against mentioned microorganisms at 250 and 500mg/kg concentration. *In vitro* Fenton reaction, *Z. officinale* and other plant constituents have shown the potent antioxidant property. Also, the anti-cough forming activity was exhibited by *Z. officinale* as compared to standard (Benadryl) using SGOT and SGPT enzymes.[16]

Marketed formulations: Immune boosting ginger tea, Herbalife Afresh, Amul milk including tulsi and ginger for boosting the immunity, Pain kill oil, J.P. Liver syrup (Jamuna Pharma), Abana, Gasex (Himalaya Drug Company), Hajmola (Dabur), Strepsils (Boots Piramal Healthcare), and Sage Massaj oil (Sage Herbals).

It is suggested to consume ginger on daily basis in order to fight cough and cold like symptoms which is a major concern in COVID-19. Now a days, to boost immunity against COVID-19 ginger-tulsi tea, lemon- ginger drink, raw ginger root, ginger-honey drink, ginger powder etc are recommended.[6]

V. Eucalyptus

Eucalyptus globulus and other subspecies of family Myrtaceae, consists of essential oil commonly known as Nilgiri obtained by the distillation of fresh leaves. Mostly, it is used with steam inhalation for cold and cough since ancient times.[17]

Constituents: The plant contains volatile oils such as 1, 8 cineole-eucalyptol; p-cymene, alpha-pinene, sesquiterpenes like aromadendrene; aldehydes and ketones and alcohols. [17]

Pharmacological activities: The leaf preparations are used as a tonic, stimulant, stomachic (dyspepsia), in typhoid fever, asthma, whooping cough etc. Various respiratory related ailments,

bronchitis, asthma, sore throat, cold, can be treated by taking a vapor bath with eucalyptus. Also it has allied properties such as stimulant, antiseptic, flavoring agent, aromatic, deodorant, expectorant etc. Eucalyptus is found to stimulate immune system response according to findings published in BMC immunology journal. It enhances immune system's phagocytic response to pathogens in a rat model. Another review article has also discussed its antiviral and antimicrobial properties. [18] Maryam Sadat Sadatrasul et. al., carried out a study in which emulsions of hydroalcoholic leaf extract of eucalyptus were formulated and its antiviral activity was determined. Further, the emulsion was tested against Madin-Darbey Canine Kidney (MDCK) cells infected with A/H1N1 virus (Swine flu). The hemagglutination (HA) and cell culture infectious dose 50% ($CCID_{50}$) assays were carried out to measure viral titers. This viral binding study showed that the oil-in-water emulsions containing 2% extract inhibited virus replication. Therefore, this formulation can be suggested to prevent transmission of influenza virus.[19]

Marketed formulations: USFDA approved Soulflower Eucalyptus Essential oil, Organic eucalyptus oil, Deva Eucalyptus Essential oil.

VI. Turmeric

Turmeric- *Curcuma longa* consists of the dried rhizomes generally called as Haldi or Kurkum belonging to the family Zingiberaceae.[20] It is safe, effective, easily available and regularly used in cooking of Indian food.

Constituents: The main active constituents of *Curcuma longa* are demethoxycurcumin, curcumin and diacetylcurcumin. Some essential oils such as tumerone, germacrone, atlantone, and zingiberene are also present. These oils are known to boost immunity related functions, blood circulation advancement, accelerate elimination of toxins from the body and improve digestion. [20]

Pharmacological activities: *Curcuma longa* exhibits anti-inflammatory and immunomodulatory activity. It is briefly used as a tonic, stomachic (aid in digestion and stimulate appetite), carminative, exhibits anthelmintic activity and acts as laxative. It is also commonly used for treating fever, gastritis, dysentery, cough (chest congestion), increased cholesterol, hypertension, rheumatoid arthritis, jaundice, problems related to liver and gall bladder, wounds (diabetes), urinary tract infections, menstrual discomfort and skin disorders.[20] Avasarala et. al., performed an experimental work on mouse infected with virus induced acute respiratory distress syndrome, wherein curcumin inhibited fibrosis by modulating the inflammatory response. Curcumin also modified chemokines/ cytokines including IL-6, IL-10, IFNγ and MCP-1 from both the inflammatory infiltrate and lung tissue through a reduction in the modulation of phosphorylated NFKβ65. Curcumin also significantly reduced TGFβR11 which is required for TGFβ signaling.[21]

Marketed formulations: Turmeric juice (Basic Ayurveda), Amul Turmeric milk for immunity boosting, Turmeric 60 capsules/ 36g (Maharishi Ayurveda).

VII. Tulsi

Sacred basil- *Ocimum sanctum* Linn. (Family - Labiatae) traditionally called as Tulsi.[22] All parts of tulsi are utilized for medicinal purpose, especially leaves. The plant is considered to be sacred in our Indian culture and so planted outside of many houses which make it readily available for use.

Constituents: The leaves of *Ocimum sanctum* contain volatile oils comprising of eugenol and methyl eugenol. The aqueous leaf extract of *Ocimum sanctum* reported to contain two flavonoids orientin and vicenin and phenolic compounds such as cirisilineol, circimaritin, rosameric acid, apigenin and isothymusin exhibiting antioxidant activity.[22]

Pharmacological activities: Tulsi is recommended to be used as a home remedy for prevention and treatment of wide range of illnesses such as common cold, cough, sore throat, fever (malarial), fatigue, earache, headache (migraine), digestive disorders (flatulence, colic pain, diarrhea), bronchitis, asthma, hepatic diseases, influenza, skin diseases, wound, insomnia, arthritis and as an antidote for snake bite and scorpion sting. In traditional medicine, the leaves are consumed daily to improve memory. The consumption of tulsi leaves cures mouth ulcer and infections; drinking water containing leaves can

kill germs present in it.[22] *Ocimum sanctum* is used in the management of pain, diarrhea, cough and fever which are the common symptoms of COVID-19. It has been used in the management of fever ranging from normal fever to malarial fever.[23] Also, it is good for boosting up the immune system of the body and aid to protect from threatening virus and bacteria.[24] Vinaya M et. al., conducted a single-blind cross-over study on *Ocimum sanctum* Linn. to evaluate its bronchodilation potential in asthmatic patients. The results depicted that *Ocimum sanctum* 200mg taken twice daily produced progress in both, FEV1 (Forced Expiratory Volume) and PEFR (Peak Expiratory Flow Rate) values on 4th and 7th day similar to Salbutamol 2mg when consumed twice daily.[26]

Marketed formulations: Adulsa cough syrup (Manbro), Amul Tulsi milk for immunity boosting, Tulsi Ghanvati (Patanjali), Dabur Honitus (Herbal cough remedy).

VIII. Chhota Gokhru

Chhota Gokhru- *Tribulus terrestris* Linn., the dried ripe seed belonging to family Zygophyllaceae. It is a saponin rich plant with other known components being flavonoids, alkaloids, lignanamides and cinnamic acids.[27]

Constituents: *Tribulus terrestris* contain numerous bioactive phytochemicals, such as steroidal saponins, flavonoids, glycosides, phytosterols, tannins, terpenoids, amide derivatives, amino acids and proteins.[26] Fruits contain major bioactive compounds like six cinnamic amides and ferulic acid which shows inhibition of Papain-like proteinase (PLpro) which is considered as major protein target of COVID-19. Papain-like protease (PLpro) shows an essential proteolytic enzyme for protection to pathogenic virus and bacteria. The methanol extract of fruits are reported as potent inhibitor of papain-like protease (PLpro).[27]

Pharmacological activities: It is mostly used for cough, chest pain, eczema, enlarged prostate and cancer. *Tribulus terrestris* are renowned for its use in pharmaceutical preparations and food supplements. It is popular as a general health supplement and as an ingredient in testosterone booster supplements.[27] Mallaiah et. al., performed a research work on evaluation of immunomodulatory activity of *Tribulus terrestris* in animal model. In this study, immunomodulatory activity of *Tribulus terrestris* was evaluated by using immunological studies like phagocytic test, carbon clearance test, humeral antibody titer (hat) and delayed type hypersensitivity (dth) response, t- cell population (rosette and e-rosette form) test and drug induced myelosuppression test. It was observed that *Tribulus terrestris* exhibited significant immunostimulatory effect.[28] M. Qiu et. al., examined the activity of Terrestrosin D, a constituent isolated from *Tribulus terrestris* for inflammation and fibrosis in murine pulmonary tissues. The inflammatory response was suppressed from the initial stage (reduction of IL-8 levels), with no “by passing” effects to initiate downstream process of inflammation. The co-administration of Terrestrosin D with Bleomycin in the pulmonary tissues of mice significantly reduced the inflammatory and fibrotic changes were observed in the classic bleomycin models.[29]

Marketed formulations: Healthy Hey Nutrition (extra strength 60% saponins) 700mg /serving 120 capsules.

IX. Ashwagandha

Indian Ginseng- *Withania somnifera* commonly called Ashwagandha belonging to Solanaceae family consists of roots and stems. It is present in Patanjali's Coronil tablets along with giloy and tulsi, which is marketed as an immunity supplement. It also possesses antioxidant properties and reduces the level of stress hormone Cortisol which increases when suffering from the deadly disease like COVID-19.[30]

Constituents: It contains phytoconstituents like withanolide A and B, withaferin A, withanone and withanosides. The main constituent present is an alkaloid withanine. Other compounds include pseudowithanine, hygrine, anahygrine somniferine, pseudotropine, tropine, isopellederine, anaferine, and steroid lactones. The leaves contain steroid lactone, commonly known as withanolides.[31]

Pharmacological activities: *Withania somnifera* would be a useful in the management of COVID-19 through modulation of host (Type 1 helper T lymphocytes) Th-1/Th-2 (Type 2 helper T

lymphocytes) immunity. The potential mechanism of action is beneficial in inducing antiviral immunity, which includes increased IFN-gamma responses with optimal anti-inflammatory activity and down regulation of IL-1, IL-6, TNF-alpha and other inflammatory mediators which are related to the clinical targets of COVID-19.[32] As reported in literature, several withanolides isolated from *Withania somnifera* possess both immunosuppressive and immunostimulatory properties.[32] It has proved its rejuvenating and life-prolonging property. *Withania somnifera* is mostly used as a tonic to calm the mind, reduce lethargy, increase stamina and improve sleep.[31] Oberholzer et. al., conducted a study on BALB/C mice induced asthma to investigate the effects of *Withania somnifera*, selenium and hydrocortisone on their blood count and bronchial lavage. *Withania somnifera* alone and in combination with selenium exhibited reduced cell number in blood compared to selenium alone. The study concluded that *Withania somnifera* considerably reduced white blood cells in both blood smear and bronchial lavage, signifying its anti-inflammatory potential and prove its effectiveness in the treatment of asthma.[34]

Marketed formulations: Ashwagandha spiced green herbal tea (Ban Labs), Coronil tablet (Patanjali), Ashwagandha capsules (Organic India).

X. Giloy

Giloy- *Tinospora cordifolia* is a herbaceous vine widely called as Guduchi, belonging to the family Menispermaceae and indigenous to tropical regions of the Indian subcontinent.[35]

Constituents: The chemical constituents present in *Tinospora cordifolia* are alkaloids, glycosides, hormones, phenolics, aliphatic compound, polysaccharides, protein-rich leaves, calcium and phosphorus [35]. The reported alkaloids are bitter gilonin, non- glycoside gilonin gilosterol and berberine. Also, tinosporaside, tinosporide, cordifol, cordifolide, columbin, b-sitosterol are present in it.[36]

Pharmacological activities: *Tinospora cordifolia* stem is one of the major part of Ayurvedic medicinal preparations used in general debility, dyspepsia, cough and urinary diseases. It has shown immunomodulatory activity, macrophage activation and immunostimulation effect against viral infections.[35] The extracts have multiple medicinal properties such as antibacterial, antiallergic, antidiabetic, analgesic, diuretic and anticancer. This Ayurvedic herb is a powerhouse of antioxidants that neutralize free radicals and prevent inflammation. Also, it purifies blood, boosts immunity, flushes out toxins from the body and fights against bacteria and virus effectively. Consuming giloy juice is helpful in reducing fever which is one of the indicative sign of COVID-19. It also helps in tackling another symptoms of COVID-19 like cough, cold and breathing problems.[37] Sagar and his coworkers have performed a study on evaluating the effectiveness of compounds isolated from *Tinospora* against SARS- COV-2 targets. The binding efficacy of isolated compounds such as berberine, tinocordiside, cordifoliside A, jatrorrhizine, magnoflorine, isocolumbin, sinapic acid, syringin and palmatine were tested against surface glycoprotein (6VSB) and receptor binding domain (6M0J), which are responsible for virus attachment to the host cell and RNA polymerase (6M71) and main protease (6Y84) responsible for virus replication in the host cell using *in-silico* tools. The results proved that compounds isolated from *Tinospora cordifolia* showed high binding efficacy against mentioned targets involved in virus attachment to host receptor and replication of the virus.[38]

Marketed formulations: Giloy juice (Baidyanath), Giloy juice (Patanjali), Giloy ki ghanvati (Dabur).

2. CONCLUSIONS

As the global pandemic of COVID-19 still persists, it is a very crucial time to investigate an active drug for therapeutic treatment. Herbs/ plants have reported low toxicity compare to synthetic drugs and have a potential to build and maintain immune system of an individual, which can be an effective solution for this contagion. Various plants *Toona sinensis Roem*[39], *Glycyrrhiza radix*[40], *Lycoris radiata*[41], *Rhizoma cibotii*[42] are reported to inhibit SARS-CoV-1 replication when tested against infected Vero cells and can provide basis for the research work and development of medicine or

even vaccines. The Ministry of AYUSH has also published following guidelines for enhancing the immunity which includes spices like haldi, jeera, dhaniya and garlic to be consumed in daily diet, amla based Chyavanprash, herbal tea/ decoction (kadha) prepared from tulsi, dalchini, kalimirch, shunthi and manuka and golden milk containing haldi powder in hot milk is recommended. Along with this, vitamins, nutrients, herbs, nutraceuticals and probiotics are also useful in boosting the immunity and fighting cold- flu like symptoms.[6]

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