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Natural herbs as immunity booster against infectious diseases like Covid-19.- A systematic review

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Abstract

Immune system is a biological structure in humans. Its function is to protect human body and to fight against bacteria, viruses and environmental agents. Viral diseases like COVID-19 can only be prevented by a strong immune system. So far no effective drug or vaccine has been developed against COVID-19, but inclusion of natural herbs in diets may boost immunity. This review is conducted to shed light on importance of natural herbs and their role in improving immunity against COVID-19. Findings revealed that a variety of natural herbs like *Rhus coriaria* (Sumac), *Zingiber officinale* (Ginger), *Allium sativum* (Garlic), *Ocimum sanctum* (Tulsi), *Cassia angustifolia* (Sennamakkahi) *Licorice*, *Camella sinesis* (Green tea), Citrus and Limon have been claimed to be very effective in boosting the immunity against infectious diseases like COVID-19.

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Introduction

Nutrition has an important role in the prevention of fatal infections like COVID-19 by reducing multiple risk factors. Functional food is required for living, physical and mental health, and for the improvement of physiological function (Abuajah *et al.*, 2015). The immune system always remains active and acts to distinguish self from non- self, therefore protecting the host. Nutrients contribute a lot to maintain this physiological phenomenon which is suppressed with under-nutrition (Calder and Kew 2002).

For the efficient functioning of the immune system, vitamins (A, B6, C, and E), minerals (Se, Fe, Cu, Zn), and essential fatty acid (linoleic acid) are crucial for the body (Calder and Kew 2002). Additionally, natural herbs are one of the important and effective methods through which immunity of person becomes strong. Herbs enhance the action of immune properties in a person like herbs increase the cytokine expression; increase the activity of CD8 and CD4 T cells, and natural killer cells (Sakure *et al.,* 2008) by producing phytochemicals and other chemicals. Phytochemicals have biological properties as stimulation of the immune system (Carratu and Sanzini 2005).

People of the whole world is worried about this pandemic disease (COVID-19) and they have not find any positive treatment or vaccine. Literature report that compounds like anti-oxidants, phytochemicals, anti-inflammatory that help the immune system to fight against viruses.

In this study, we have summarized different herbs *Rhus coriaria* (Sumac), *Zingiber officinale* (Ginger), *Allium sativum* (Garlic), *Ocimum sanctum* (Tulsi), and *Cassia angustifolia* (Sennamakkahi) licorice, green tea that boost up immunity by producing different chemicals. This review would help researchers in evaluating the effects of different natural herbs for boosting of immunity, and how strong the immune system is necessary for the fighting infections against COVID-19.

Materials and methods

A systematic literature search was performed in databases i.e. PubMed, Embase (Elsevier), Google Scholar, and the World Health Organization, to identify the researches addressing the role of natural herb in enhancing immune system and helps in fighting viruses. The MeSH terms and keywords like efficacy, natural herbs, remedies, infections, viral diseases, immune system, immunity, *Rhus coriaria* (Sumac), *Zingiber officinale* (Ginger), *Allium sativum* (Garlic), *Ocimum sanctum* (Tulsi), and *Cassia angustifolia, Licorice* (Sennamakkahi), green tea were combined along with Boolean operators to identify the related articles.

Findings and discussion

Herbs are not only used as food stuff but also has a pharmaceutical use. In past years, many types of research and studies are made on the medicinal role of herbs and due to these researches, many new herbs and their constituents were discovered that play a therapeutic role. But the main focus is on those herbs that enhance immunity. Such as licorice, green tea. Because it is said that licorice has various therapeutic effects, e.g., antidote, anti-coagulant, analgesic, antimicrobial, and non -mutagenic. In addition to licorice, many other herbs contain important oxidation suppressive compounds that provide defense against many lethal infections or viral infections (Huang *et al.,* 2008). The other herbs are *Rhus coriaria* (Sumac), *Zingiber officinale* (Ginger), *Allium sativum* (Garlic), *Ocimum sanctum* (Tulsi), and *Cassia angustifolia* (Sennamakkahi). Systematic review of natural herbs with Immunity is shown in table no. 1, while the constituents and mechanism through which these herbs enhance immunity is discussed below;

Rhus coriaria L. Anacardiaceous (Sumac)

Sumac is conventionally used in turkey and middle-east. The fruit is red and contains only one seed. Many studies suggest that the leaves of sumac contain many phytochemicals i.e. flavonoids that are responsible for its therapeutic use. Rhuscoriaria is an essential plant and it is popularly used as a spice in Mediterranean diet because of its health maintain characteristics (Kosar *et al.,* 2007).

Table 1. Systemic review of natural herbs with immunity.

Ingredients	Data collection	Method	Findings	Reference
Rhus coriaria L. Anacardiaceous (Sumac)	Blood serum of sample was collected by centrifugation and analyzed lysozyme activity.	Trout was collected with an average weight about 38g and fed basal diet for first two weeks and then fed basal diet mixed with sumac powder.	Increase in immunity and resistance to microorganisms	(Gharaei *et al.* 2020)
Zingiber officinale (Ginger)	Blood of broilers was collected and performed analysis of variance test (ANOVA) and analyze humoral immunity	Broilers were obtained and place them in cages and divide them into groups and one group fed diet mixed with ginger and the other without ginger	Increase in humoral immunity	(Azhir *et al.* 2012)
Allium sativum (Garlic)	Blood of sample was collected and perform chemical test and check plasma proteins level Perform hematology test and check level of WBCs	150 Broilers were obtained and randomly divided about 30 broilers/treatment group First broilers fed basal diet for two weeks and then add garlic powder	Increase in level of WBCs	(Fadlalla *et al.* 2010)
Ocimum sanctum (Tulsi)	Through Erythrocyte (E)-rosette formation test,	A group of rats treat with extracts of tulsi was exposed to typhoid antigen and sheep red blood cells and then perform given test	Increase in antibodies	(Mondal *et al.* 2009)
	Count anti-sheep red blood cells	A group of rats also treat with leaves of tulsi derived through steam distillation	Increase in humoral immunity	
Glycyrrhiza glabra L. (Licorice)	Through ELISA and Real-time PCR test	Animal (pigs) were obtained and divided into groups (8 animals/group) and fed Diet with licorice. The IgA antibody level was analyzed at day 50 and 51	Increase in antibody production and immunity	(Katayama *et al.* 2011)
Cassia angustifolia (Sennamakkahi)	Blood of mice were collected in EDTA-vacutainers and perform DLC test	A group of mice was obtained and divided into five groups (4mice/group) two groups are treated with normal saline and other three group with extract of senna makkhi	Increase in WBCs Increase in immunity	(Bagwe *et al.* 2019)
*Camellia sinensis (*Green tea)	Hematological analysis and DLC test	A group of mice was obtained and divided into four groups each group consist of six members. One group was control group and other three was experimental group. Control group fed normal diet and other three group fed epigallocatechin-3-gallate containing diet	Increase in leukocytes	(Sharma *et al.* 2017)
Citrus and Limon	Hematological analysis and also perform Nitro blue tetrazolium	A group of fish was collected and distributed in aquarium and fed diet mixed with oils of citrus Limon and also injected with a bacteria E.tarda	Increase in white blood cell count and increase in immune response	(Baba *et al.* 2016)

Besides this, *R. coriaria* also prevents cancer, fever, and protect our genetic material. It also has disinfectant, antimicrobial, oxidation suppressive, heart and liver protection, and glucose Maintenance, properties, which support its conventional use. Many past types of research have suggested that sumac contain hydroxybenzoic compounds, such as hydrolyze tannins, pigments i.e. anthocyanins, and also organic acids such as 2-Hydroxybutanedioic and 2-Hydroxypropane-1,2,3-tricarboxylic acid. (Abu-Reidah *et al.,* 2015) the organic acid component of *Rhus coriaria* is responsible for its acidic sour taste. Conventionally, in medicine, *Rhus coriaria* is used as an astringent agent (Sakhr and El Khatib 2020).

The antimicrobial activity of *Rhus coriaria* extract had been examined at different concentrations through the disc diffusion method or MIC (minimum inhibitory concentration) (Kossah *et al.,* 2013).

Zingiber officinale (Ginger)

It is commonly known as Ginger belongs to the genus *Zingiber* from Zingiberaceae (Han *et al.*, 2013). Currently, it is reported that it has biological activities, like antioxidant, antimicrobial, anti-inflammatory, and anticancer (Zhang *et al.,* 2016; Nile and Park 2015; Kumar *et al.,* 2014). Further, it is studied that it has potential against prevention and management of many diseases like respiratory disorders, obesity, diabetes mellitus, emesis, headaches, and induced nausea (Suk *et al.*, 2017; Wei *et al.,* 2017; Akinyemi *et al.,* 2015; Ho *et al.,* 2013; Stoner 2013; Townsend *et al.,* 2013; Walstab *et al.,* 2013). Chronic inflammation leads to a low immune response which enhances the chances of illness (Deng *et al.,* 2006) and patients having chronic immune-mediated inflammatory diseases have a high risk of this infection (Schett *et al.,* 2020). Having strong anti-inflammatory and antimicrobial properties, it helps in boosting the immune response by reducing inflammation. Due to these anti-inflammatory properties, it can be used against Covid-19 for boosting the immunity (Mao *et al.,* 2019; Whitfield).

Allium sativum (Garlic)

It is traditionally known as garlic; the most abundant compound has antioxidant metabolites (Chan *et al.* 2019; Colín-González *et al.,* 2012). It has sulfur-containing amino acids and other compounds that it does not increase just immune system activities but also antiviral activities of the body against many viruses like simplex and influenza B reported by many scholars. Many factors like physical injury, mental tension, inadequate nutrition, chemical pollution, enormous pressure are continuously disturbing the immune system. It can be compensated with nutrients like garlic as it has the potential for the maintenance of health (Salman *et al.,* 1999) and booting immune system against infectious diseases (Abdullah *et al.*, 1988; Onyeagba *et al.,* 2004).

When an experiment was done on HIV patients in the USA or viral infected patients in China during bone marrow transplant, it was seen that garlic extract enhances the activity of natural killer cells and possesses a "potent antiviral activity" (Josling 2001). It can be used as prevention, treatment, and reduction of reinfection (Mekonen *et al.*, 2019).

Ocimum sanctum (Tulsi)

In the Indian language, *Ocimum sanctum* is called 'tulsi' or in the English language, it is called 'holy basil'. It is a soft, straight, fragrant bush found throughout India. It is mostly grown in gardens. Conventionally, in medicine, several parts of *Ocimum sanctum* have been used for the treatment of respiratory disorders, skin diseases, chronic fever, joint pain, and insect bite. Previous researches also suggested *that Ocimum sanctum* has antifertility, non-mutagenic, antimicrobial, glucose, liver and heart maintenance, antitoxin, pain-relieving, stimulatory, and properties. It also protects from nausea. The leaves of *Ocimun sanctum* are a good antidote for common colds. The oils that are derived from the leaflet of *Ocimum sanctum* inhibit the growth of bacteria when bacteria were grown outside in a culture i.e. *Escherichia coli, Bacillus anthracis*, and *Pseudomonas aeruginosa* that shows antimicrobial properties of *Ocimun sanctum*.

The essential constituent of oils that are derived from leaflets of *Ocimum sanctum* through steam distillation is eugenol, carvacrol, methyl eugenol, and caryophyllene. But Eugenol is the most potent component of oils that is responsible for the medicinal use of *Ocimum sanctum* (Prakash and Gupta 2005). In an experiment, a decoction of Tulsi leaves in liquid form was mixed within the diet of diabetic rats and it was seen that there was a great reduction in blood glucose level, serum lipid level and glucose tolerance level was also improved. And it was also noticed that there was an increase in oxidation and free radicals' suppressive enzymes i.e. superoxide dismutase, catalase, glutathione peroxidase, glutathione transferases and antioxidants like glutathione.

This experiment proved that *Ocimum sanctum* has medicinal properties like antidiabetic, antilipidemic, and antioxidant (Mohan *et al.,* 2011).

Glycyrrhiza glabra L. *(Licorice)*

Licorice is a common herb that is conventionally used as a therapeutic herb in China. Researchers suggest that licorice consists of almost more than 20triterpenoids and 300 flavonoids that are responsible for the medicinal activities of licorice. These components exhibit antiviral, antimicrobial, anti-inflammatory, antitumor, and other properties.

The parts of licorice herb that are mostly used in medicine are its roots and rhizomes. As viral and microbial diseases spread rapidly in many countries it is important to develop some antiviral or antimicrobial agents and, in this circumstance, licorice got great attention due to its superb activities.

The flavonoids and triterpenoids of licorice are glycyrrhizic acids (GL), 18beta-Glycyrrhetinic acid (GA),7,4'-Dihydroxy flavanone (LTG), chalconoid (LCA), retrochalcone and glabridin are the dynamic constituents which fight against viral infections. But the glycyrrhizic acid is the most potent antiviral constituent that performs its role by declining viral activity through restraining gene transcription, translation and replication, decreasing adherence and strain, and binding of amphoterin to DNA.GL also increases the working of the infected individual cell by stopping the degradation of IkB, enhancing the growth of T lymphocytes, or decreasing cell death of the host. GA performs its role against the virus by decreasing virus replication, or attachment to the host cell or by increasing activity of host cell (Wang *et al.,* 2015). Glycyrrhizin acid restrain the cell death of liver, monitoring immune system activities, inhibit uncontrolled cell growth and provide protection against viral infections (Noreen *et al.,* 2020).

Cassia angustifolia (Sennamakkahi)

Sennamakkhi is extensively used because of its various advantages. It belongs to family Leguminosae. *Cassia angustifolia* is widely used as a conventional therapeutic herb in China, India, Pakistan, Africa, and also in the western allopathic system of medicine. It is mostly used in the treatment of respiratory diseases, skin diseases, gastrointestinal diseases, or depression. For the treatment of respiratory diseases dried leaves of *Cassia angustifolia* are ground to make powder then 2g of powdered leaves are mixed with equal quantity of powdered rose petals. Then 5-10g of this mixture is given with water to patients for five days for the treatment of respiratory disorders (Sultana *et al*., 2012).

Camellia sinensis (Green tea)

The pharmaceutic and curative consequences of green tea are about 5000 years old. The basic chemical components of green tea are polyhydroxybenzoids, caffeine, and protein constituents. In addition to these, green tea also encompasses flavonoids. Flavonoids are thought to possess antioxidant properties that have many favorable consequences such as they decrease inflammation and also act as a disinfectant (Sharangi 2009).

The recent investigation also evaluates that there is a latent component in green tea i.e. phytochemical epigallocatechin-3-gallate (EGCG). EGCG performs many functions such as it accelerates the regularity of the circulatory system, increases the durability of immune reactions, and diminish the production of non-specific antibodies and also lightens the inflammatory and oxidative strain (Sharma *et al*. 2017).

Citrus and Limon (Lemon)

From the family Rutaceae; Citrus and Limon (L.) Burm. F. is a bush having yellow edible fruits and evergreen leaves. The important oils and juices extracted from the raw material of this pod. These fruits have exceptional nutritious characteristics, but it is remarkable due to its useful biological and physiological actions (Klimek-Szczykutowicz *et al.,* 2020). Davis reported that vitamin C is accumulated in citrus fruits, which aids in inflammatory response by activation of transporting vitamin C into cells during times of stress.

Vitamin C is essential for optimum growth for maintenance and also acts as an immune-modulating (Tewary and Patra 2008).

Vitamin C is a very potent antioxidant agent to boost your mechanism defense of the body (Pham-Huy *et al.,* 89 2008). Research has shown that high consumption of vitamin C can boost the number of antioxidant enzymes in your body fluids by over 30%. This empowers your body's natural defense to combat oxidative stress and protect you against acute and chronic ailments (Kim *et al.,* 2003) Okoth *et al.*, (2016). It is suggested that oil extracted from citrus lemon has a significant effect on the immune system of fish. Citrus peel oils show strong antimicrobial activity while fruits of citrus have antioxidant activity (Zou *et al.*, 2016).

Conclusion

COVID-19 is a serious respiratory disorder in human-caused by a coronavirus that weak the immune system. Up till now, there is no effective drug or vaccine developed against it. Literature showed that only a strong immune system can fight against infectious diseases like COVID-19. Immune system can be boost up with herbs like *Rhus coriaria* (Sumac), *Zingiber officinale* (Ginger), *Allium sativum* (Garlic), *Ocimum Sanctum* (Tulsi), and *Cassia angustifolia* (Sennamakkahi), *licorice*, and green tea as these are rich in immunity-boosting chemicals like i.e. flavonoids and triterpenoids, antioxidants, anti-inflammatory, Vitamin C, linoleic acid and many other nutritive compounds. This review develops understanding and awareness among individuals how they can boost their immune system. It also helps food scientists to conduct research on these herbs and identify how these herbs are useful in the treatment of COVID-19.

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