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A REVIEW: THERAPEUTIC POTENTIAL OF NUTRACEUTICALS MORINGA OLIFERA & ALOE VERA AS IMMUNITY BOOSTER IN COVID- 19 INFECTION

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Abstract

Nutraceuticals are dietary supplements, utilized to ameliorate health, delay senescence, prevent diseases, and support the proper functioning of the human body. The world woke up in 2020 with a new virus called coronavirus 2019 (COVID-19). The virus spread easily from Wuhan, a western province in China to the whole world and caused a pandemic situation. Our body is always exposed to mysterious invaders which can cause diseases and infections. The immune system enables to keep these contagious microorganisms at bay and protects our body depending on the strength of immune system. The nutrients like vitamins, minerals, fatty acids, amino acids etc. play a significant role in the host immunity. Moringa is a miracle tree whose leaves are rich in number of vital components that improves the body immunity. Aloe vera is one of the most important medicinal agents in various alternative systems of medical scientific studies have shown that Aloe vera has anti-inflammatory, anti-oxidative, immunomodulatory and bronchodilator. These two herbal plant can boost the immunity of healthy and sick patients, thereby giving a protection against covid-19. So, this review covers all the information about to improve immune response in covid-19 viral infection by the use of herbal plant like Moringa olifera and Aloe vera .

Keywords: **Covid 19, Immunity booster, Nutraceutical, Moringa olifera, Aloe vera.**

1. INTRODUCTION

Nutraceuticals are food-derived products that are claimed to give additional health advantages beyond the fundamental nutritional content of foods. The term "nutraceutical" refers to herbal products that have been isolated [1]. The Coronavirus 2 of the Severe Acute Respiratory Syndrome (SARS-CoV-2) affects upper respiratory tract epithelial cells, causing mild symptoms. When the virus infects the alveoli of the lungs, it can cause severe pneumonia, which can lead to respiratory failure and acute respiratory distress syndrome (ARDS) [2]. The Moringa oleifera commonly referred as “Moringa.” When compared to fruits and vegetables that contain these nutrients, moringa leaves had a higher concentration of important minerals and vitamins. Yogurt, milk, spinach, banana, and carrot all have less protein, calcium, iron, potassium, and vitamin A than M. oleifera leaves [3,4]. Aloe vera (Asphodelaceae) is a well-known and widely used for centuries for its health, beauty,medicinal and skin care properties. These two herbal plant can boost the immunity of healthy and sick patients, thereby giving a protection against covid-19 [5].

The reasons for the transition to nutraceuticals are as follows: [6–10]

1. Increasing numbers of consumers, concerned about healthcare costs.

2. Nutraceuticals are being used by those who are dissatisfied with pharmaceutical agents for enhancing health and preventing chronic disease.

3. Health care provider recognize the fact that our heavily processed food supply, coming from crops grown with chemical fertilizers, pesticides, herbicides, and often genetically modified seeds, lacks sufficient nutrients necessary for optimum Health.

4. People believing more in prevention than a cure.

5. People who suffer from chronic illnesses for which allopathic treatment has failed to provide a cure.

6. Economically challenged patients.

The US Food and Drug Administration (FDA) has not approved nutraceuticals for health benefits or disease prevention, with a few exceptions; however, nutraceutical makers have marketed them as health-promoting substances.

1.1 MERITS OF NUTRACEUTICALS

Nutraceuticals may provide a number of advantages, including the ones listed below [11].

a. It's possible that our diet's health value will improve.

b. May assist us in avoiding some medical issues.

c. Traditional medicine may be seen as more "natural" and less prone to have unpleasant side effects.

d. May have a psychological benefit from doing something for one self.

e. May easily be available and economically affordable.

f. May present food for populations with special needs (e.g., nutrient-dense foods for the elderly).

g. May help us live longer.

2. POTENTIAL NUTRACEUTICALS FOR COVID

"Immune boosting" is a hot issue in the wake of the coronavirus pandemic, alongside a slew of speculative cures, treatments, and prevention methods [12]. This belief is so widespread among laypeople that "improving the body's immune system" is the most common rationale for taking nutritional supplements. Vitamins, minerals, antioxidants, probiotics, and "functional foods," as well as other complementary and alternative medicine (CAM) techniques, are all part of the "immune boosters" market [13,14]. A balanced diet consists of a range of foods in suitable proportions of protein, carbs, fats, minerals, and vitamins, among other things. It contains all of the nutrients necessary for a healthy body and a robust immune system. The majority of poor people in India eat a restricted diet every day, which can lead to dietary deficiencies. Furthermore, due to changing lifestyles, the middle and upper classes today consume more junk and processed food. The western diet is low in nutrients and high in calories, refined sugars, salt, carbs, and saturated fats, which can contribute to increased inflammation and weakened immunity, increasing the risk of viral infections like SARS-CoV-2. SARS-CoV-2 has disrupted global health and economic wellbeing since the beginning of 2020. The regional office of World Health

Organization (WHO) in China was first alerted to the virus infection in Wuhan on December 31, 2019 and termed the infection as an epidemic on March 11, 2020. Since then, laboratories across the globe have been collaborating to develop vaccines and therapeutic agents for this novel coronavirus [15].

2.1. A NATURAL IMMUNITY BOOSTER:

Herbs are known for their several health benefits. They are anti-oxidants, immunomodulators, anti-microbials, anti-inflammatory, aid in digestion. Herbal plants that boost immune system stimulate the activity of cells responsible for fighting infections [16]. These natural immune boosters are an important tool in our current war against coronavirus infection. About Boosting immunity naturally over 80% Of the earth's population depends on plants that increase immunity and promote healing. However, one very important function of herbs is they help cleanse toxins and in-turn help boost our immunity [17].

2.1.1 MORINGA OLEIFERA

Moringa, also known as Sahjan, Horseradish tree, Ben tree, or Drumstick tree, has been used for thousands of years for its health advantages. Moringa belongs to family Moringaceae and it has 14 species, but most commonly grown species is *Moringa oleifera* which is native to India, Africa, Arabia, Southeast Asia, South America, Pacific and Caribbean Islands. Moringa has extraordinary therapeutic characteristics in all of its parts, making it a very easy and easily available natural source for boosting human immune systems [18]. Leaves of moringa oleifera are shown in Fig.1.

Fig. 1 Moringa oleifera Leaves

BIOACTIVE CONSTITUENTS OF MORINGA

Moringa oleifera contains components including vitamin, polyphenols such as (flavonoids, phenolics acid), Alkaloids, glucosinolates & Isothiocyonates, tannins, and saponins.

Moringa oleifera leaves are good source of Flavonoids. Flavonoids ingredients of moringa include myrecytin , quercetin, kaempferol [19].

Phenolic acid are a sub group of phenolic compound derived from hydroxybenzoic acid & hydroxycinnamic acid naturally presents in plants. Chlorogenic acid (CGA) is an ester of dihydrocinnamic acid and a major phenolic acid in moringa oleifera [20].

Alkaloids are a group of chemical compounds, which contain mostly basic nitrogen atoms. Several of these compounds, including *N*,α-L-rhamnopyranosyl vincosamide, phenylacetonitrile pyrrolemarumine, 4′-hydroxyphenylethanamide-α-L-rhamnopyranoside and its glucopyranosyl derivative, have been isolated from *Moringa Oleifera* leaves [20].

Moringa oleifera have pharmacologic properties such as Hypolipidemic, Antioxidant, Anti-inflammatory, immunomodulatory, Hepatoprotective, Antihyperglycemic, anticancer effect [21].

USE IN COVID-19 INFECTION

Moringa oleifera is a plant that is high in vitamin C, potassium, calcium, protein, iron, and amino acids and is frequently used as a nutritional supplement [22,23]. These nutrients are responsible for muscle growth after M. oleifera ingestion. M. oleifera has been shown in studies to serve as an antioxidant, immune system booster, lower blood pressure, and reduce fat in the blood and body [24]. Molecular peptide docking proved the effect of M. oleifera on covid-19. They found the presence of flavonoid which may interact with 15 peptides of SARS Cov-2 and reduce the activity of the virus. Their findings revealed that the antiviral activity of M. oleifera is due to the presence of those flavonoids [25].

Moreover, used computational approaches to screen the potential of the compounds in M. oleifera on SARS- Cov-2. Among 294 phytochemicals compounds of M. oleifera they found that two of them (Kaempfenol-3-o-rutinoside and vitexin) showed good stability and high binding to the SARS-CoV-2 receptors [26].

These compounds are also flavonoids, and further confirmed the findings [25].Demonstrated that the antiviral activity of M. oleifera was dependent on the presence of three flavonoids in the plant. These three flavonoids are isorhamnetin, kaempferol and apigenin. They displayed good binding by virtual screening and dynamic simulations [27]. In addition, confirmed the antiviral activity of M. oleifera on covid-19 by performing in silico molecular docking and dynamic studies. The presence of ellagic acid and apigenin is responsible for the antiviral activity of M. oleifera. They evaluated the pharmacokinetics and toxicology profiles of these compounds and revealed the safety of the plant. The molecular docking of these compounds showed clearly their druggability [28]. The binding properties between covid-19 (the main protease (M pro)) and several compounds of M. oleifera by performing protein-ligand docking. 12 compounds (morphine, kaempferol, quercetin, pterygospermin, benzoic acid, gallic acid, benzyl isothiocyanate, niazirin, niaziminin, niazinin, o-ethyl-carbamothionate and niazirinin) found in M. oleifera were evaluated. After docking, the result demonstrated that only niaziminin bound strongly to the Mpro, probably by it OH groups. Niaziminin could form hydrogen bonds with the sequences Glu 166 and Phe 140 of the Mpro of covid-19 [29]. This was confirmed by Ullah and Ullah, who also evaluated the binding of natural and synthetic inhibitors to Mpro as promising vaccine strategies against covid-19 [30]. Encapsulated M. oleifera in electrospum nanofiber and evaluated its effect on covid-19. The nanofibers were able to control the viruses' particles and they developed a new face mask to protect safe and sick people (31). These moringa olifera is used natural drugs showed promising efficacy against covid 19 to boost immunity of healthy people & reboost the immunity of sick people under this covid -19 pandemic [32].

2.1.2. ALOE VERA

The scientific name of *Aloe vera* is *Aloe barbadensis is Miller*. Is a well-known herbaceous plant, aloe vera belongs to *Liliaceae* family. There are more than 300 species of plants which are has been widely used as a therapeutic, cosmetic and nutraceutical and herbal medicine for centuries. Aloe vera is used based on scientific evidence antifungal, antidiabetic, anti-inflammatory, analgesic, anticancer, antimicrobial, antioxidant, antiproliferative, Gastric mucosal protection, hepatoprotective, hypolipidaemic, immunomodulatory, antimutagenic, radioprotective and wound healing[33,34].

Fig. 2 Aloe vera

BIOACTIVE CONSTITUENTS OF ALOE VERA

Aloe vera contains various components, including Anthraquinone, carbohydrates, Enzymes, inorganic compound, oraganic compound and lipid non essenctial and essential amino acids, proteins saccharides, vitamins, sterols [35]. There Is great variation of therapeutically eloquent substances produced by aloe vera which have eminent significance in many areas of many medicine. An entirety of 75 compounds is present in the leaf of aloe , and each one has a variety of remedial properties. these include lignin(capacity of penetrating the human skin),saponins(antiseptic property as well as foaming agent),anthraquinones(aloin, isobarbaloin ,anthracene, emodin ,ester of cinnamoic acid, chrysophanic acid, barbaloin, anthranol, aloectic acid, aloe emodin and ethereal oil),minerals(calcium, manganese, sodium, copper, magnesium potassium, zinc chromium and iron), vitamins (vit A, C, E,B_{12} and choline), amino acids (20 of 22 required amino acids and seven of eight essential ones),enzymes peroxidase,aliiase,catalase,lipase,cellulase,carbxypeptidase,amylase and alkaline phosphate) and sugars (monosaccharides and polysaccharides) [36,37].

USE IN COVID-19 INFECTION

Antiviral activity of aloe vera and Some of its phytochemicals is well documented. Fractions of the gel containing lectins isolated from the plants have been shown to directly inhibit the proliferation of CMC (Cytomegalovirus) in cell cultures [38]. A.vera chrysophanic acid achieves 50% inhibition of viral replication in type 2 and 3 polioviruses at concen of 0.21 and 0.02 ug/ml. these actions may be due to indirect or direct effects. Indirect effect is due to stimulation of the immune system and direct effect is due to anthraquinones. The anthraquinone aloin inactivates various enveloped viruses such as herpes simplex, varicella zoster and influenza [39]. Aloe-emodin inhibits the cleavage of 3C-like protease, an enzyme that plays an important role in viral replication by acting on the proteolytic process at the replicase level [40]. Aloe vera is a high-potential anti-COVID-19 plant drug candidate for the management of this disease in the Democratic Republic of the Congo. Indeed, several experimental studies have shown that the Aloe vera plant is endowed with formidable virucidal properties with a broad spectrum of action [41]. A.vera ethanol extract (AVE) reportedly has significant anti-influenza virus activity [30]. One of the anthraquinones, named emodin of Aloe vera, has been reported to have antiviral activities to some kind of viruses, such as human cytomegalovirus, herpes simplex virus type 1 ,poliovirus and SARS COV-1 [42,43]. Antiviral activity is in general due to anthraquinones. However, several individual compounds involved in antiviral activity were identified in *Aloe vera* including quercetin, catechin hydrate, kaempferol, acemannan, azidothymidine, acyclovir, aloin, emodin [44,45].

The neutrophils from COVID-19 display an activation status. Inflammation and hemorrhagic lesions in COVID-19 patients' lungs can be exacerbated by neutrophil activation and degranulation Lymphopenia and a higher neutrophil-lymphocyte ratio also happen in patients with severe COVID-19 [46] Patients with COVID-19 exhibited high circulating levels of calprotectin (a neutrophil activation marker) and its quantities were higher in patients who had progressed to the severe form of the disease [47].

2.1 VITAMINS AND MICRONUTRIENTS AND THEIR ROLE IN IMMUNITY BOOSTER

2.1.1. VITAMIN A

i) It is known as an anti-inflammatory vitamin because it strengthens the immune system and regulates cellular and humoral immunological processes [48]

(ii) Necessary to generate antibodies against antigens and for normal functioning of macrophages and neutrophils [49].

(iv) The components of innate immunity, as well as their inflammatory responses, were impaired by vitamin A deficiency (VAD) [50].

2.1.2. VITAMIN B

(i) Vitamin B1 (Thiamin) influences anti-inflammatory property and its deficiency causes T cell infiltration [51].

2.1.3. VITAMIN C

(i) Vitamin C has been linked to the immune system's strengthening and enhancement [52].

(ii) Vitamin C is an antibacterial agent that is found in the human immune system [53].

(iii) Vitamin C elicited antiviral immune responses in vivo, particularly against influenza virus.

(iv) Supplementing with vitamin C can help asthmatic patients cope with the symptoms of respiratory infections.

(v) Vitamin C has antibacterial effects, and a deficit causes a decrease in microbial infection resistance [54].

2.1.4. CALCIUM

(i) An increase in [Ca2+] is linked to the activation of immune system cells.

(ii) Calcium (Ca2+) is a multifunctional Cation capable of acting as a second messenger in various immune cell groups including T and B lymphocytes, macrophages, mast cells, etc [55]

2.1.5. ZINC

(i) Zinc is required for immune cell development and differentiation as well as appropriate function [56].

(ii) Zinc promotes CD8+T cell proliferation by modulating cytokine release

(iii) Zinc deficiency impaired neutrophil phagocytic activity, chemotactic responses of both macrophages and monocytes, and immune cell ability to destroy infections.

(iv) Zinc supplementation in the diet has been demonstrated to lessen the severity of acute lower respiratory tract infections [57].

2.1.6. IRON SALTS

(i) Iron salts are thought to play a role in immunity.

(ii) Iron deficiency is linked to a decrease in cell-mediated and innate immunity, making elderly people more susceptible to infections

2.1.7 COPPER

(i) Copper is a powerful virucidal agent.

(ii) Copper deficiency impacts immune function and is known to reduce the killing ability of natural killer cells (NK cells) [58].

2.1.8 MAGNESIUM

(i) There is a strong relation between Mg and the immune system [59]

(ii) Magnesium insufficiency is linked to immune system dysfunction, both humoral and cell-mediated [60].

2.2 POST COVID SCENARIO OF NUTRACEUTICALS

At present Covid-19 pandemic has to a great extent increased the importance of preventive health care in general public. The preventive health care aspect has become the important line of defence in the current Covid pandemic scenario where people are more and more relying upon the nutraceuticals for boosting their immunity.

This industry has risen in the past few years and recently got a boost due to the ongoing pandemic. The focus on preventive healthcare has contributed exceptionally to the growth of this sector. The population across India has begun to believe in immunity-boosting supplements and has led to a significant shift in buying patterns and market behaviour. The general public is relying more on such immunity boosting nutraceuticals. Vitamin capsules, chewable tablets and gummies are examples of the open-minded buying behaviour of consumers of healthcare products. Vitamin and zinc supplements are also those commonly prescribed by doctors during the pandemic. Shifting from curative aspects to preventive measures has made a growth path for the nutraceuticals market in India [61].

2.3 CRITICISM REVOLVING AROUND NUTRACEUTICALS

Since the nutraceuticals are not largely regulated they have also come under the scanner whether as to they provide more health benefits than risks to the consumers [62] The evidence for the efficacy of many of these products remains anecdotal or, at best, based on hints of benefit from small or poorly controlled studies. legal consequences are bound to arise when their claims do not match the evidence. One case is that, scientists disputed the benefits of nutraceuticals like probiotics in Danone yogurt and the company was later forced to pay millions for falsely claiming that its products Actimel and Activia boosted the immune system [58]. Steven Nissen, chairman of cardiology at the Cleveland Clinic, said, "The concept of multivitamin supplements was sold to Americans by an eager nutraceutical industry to generate profits. There was never any scientific data supporting their usage." Steven Nissen, chairman of cardiology at the Cleveland Clinic, said, " The idea of multivitamin supplements was marketed to Americans by a profit-hungry nutraceutical sector. There was never any scientific evidence to back up their use[63].

3.CONCLUSION

The promotion of the consumption of these two herbal medicines is welcome to combat the Covid-19. By interacting with the receptor of this virus, Moringa and aloe vera helps to control the inflammation part of the covid-19. These two products can boost the immunity of healthy and sick patients, thereby giving a protection against covid-19. These products might be used by the world population in this pandemic situation. Further research needs to be conducted to evaluate the impact of this combination.

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