Asian Journal of Chemistry; Vol. 33, No. 4 (2021), 691-700

ASIAN JOURNAL OF CHEMISTRY

https://doi.org/10.14233/ajchem.2021.23114

REVIEW

Review on Boosting up Body's Natural Defence Mechanism and Suppression of Symptoms against SARS-CoV-2 (Covid-19)

G.S. VAIDYANATHAN[1], B. AISHWARYA[1], IBRAHEM AHMAD[1], S. PERIYAR SELVAM[1,*], M. MAHESH KUMAR[1] and E. ROTIMI SADIKU[2]

[1]Department of Food Process Engineering, Postharvest Research Lab, School of Bioengineering, SRM Institute of Science and Technology, Potheri, Kattankulathur-603203, India
[2]Institute of NanoEngineering Research (INER), Department of Chemical, Metallurgical and Materials Engineering (Polymer Division), Tshwane University of Technology, Staatsartillerie Rd, 0183, Pretoria West Campus, South Africa

*Corresponding author: E-mail: periyar.india@gmail.com; periyars@srmist.edu.in

Received: 1 January 2021; *Accepted*: 2 February 2021; *Published online*: 20 March 2021; AJC-20270

The prevailing global health crisis, posed by the pandemic COVID-19, has threatened the livelihood of the public around the world. The dramatic coronavirus surge (2019-nCoV) is denoted as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Initially, this deadly ailment was identified to have originated from bats and thereafter, passed on to human beings, in December 2019 *via* unknown modes of biological transmission in Wuhan, China. One of the leading causes of COVID-19 mortality could be attributed to respiratory failure (hypoxemic or hypercapnic) due to acute respiratory distress. From an immunological perspective, the virus triggers secondary haemophagocytic lymphohistiocytosis, which results in fulminant, followed by fatal hypercytokinaemia alongside multiple organ failure, which happens in adults, in most of the predominant cases. As several scientific communities and researchers, tirelessly strive to find a suitable cure since there is a need for finding a registered medication/vaccine against COVID-19, it becomes quite pertinent for boosting our immune system. As the immune system, supports the body's ability, as a fortress, to defend against pathogenic microbes, comprising of viruses, fungi, bacteria and protozoan species, thereby restricting infection. This review emphasizes the utilization of naturally-derived or otherwise plant-based supplements/foods that facilitate in enhancing or boosting the immunity against COVID-19, irrespective of one's age. For a healthy lifestyle, the use of micro and macronutrients, such as: magnesium, zinc, vitamin-rich foods, especially vitamins C, D and E, since health could be enhanced and an individual could be further aided to overcome the infection. This report, majorly investigates the significance of antioxidants and their roles as immune boosters, through determining the various vitamins C and D-rich compounds, alongside the various secondary metabolites-endowed foods from various sources, which could most likely facilitate in improving immunity and thereby, controlling COVID-19.

Keywords: SARS-CoV-2, COVID-19, Immune system, Micronutrients, Vitamins.

INTRODUCTION

The latest 2019 coronavirus (2019-nCoV) or severe acute respiratory syndrome corona Virus 2 (SARS-CoV-2) is from the Wuhan Province, Chinese origin [1]. Globally as of, 28 November 2020, there have been 61,036,793 confirmed cases of COVID-19, including 1,433,316 deaths, reported to WHO, so far suggesting that COVID-19 is a significant pandemic, resulting in a global health epidemic with a possible or future impact on people of all countries [2]. This epidemic, especially among vulnerable communities, *e.g.*, health care workers, by now, has had a substantial consequence on the psychological wellbeing of the world population [3]. These psychiatric effects can, often unflatteringly, alter immune function, in addition to inducing distress of their own. A high risk of causing viral upper respiratory infections, is associated with psychosocial causes, such as: anxiety, fatigue and depression [4] and the body's natural defence reaction to the influenza vaccine, more commonly known as the flu shot, may also be compromised [5]. Such research shows that the relationship between the psychological and body's natural defence mechanisms to COVID-19 is naturally admirable, therefore, demands addit-

ional consideration. Thus, recommending the use of antioxidants such as vitamins C, D and E, use of micronutrients, such as magnesium, zinc, alongside the several secondary metabolites-endowed foods from various sources, which could most likely facilitate in improving immunity and thereby, controlling COVID-19 (Fig. 1).

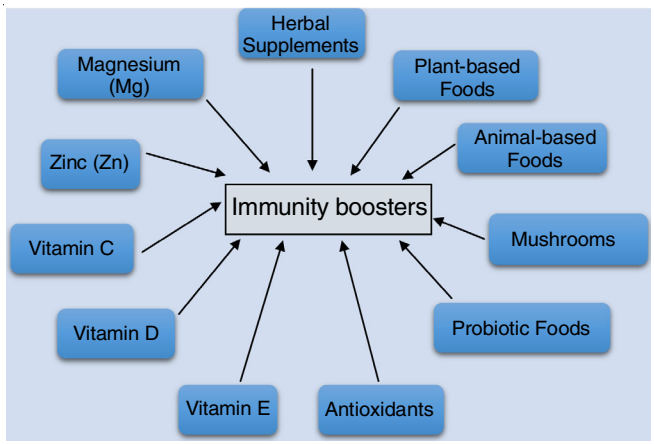

Fig. 1. Different food products/minerals used for boosting immunity in the human body

Various indigenous systems, such as: Siddha, Ayurveda and Unani, which are commonly used by a diverse segment of society, are currently followed throughout India. The Ministry of AYUSH, Government of India included Ayurveda and Yoga Interventions for integrated management of COVID into the 'National Clinical Management Protocol: COVID' during the crisis, in reaction to the COVID-19 calamity and made them available to the public [6]. The following review explores the various plant-based derivatives, which can be administered orally or simply ingested as a part of one's daily food intake, can be beneficial in improving the immune system, thereby facilitating in recovering as well as defending against COVID-19, to a significant extent.

Reports from Department of Ayush, with regards to the Ayurveda scriptures suggested an intervention, involving Ashwagandha (*Withania somnifera*), followed by species like Guduchi (*Tinospora cordifolia*) and Pippali (*Piper longum*) as Ayush, extensively have studied for clinical safety, under the needful regulatory compliance. From the medicines (and/or their ingredients) showcase high affinity over potential targets over SARS-CoV-2 also from the inferred from *in silico* studies with their activities involving attributes of immune-modulator, antiviral (involving other forms of viruses which serve as causative agents against respiratory/influenza based illnesses), antipyretic and anti-inflammatory effects were well documented [7].

Furthermore, from the recommended interventions concerning with Ayurveda and Yoga, which are in practice since long and some are even reported with immunomodulatory effect reported centuries before and are time tested on their effectiveness in clinical applications as immune modulators with proven pharmacological benefits against viral infections which exhibit COVID-19 like symptoms *viz.* respiratory tract illness, fever [8]. From the recent and relevant scientific evidences which showed promising trends from the defined preliminary reports on studies which showed that Ayurvedic preparations involving guduchi (*Tinospora cordifolia*) with aqueous extract, comprising of mixture: guduchi + pippali (*Tinospora cordifolia* + *Piper longum*); aqueous extracts and AYUSH 64 that recommended on the inclusion of National protocol among asymptomatic cases as well as for mild-to-moderate COVID-19 cases. These interventions are likely to be useful for cases recommended home care through strategies like Sanjeevani OPD. ashwagandha (*Withania somnifera*) aqueous extract and guduchi (*Tinospora cordifolia*) aqueous extract are recommended for inclusion in National protocol for prophylactic care against COVID-19 in high risk individuals [9].

The following subsection in this review article emphasizes the major immune-boosting foods, supported by relevant and recent literature sources that provide the scientific significance, governing their functional attributes in improving the immune system.

Overview on healthier immune system and their impact on COVID-19

SARS-COV-2 represents a significant number of CoVs associated with various respiratory disorders with varying degrees of severity, beginning with a basic common cold, with more deteriorating symptoms contributing to pneumonia and bronchitis [10]. Due to its high genetic nucleotide substitution rate and recombination [11]. CoV2 has now been considered as a fast spreading virus. There are six known HCoVs from investigations, to date, namely: HCoV-NL63, HCoV-229E, HCoV-OC43, ARS Corona virus (SARS-CoV), HCoV-HKU1 and CRS; out of which, HCoV-HKU1, HCoV-OC43, HCoV-229E and HCoV-NL63 are globally active and have affected the human population and also serving as a contributor, hence, posing over 1/3rd of the most prevalent types of cold infections acquired in humans [12]. While considering severe cases, the aforementioned HCoVs could impact fatal pneumonia, followed by bronchiolitis, especially among the elderly, as well as children and most prone for patients who are immune-compromised [13]. Besides that, respiratory diseases, could lead to neurological and enteric diseases [14].

From the immunological perspective that governs the disease, it could be said that COVID-19 pathogenicity is significantly more susceptible among individuals with low immunity, especially the younger citizens [15]. Consider the body immune system, which primarily depends on thriving, helps the microflora like bacteria that have a synergistic impact on the gut that primarily protects the body against various ailments. It remains particularly vulnerable to multiple illnesses with the weakened/damaged immune system, which therefore, makes it very opportunistic for the human body to be infected by COVID-19 virus, thereby leading to numerous diseases. Plant-based foods as well as bacterial-based diets have an overall beneficial effect on the intestinal micro flora, which make up 85% of the body's natural defence mechanism [16].

The morphological properties and chemical structure of the COVID-19 virus are same as of another human surrogate

Corona virus, on the available data for environmental and effective clotting action [17]. It is important to follow all suitable preventive actions in order to keep safe and healthy until comprehensive and adequate treatments or a novel coronavirus vaccine is available. While considering COVID-19 reports, which showed that humans have a long history of adapting to the coronavirus, this indicates that the virus is more virulent than the influenza virus. However, most humans have some degree of immunity against the influenza virus, which is not showcasing virulence like that of COVID-19 [18]. This explains the efforts being made by health organizations to constantly update the human body's immunity to the coronavirus.

Plant based metabolites and nutritional significance of plant derived food products in boosting the immune response and suppression of SARS-CoV-2 symptoms

Micronutrients (Zn and Mg): It is primarily used for DNA synthesis as well as cell proliferation; essential micronutrients could appear as an effective immune booster [19]. Both Zn and Mg promote the modulation of adaptive as well as innate immune response and cell signalling pathways, followed by the development of immune cells [20]. They serve as an essential micronutrient, especially in the case of Zn, which is abundant in shellfish and red meat [21]. It is regarded as a vital mineral that aids in the appropriate regulation of the body's defence system. In case of magnesium, it serves as an essential electrolyte that facilitates the strengthening of the body's natural immune system and triggering the development of natural killer cells and lymphocytic cells. In addition, it serves as a key energy source for the cell, known as ATP, which is quite crucial for proper cellular functioning. Magnesium aids in the adequate and appropriate development of haemoglobin since it is essential for delivering oxygen for the lungs and also to the whole human body, thereby contributing especially to combat COVID-19, as the disease primarily, targets the pulmonary system [22]. Food products, such as high cocoa content chocolate, avocados, turtle beans and whole grain, rich in magnesium could be taken as a part of the dietary intake [23].

In case of zinc, plant-based foods, which are for human consumption, comprise of: chickpeas, beans, lentils, tofu, cashew nuts, chia seeds, hemp seeds, walnuts, ground linseed, pumpkin seeds, hemp seeds, quinoa and wholemeal bread. From investigation, Zn is regarded as a suitable and supportive treatment approach in the treatment of COVID-19 as a result of their immunomodulatory effect and from their direct antiviral effect as reported [24]. Despite the existing sources that happen to only mechanistically discuss on the anti-COVID-19 effects, impacted with the use of zinc, happens to be vague till now. Moreover, earlier reports have shown a positive impact governing the administration of chloroquine, which is a zinc ionophore product that increases Zn^{2+} flux to the cells [25]. Moreover, the researchers proposed that chloroquine-mediated zinc inflow might underlie the anticancer nature of the compound. In this particular instance of another form of Zn associated method to COVID-19 modulation, Zn ions targeted in the structure of viral proteins are elaborated. In particular, it has been shown to destabilize its protein with induced Zn^{2+}-disulfiram induction by using papain-like protease for Middle East respiratory syndrome-related coronavirus (MERS-CoV) as well as SARS-CoV-1 attribute [26].

While considering those reports emphasizing with Mg in the treatment against COVID-19, it was found that hypokalaemia condition has prevalently, been observed in case of the critically ill corona affected patients. In the latest information released by China, it is stated that 93% cases with extreme as well as critically ill patients, were suffering due to COVID-19, were found to exhibit hypokalaemia [27]. From the investigation so far, Mg as a supplementation from food intake, might reveal quite useful information for managing against the stress, which is triggered by the pandemic and also to lower post-traumatic stress disorder (PTSD), which eventually might plague COVID-19's survivors, the common people as well as health professionals, who experience such important changes in their habits as well as with their life-styles.

Vitamins: C, D and E rich plant-based foods: There is a strong determination of natural metabolic and vitamin D function [28]. Within the external intake of the body system, the outer skin as vitamin D3, is developed with a thermal reaction after the association of ultraviolet B (UVB) radiation with dehydrocholesterol that is present in the skin. Oral D3 is substituted in the liver by a metabolite of 25 (OH) D and then in the kidneys or other organs by 1, 25 (OH) 2D (calcitriol) hormones. Many of the vitamin D's molecular effects come on or after transferring the calcitriol in organs into vitamin D/calcitriol receptors, a protein restraining on DNA contact that interacts, specifically with the modulation of the sequence, affecting individual genes and controls complexes of genetically lively chromatin. The transcript product is active inmodifications, formally and epigenetically. The well-recognized work of vitamin D3 is to aid in stabilizing serum calcium levels in the body, while parathyroid hormone (PTH) has many important functions for the organism in the feedback loop.

The reconsideration of patient medical history around the world, has been regularly correlated with the prevalent low vitamin D status associated with COVID-19, since the advent of COVID-19. In a study, undertaken in 20 European countries, vitamin D eminence is linked with a great risk of death due to infection [29]. Thus, the threat of COVID-19 illness is impacted by vitamin D eminence, with incidence and mortality not being fully reported. Renin and its potential connection to vitamin D, as an inverse endocrine regulator of the angiotensin system, is a very interesting hypothesis. During an *in vivo* research, vitamin D also served as a down-regulator of renin [30]. Renin and angiotensin II levels were significantly improved in the VDR-null mice. Hypertension and target-organ damage were also documented to have occurred in mice [31]. The non-specific immune system of humans, not only produces anti-inflammatory, but also pro-inflammatory cytokines, in reaction to any bacterial or viral diseases, as studied in different patients with coronavirus disease. The 1, 25 (OH) 2D3 primarily causes reactions, influenced *via* T-type auxiliary type T1, by attempting to subdue inflammatory cytokine output of IL2 and interferon-gamma (INFπ). Vitamin D is an important immune modulator. Each 1, 25 (OH) 2D3 T helper, promotes the development of

type 2 (Th2) cell cytokines, thereby, enhancing the indirect resistance of Th1 cells by helping them to activate the functions that are impaired by various cell types [32]. In addition, 1, 25 (OH) 2D3 stimulates the initiation of regulatory T cells (Tregs), which thereby, prevents inflammatory progresses, given in Fig. 2. The serum 25-hydroxyvitamin D[25(OH)D] ratio, declines as age increases, which might be meaningful for COVID-19, for example with the case fatality fate (CFR); increase in age is attributed to low levels of 7-dehydrosterol cholesterol in the skin, due to reduced sun exposure and development of condensed vitamin D. In comparison, the introduction of certain fertility medications, use of several anti-neoplastic, endocrine medicines, anti-inflammatory agents, endocrine medicines, anti-PT epileptics, anti-retroviral, anti-hypertensive or specific antibiotics, may also regulate serum 25 (OH) D concentrations of septic receptor deficiency in individuals. Typically, opioid use escalates with aging in humans. Supplementation of calciferol increases the development of genes, linked to antioxidants (glutathione reductase and the glutamate-cysteine ligase subunit controller). Ascorbic acid (vitamin C), having extraordinary anti-microbial activities, is thus, prescribed for the prevention and treatment of COVID-19 and also recommended to increase glutathione output.

In infants, adults or the elderly, vitamin C is a crucial factor in increasing immunity. Different fruits with abundant vitamin C content, such as bananas, papaya, kiwi, kale and guava can be used for regular food intake. In addition, certain vegetables, such as eggplant, bell pepper, beet, spinach and cauliflower, are also opulent in vitamin C and are designated as a better option for the immune system. Immune boosters, include spinach, mushrooms, kiwi, berries and bananas [33]. The immunity of the elderly is significantly improved by consuming these foods. Vitamin C is an antioxidant for the body's immune cells, liver and lung epithelium cells as well as for the suppression of immune-suppressive effects [34].

For the maintenance of general health, including the immune system of the elderly people, vitamin E is essential. It is a dominant antioxidant, which protects the human body against various infectious microorganisms. Vitamin E is rich in soaked badam, peanut butter, sunflower kernels and cobnuts.

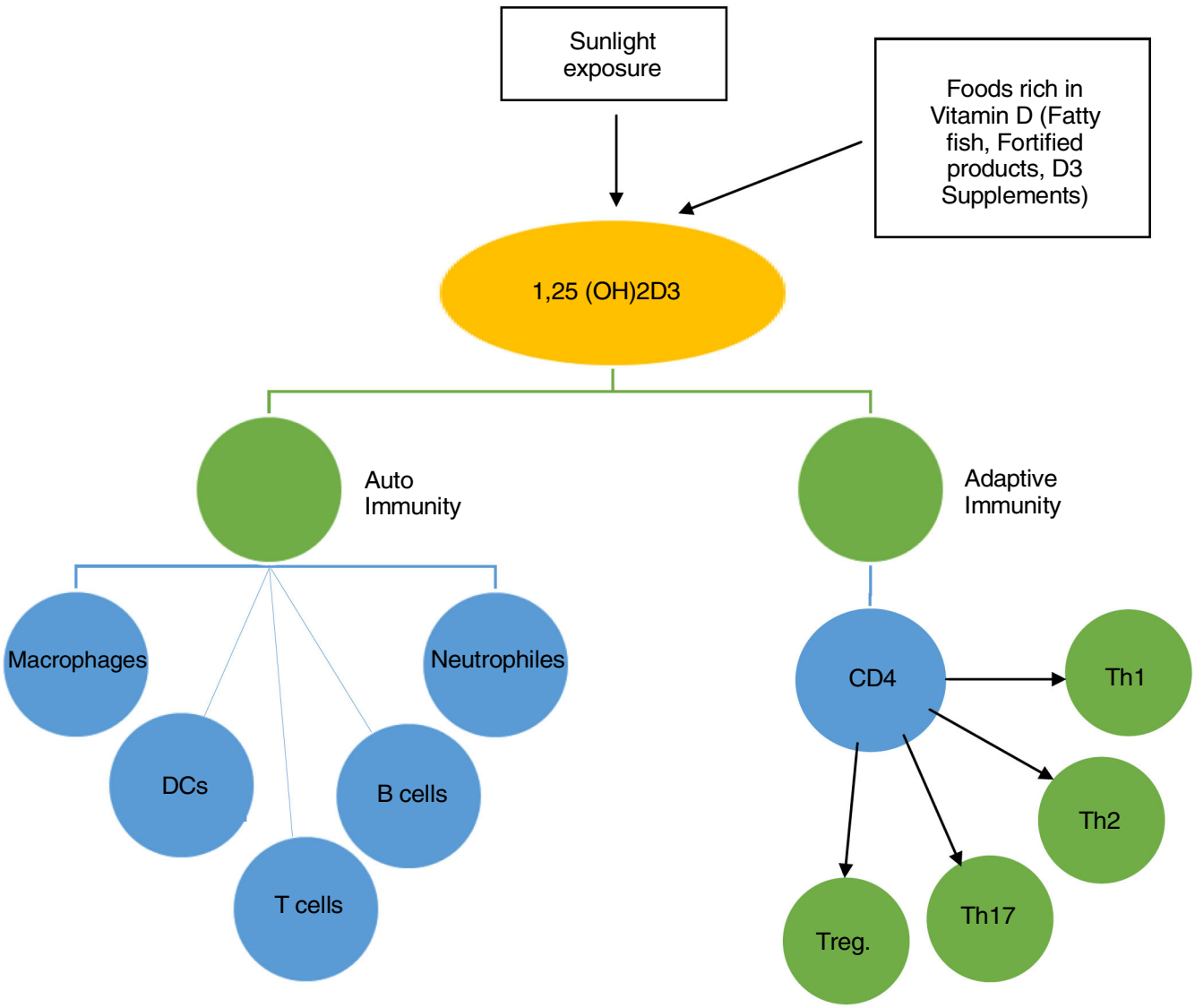

Fig. 2. Representation of immunity developed by calcitriol (vitamin D) in human body

These, essentially, serve as a particular chain breaker in order to achieve the daily dose of vitamin E (an antioxidant, which stops phospholipid peroxidation from spreading). It is also known as a radical paroxysmic scavenger, since it protects plasma membrane lipoproteins and polyunsaturated fats [35]. For oxidative lipid degradation and free-radical production *in vivo*, F-isoprostane quantification is the most optimal approach [36]. Enhanced F2-isoprostane and its effects can be minimized with the consumption of vitamin E supplements. As part of efforts in sustaining an immune response, vitamin E exhibits an essential role. Such a minor defect may affect the immune system or they may enhance aging and cytological immunity, if substituted at higher rates than suggested [37].

Herbal supplements: Herbs, such as black cumin and garlic are identified as boosters of immunity. Not only does the use of these herbs in tea or the everyday diet, strengthen the stomach, it also increases immunity. In Traditional Chinese Medicine (TCM), herbal medicines are well known. The TCM has a long tradition and it is an important component, in curing or inhibiting specific infectious diseases. During 2003 SARS outbreak, TCM action has had remarkably beneficial effects [38].

Similar to Qingfei Paidu decoction (QPD), Gancao Ganjiang decoction (GGD), Qing-fei-tou-xiefu-zhen-grecette, Shegan-mahuang decoction, *etc.*, TCM concentrated on the overall main origin of patients with pneumonia due to COVID-19, since they could have favourable medicaments. The QPD, which consists of: *Ephedra sinica* (*Ephedrae Herba*), *Glycyrrhiza uralensis/ Glycyrrhiza glabra (Glycyrrhizae radix et Rhizoma Praeprata cum Melle*), *Prunus armeniaca* (*Semen Armeniacae Amarum*), *Aster tataricus* (*Asteris Radix et Rhizoma*), *Polyporus umbellatus*, *Gypsum fibrosum*, *Cinnamomi ramulus (Gui Zhi)*, *Atractylodes macrocephala* (*Atractylodis macrocephalae Rhizoma*), *Wolfiporia extensa* (*Poria*), *Alisma plantago-aquatica* (*Alismatis rhizoma*), *Scutellaria pekinensis* (*Scutellariae radix*), *Bupleurum scorzonerifolium* (*Bupleuri radix*), *Zingiber officinale* (*Zingiberis rhizoma recens*), *Pinelliae rhizoma praepratum cum Zingibere et Alumine*), *Tussilago farfara* (*Farfarae flos*), *Citrus aurantium* (*Aurantii fructus Immaturus*), *Iris domestica* (*Belamcandae rhizoma*), *Asarum sieboldii* (*Asari radix et Rhizoma*), *Dioscorea villosa* (*Dioscoreae rhizoma*), *Citrus reticulata* (*Citri reticulatae Pericarpium*) and *Pogostemon cablin* (Guang-Huo-Xiang/*Pogostemonis Herba*) had been introduced in China during the COVID-19 crisis, as a common therapy for cure concepts [39].

For instance, in order to prove its efficacy, it was detected among patients with COVID by hand-operated TCM. The male patient was on an official call to Wuhan a few days prior to the onset of the infection [40]. There was a recurring rise in temperature and cough after admission and the lungs were not easily noticeable. Western antibiotics, such as the intravenous injection of goniclovir, capsules of oseltamivir phosphate (orally) and aerosols of Recombinant Human Interferon A1b, were initially administered. Even though the nucleic acid testing (NAT)/blood testing came out to be negative, the findings of chest computed tomography (CAT scan), revealed an enlargement in the combination and density of both lungs' vitreous darkening, which was more challenging than admission. The acute disease was related to the success of the heat syndrome of the patient, which was intense for study, hence, QPD was used. In addition, the "Disease Prevention Therapy" framework was expressed in COVID preventive and regulatory behaviours. The precautionary measures of TCM should include various sporting activities, consciousness, medication and proper nutrition in addition to the contagious ailments documented in the course of the Han dynasty [40].

The advantages of TCM, in differential syndromes, should be administered for the care and prevention of COVID and should minimize all health issues and mortality. Furthermore, experimental studies on TCM with the obvious therapeutic promise of COVID-19, should be essentially, carried out thoroughly in order to analyze the mode of operation, thereby, allowing the consideration of COVID-19 in detail [41].

Whilst considering Myanmar based Traditional Medicine which has flourished over thousands of years and becomes quite a distinct entity, which emerged as a delicate and yet useful and also a significant study area of community health with a preventive, rehabilitative and curative aspects. Myanmar Traditional Medicine also includes basic Myanmar traditional subjects of beliefs, practice, culture, numerous treatises in medicine and diverse approaches on prescribing wide range of traditional medications that are strong and effective. It is now, time to act upon Myanmar traditional medicine to be Good Medical Practice (GMP) through proper standardization and quality assurance. Reports also showed that by boiling jaggery with betel (*Piper betle*) leaves, as rhizome liquid was reported to consumed as cure for influenza and also as a digestive aid and blood purifier among new mothers and reports concerning with immunomodulatory effect of *Plumeria rubra* L were documented from the study [42].

Similar to Indian and Chinese medications, there has been a substantial increase in the ubiquitous nature of herbal supplements among various Asian countries so far. With an increase over the demand has far been outpacing the availability over the existing plant based raw materials, with Thailand's prominent exports on herbal plants are utilized for several immunomodulatory effects and in pharmaceutical and perfumeries [43]. Besides Thai traditional massage or "Nuad Thai", hot herbal compresses, or herbal steam baths were also found to have beneficiary effect among the asymptomatic individuals to rejuvenate their body which in turn is essential for the human health [44].

Antioxidants: As an antioxidant, glutathione is well-known for its antioxidant potential in the body that affects free radicals and further participates in the regeneration of tissue, produces useful chemicals and synthesizes proteins used by the body's natural defence mechanism. *N*-Acetyl-cysteine (NAC) facilitates the synthesis of glutathione (GSH) as well as serves as an important enhancement [45]. Studies related to animal samples with remaining viral diseases have demonstrated that NAC, not only decreases harshness and symptoms, but also reduces the time with cellular repair and defence by aggregation. In doses of 500 to 600 mg, NAC is generally administered. Approximately 600 mg/IV-40000 mg of glutathione may also

be provided with a prescription from a designated healthcare provider [46].

Quercetin-based bioflavonoid is endowed primarily and in a wide degree of fruits as well as vegetables. Animals as well as research *in vitro* studies, indicated quercetin preventive ability for a wide range of viral infections, involving Corona virus (SARS-COV) [47]. Quercetin further attributes their role on the assumption of achieving antioxidant capability and defends the lung tissue. An adequate mixture of bromelain with Vitamin C is also an available option as a health supplement. The recommendation lies within the range of 500 to 1000 mg/day. The main food sources, include: greens, *Anethum graveolens* (dill/savaa), apples, fennel leaves, onion, parsley, varieties of grapes, chillies and green and black tea [48].

Food derivatives or supplements and their medicinal values concerning with immune boosting and respiratory disorders: A detailed survey on some of the majorly available natural and/or plant-based foods, mushrooms, animal based foods and probiotic foods are shown in Table-1 with supporting literatures, alongside their functional attributes and the key active compounds/ingredients.

Conclusion

It should be noted that certain people with poor immunity become significantly more vulnerable to COVID-19 during the pandemic scenario. In order to deal with the growing cases of COVID-19, an optimal prevention plan is crucial for individuals, before a conclusive solution is put in place or devised

TABLE-1
LIST OF FOODS/DERIVATIVES AND THEIR FUNCTIONAL ATTRIBUTES IN IMMUNE BOOSTING AND RESPIRATORY DISORDERS

Food products/ derivatives	Active compounds/Ingredients	Functional attributes	Ref.
		Plant based foods	
Almonds	β-sitosterol and α-tocopherol	These fatty acids that are endowed majorly in almonds facilitate in enhancing the immune function of the body greatly and is suggested to soak the almond seeds before consumption	[49]
Aloe vera	Vitamins A (β-carotene), C and E	Modulates immune system	[50]
Amla	Vitamin-C	Pose as an effective immune booster and disease prevention	[51]
Betel leaves	Good level of phenol, Allyl pyrocatechol and isoflavones content	The application of betel leaves in combination with Ayurvedic herbal supplement (*Swarna bhasma*) was observed to be posing as a suitable immunomodulator to combat COVID infection among the unaffected people.	[52]
Black pepper	Piperdardiine, piperanine	The chemical constituents from pepper such as piperdardiine, piperanine, are significantly effective against COVID-19 from the molecular docking studies performed.	[53]
Camphor	Camphor	Immune booster acts as prophylactic. Suggested as an effective homeopathic medication for treating against COVID-19	[54]
Cinnamon	Cinnamaldehyde, cinnamate, cinnamic acid and numerous essential oils	Serves as an effective immune booster. Suggested as an effective Indian traditional medicine by AYUSH in treatment for SARS-CoV-2 (nCOVID-19)	[55]
Cumin	Thymoquinone, Nigellidine and α-hederin	These metabolites derived from *Nigella sativa* (Black Cumin) can pose as a potential influencer for reinforcing immune response from the molecular grounds.	[56]
Dill	Carvone, α-phellandrene, limonene and other phytochemical compounds such as diterpene, cineole, pinene,furanocoumarin, isomyristicin, paramyrcene, myrcene, dihydrocarvone, dilapiole, dilapiole, apiole, dilapiole, myristicin and myristin.	Serve as a chemopreventive agent in curing against respiratory disorders and as an effective immune booster possesses antiviral potential	[57]
Eucalyptus oil	Eucalyptol, α-terpineol	Extremely effective as a respiratory decongestant and as an immune booster. For COVID-19, it could pose as an integrative therapeutic medicinal therapy.	[58]
Garlic	Alliin	Exhibit immunomodulatory effect and facilitate in anti-inflammatory impact	[59]
Green tea	Theophylline	Treatment of lung-related disorders such as wheezing, shortness of breath and cough induced chronic bronchitis, asthma, emphysema, *etc.* It unwinds thereby unlocking air openings in the lungs, making breathing comfortable.	[60]

Honey	Polyphenols found in larger levels, which are primarily comprised of flavonoids, phenolic acids and phenolic acid derivatives	Numerous micronutrients are necessary for immune competence and specifically polyphenols derived from plants (bioactive components), are much essential for reducing the release of inflammatory cytokines and since these bioactive components are widely present in honey, we can come to a decision that honey could play a major part in relieving discomfort among patients infested with COVID-19.	[61,62]
Mint, Tulsi	Limonene, menthone, menthofuran, cineole, isomenthone, isopulegol, menthol, menthyl acetate, carvone and pulegone	Suggested as a suitable nutrition or part of the diet plan during COVID-19 pandemic. Serve as an effective decongestant	[63,64]
Neem	Azadirachtin, salannin and nimbin	Possesses antiviral potential and immunomodulatory effects	[65,66]
Papaya, Oranges, Kiwi, Guava, Eggplant, Beetroots, Spinach, Bell peppers and Cauliflower	Vitamin C and E	Improves immunity	[67-69]
Plants from Kabasura kudineer	Ingredients of Ginger (Chukku); Piper longum; Clove; Dusparsha; Akarakarabha; Kokilaksha; Haritaki; Malabar nut; Ajwain; Kusta; Guduchi; Bharangi; Kalamegha; Raja pata; Musta	Treatment of chronic respiratory conditions such as colds and flu. It has analgesic, antifungal, antiviral, immunomodulatory, anti-inflammatory, antibacterial, antioxidant, antipyretic, antipyretic and antiasthmatic properties.	[70-72]
Seaweed	Secondary metabolites which include flavonoids, alkaloids, glycosides, saponins, tannins, steroids	Evidences showcased seaweed helps to increase the production of antibodies to generate an immune response against viral infections and increase the immunity. Seaweed is full of minerals, vitamins and antioxidants, so that it will improve immunity and may protect body from infectious Covid-19.	[73]
Silver beet	Vitamin-A	Effective against treatment of bronchiectasis and Cystic Fibrosis	[74]
Sunflower seeds	Vitamin-E, zinc and selenium	Suggested among one of the green foods that serves as an immune booster to the bodily system to combat COVID-19	[16]
Sweet potatoes, carrots, green leafy vegetables, pumpkin, summer squash, red/yellow bell peppers, peas, broccoli, paprika, chilli, tomato, parsley and coriander.	Excellent levels of carotene derivatives	These plant based food derivatives possess vast array of carotene derivatives, which were suggested in report to serve as a suitable immunomodulator in nutritional intake during the COVID pandemic.	[75]
Turmeric	Curcumin (Polyphenol)	Enhances several immune cells, such as many subsets of macrophages, T-lymphocytes, dendritic cells, natural killer cells and B-lymphocytes helping to minimize the intensity of immunologically etiologically complex diseases.	[76]
Various Dal varieties or Nuts	Protein	Immune boosting and suggestive of combating against COVID-19	[77]
		Animal based foods	
Eggs	Proteins, calcium, vitamin D, omega 3 fatty acids, Vitamin B12, biotin, iodine, selenium, choline, riboflavin	Serve as an effective immunity booster	[78,79]
Poultry	High in vitamin B6, moderate levels of vitamin A, iron, cobalamin, magnesium, vitamins C and E, phosphorus and coenzyme Q10 (CoQ10)	Proteins present in turkey as well as chicken are responsible for delivering certain amino acids that are utilized by the human body to develop antibodies in order to fight any bacterial/viral invasion. Likewise, consuming hot soup prepared from poultry releases gelatin/chondroitin sulfate and various micro-nutrients that aids in the maintenance of a proper gut as well as improved body's self-defence function.	[80]
Shell fishes and other Fishes (Salmon, Crabs, Mussels)	Zinc, protein rich in essential amino acids, Vitamin B and Vitamin D	Considered as a part of the major dietary intake for enhancing the immune system against COVID-19 infection.	[81]

Mushrooms as food			
White button mushroom	β-Glycan lentinan, ergosterol, β-glucans, ergothioneine, vitamin D and an antioxidant compound generally stated as flavonoid	Stimulatory action on immune responsiveness	[82]
Shiitake Mushroom	β-Glycan lentinan, ergosterol, β-glucans, ergothioneine, vitamin D and an antioxidant compound generally stated as flavonoid	Extracts of β-glucan derived from these golden oak mushroom or *Lentinula edodes* shows pulmonary cytoprotective and various immunomodulatory impact during *in vitro* studies, which is indicative of possible approach for COVID-19.	[83]
Reishi, Cordyceps, Chaga, Turkey tail and Lion's mane	β-Glycan lentinan, ergosterol, β-glucans, ergothioneine, vitamin D and an antioxidant compound generally stated as flavonoid	Their bioactive constituents were reported as suitable immune booster which could be consumed commonly in the form of food	[84]
Probiotic foods			
Yogurt, Miso, Kimchi, Kefir, Pickles, Sauerkraut, Akhuni *etc.*	Favourable microorganisms include *Streptococcus thermophilus, Lactobacillus acidophilus, Bifidobacterium bifidum, Lactobacillus delbrueckii* subsp. *bulgaricus* and *Lactobacillus helveticus*. And these probiotic strains will be our life-saving bacterial species.	Probiotic strains administered orally may promote the reduction of the incidence and seriousness of viral RTIs. Different probiotic strains reported for anti-viral and respiratory activities (not low-quality undocumented imitations) should necessarily turn out to be a portion of the armamentarium, thereby decreasing the impact as well as brutality of this pandemic, a stage where medics are prescribing medications with very less available information on the treatments for COVID-19. In addition, as a small portion of the whole plan to slow down the spread of the COVID-19 pandemic, the known prebiotics/dietary fibres (*e.g.*, fructan, galactosan) could be used to escalate the different probiotic strains and other favourable indigenous microbes in the human body.	[85]

to counteract and eradicate the deadly virus. An appropriate approach is also considered to support and further enhance/improve immunity through dietary nutrients intake, in particular the analysis succeeded in stressing some of the main issues related to plant-based foods and their crucial function and effects through the promotion of beneficial bacteria in the body system. For example, some of the popular micronutrients, such as zinc, manganese and vitamins C, D and E are studied, along with extending their herbal intake tests. Hence, the research aims to further boost immunity. There are also many individuals who choose/consume fruits, apart from plant-based foods that are rich in vital elements for boosting immunity. Fruits, such as papaya, bananas, guava and kiwi are high in vitamin C, while vegetables and spices are also recognized to contain abundant vitamin C, which is beneficial to resisting particular diseases. However, the analysis also concentrated on the various animal-based foods, probiotic foods and diverse mushrooms that could likely protect and strengthen the immune system and body activity in order to regulate the lethal COVID-19 (SARS-CoV-2).

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

REFERENCES

1. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200423-sitrep-94-covid-19.pdf?sfvrsn=b8304bf0_4.
2. https://covid19.who.int/.
3. R.P. Rajkumar, *Asian J. Psychiatr.*, **52**, 102066 (2020); https://doi.org/10.1016/j.ajp.2020.102066
4. E. Oraka, M.E. King and D.B. Callahan, *Chest*, **137**, 609 (2010); https://doi.org/10.1378/chest.09-1777
5. J.A. Whitaker, M.S. von Itzstein and G.A. Poland, *Vaccine*, **36**, 5940 (2018); https://doi.org/10.1016/j.vaccine.2018.08.040
6. D. Shankar and B. Patwardhan, *J. Ayurveda Integr. Med.*, **8**, 137 (2017); https://doi.org/10.1016/j.jaim.2017.09.001
7. G. Tillu, S. Salvi and B. Patwardhan, *J. Ayurveda Integr. Med.*, **11**, 95 (2020); https://doi.org/10.1016/j.jaim.2020.06.012
8. https://main.ayush.gov.in/event/first-report-and-recommendations-interdisciplinary-committee-integration-ayurveda-and-yoga.
9. S. Chaturvedi, N. Kumar, G. Tillu, S. Deshpande and B. Patwardhan, *Indian J. Med. Ethics*, **05**, 191 (2020); https://doi.org/10.20529/IJME.2020.058
10. Y. Yi, P.N.P. Lagniton, S. Ye, E. Li and R.H. Xu, *Int. J. Biol. Sci.*, **16**, 1753 (2020); https://doi.org/10.7150/ijbs.45134
11. S.P. Kaur and V. Gupta, *Virus Res.*, **288**, 198114 (2020); https://doi.org/10.1016/j.virusres.2020.198114
12. J. Lim, S. Jeon, H.Y. Shin, M.J. Kim, Y.M. Seong, W.J. Lee, K.W. Choe, Y.M. Kang, B. Lee and S.J. Park, *J. Korean Med. Sci.*, **35**, 79 (2020); https://doi.org/10.3346/jkms.2020.35.e79
13. A.S. Abdulamir and R.R. Hafidh, *Electron. J. Gen. Med.*, **17**, em202 (2020); https://doi.org/10.29333/ejgm/7850
14. C.A. Pérez, *Neurol. Clin. Pract.*, **10**, 371 (2020); https://doi.org/10.1212/CPJ.0000000000000836
15. J. Nikolich-Zugich, K.S. Knox, C.T. Rios, B. Natt, D. Bhattacharya and M.J. Fain, *Geroscience*, **42**, 505 (2020); https://doi.org/10.1007/s11357-020-00186-0
16. M.S. Arshad, U. Khan, A. Sadiq, W. Khalid, M. Hussain, A. Yasmeen, Z. Asghar and H. Rehana, *Food Sci. Nutr.*, **8**, 3971 (2020); https://doi.org/10.1002/fsn3.1719
17. S.V. Mohan, M. Hemalatha, H. Kopperi, I. Ranjith and A.K. Kumar, *Chem. Eng. J.*, **405**, 126893 (2021); https://doi.org/10.1016/j.cej.2020.126893
18. D. Raoult, A. Zumla, F. Locatelli, G. Ippolito and G. Kroemer, *Cell Stress*, **4**, 66 (2020); https://doi.org/10.15698/cst2020.04.216
19. J. Fuhrman, Eat for Life, HarperOne, Harper Collins (2020).

20. I. Wessels, M. Maywald and L. Rink, *Nutrients*, **9**, 1286 (2017); https://doi.org/10.3390/nu9121286
21. P.A. West, Molluscan Shellfish Depuration, CRC Press, ed. 1, pp. 275-286 (1991).
22. https://www.elektramagnesium.com.au/immune-system-defence-with-vitamin-c-and-magnesium/.
23. https://www.healthline.com/nutrition/10-foods-high-in-magnesium#section7.
24. J. Zhang, B. Xie and K. Hashimoto, *Brain Behav. Immun.*, **87**, 59 (2020); https://doi.org/10.1016/j.bbi.2020.04.046
25. J. Xue, A. Moyer, B. Peng, J. Wu, B.N. Hannafon and W.Q. Ding, *PLoS One*, **9**, e109180 (2014); https://doi.org/10.1371/journal.pone.0109180
26. M.H. Lin, D.C. Moses, C.H. Hsieh, S.C. Cheng, Y.H. Chen, C.Y. Sun and C.Y. Chou, *Antiviral Res.*, **150**, 155 (2018); https://doi.org/10.1016/j.antiviral.2017.12.015
27. R. Sheervalilou, M. Shirvalilоo, N. Dadashzadeh, S. Shirvalilou, O. Shahraki, Y. Pilehvar Soltanahmadi, H. Ghaznavi, S. Khoei and Z. Nazarlou, *J. Cell. Physiol.*, **235**, 8873 (2020); https://doi.org/10.1002/jcp.29735
28. J.W. Pike and S. Christakos, *Endocrinol. Metab. Clin. North Am.*, **46**, 815 (2017); https://doi.org/10.1016/j.ecl.2017.07.001
29. P.C. Ilie, S. Stefanescu and L. Smith, *Aging Clin. Exp. Res.*, **32**, 1195 (2020); https://doi.org/10.1007/s40520-020-01570-8
30. Y.C. Li, *Curr. Opin. Nephrol. Hypertens.*, **21**, 72 (2012); https://doi.org/10.1097/MNH.0b013e32834de4ee
31. Y.C. Li, J. Kong, M. Wei, Z.F. Chen, S.Q. Liu and L.P. Cao, *J. Clin. Invest.*, **110**, 229 (2002); https://doi.org/10.1172/JCI0215219
32. S. Christakos, P. Dhawan, A. Verstuyf, L. Verlinden and G. Carmeliet, *Physiol. Rev.*, **96**, 365 (2016); https://doi.org/10.1152/physrev.00014.2015
33. https://www.healthline.com/nutrition/vitamin-c-foods#section10.
34. A. Erol, *OSF Preprints*, (2020) https://doi.org/10.31219/osf.io/p7ex8
35. Y. Liang, P. Wei, R.W. Duke, P.D. Reaven, S.M. Harman, R.G. Cutler and C.B. Heward, *Free Radic. Biol. Med.*, **34**, 409 (2003); https://doi.org/10.1016/S0891-5849(02)01018-3
36. Y. Lin, R. Huang, N. Santanam, Y.G. Liu, S. Parthasarathy and R.P. Huang, *Cancer Lett.*, **187**, 17 (2002); https://doi.org/10.1016/S0304-3835(02)00346-4
37. A. Mastaloudis, S.W. Leonard and M.G. Traber, *Free Radic. Biol. Med.*, **31**, 911 (2001); https://doi.org/10.1016/S0891-5849(01)00667-0
38. P.C. Leung, *Am. J. Chin. Med.*, **35**, 575 (2007); https://doi.org/10.1142/S0192415X07005077
39. H. Wu, J.Q. Wang, Y.W. Yang, T.Y. Li, Y.J. Cao, Y.X. Qu, Y.-J. Jin, C.N. Zhang and Y.K. Sun, *Acta Pharm. Sin. B*, **55**, 374 (2020); https://doi.org/10.16438/j.0513-4870.2020-0136
40. Z. Xu, L. Shi, Y. Wang, J. Zhang, L. Huang, C. Zhang, S. Liu, P. Zhao, H. Liu, L. Zhu, Y. Tai, C. Bai, T. Gao, J. Song, P. Xia, J. Dong, J. Zhao and F.-S. Wang, *Lancet Respir. Med.*, **8**, 420 (2020); https://doi.org/10.1016/S2213-2600(20)30076-X
41. N. Zhu, D. Zhang, W. Wang, X. Li, B. Yang, J. Song, X. Zhao, B. Huang, W. Shi, R. Lu, P. Niu, F. Zhan, X. Ma, D. Wang, W. Xu, G. Wu, G.F. Gao and W. Tan, *N. Engl. J. Med.*, **382**, 727 (2020); https://doi.org/10.1056/NEJMoa2001017
42. R.A. DeFilipps and G.A. Krupnick, *PhytoKeys*, **102**, 1 (2018); https://doi.org/10.3897/phytokeys.102.24380
43. P. Subcharoen, Traditional Medicine in Asia, E.T.O. Printing: Bangkok, ed. 2, pp. 301-305 (2001).
44. V. Chokevivat and A. Chuthaputti, Conference paper for 6th Global Conference on Health Promotion, Bangkok, Thailand (2005).
45. G. Aldini, A. Altomare, G. Baron, G. Vistoli, M. Carini, L. Borsani and F. Sergio, *Free Radic. Res.*, **52**, 751 (2018); https://doi.org/10.1080/10715762.2018.1468564
46. S. De Flora, C. Grassi and L. Carati, *Eur. Respir. J.*, **10**, 1535 (1997); https://doi.org/10.1183/09031936.97.10071535
47. L. Yi, Z. Li, K. Yuan, X. Qu, J. Chen, G. Wang, H. Zhang, H. Luo, L. Zhu, P. Jiang, L. Chen, Y. Shen, M. Luo, G. Zuo, J. Hu, D. Duan, Y. Nie, X. Shi, W. Wang, Y. Han, T. Li, Y. Liu, M. Ding, H. Deng and X. Xu, *J. Virol.*, **78**, 11334 (2004); https://doi.org/10.1128/JVI.78.20.11334-11339.2004
48. D.M. Minich and B.I. Brown, *Nutrients*, **11**, 2073 (2019); https://doi.org/10.3390/nu11092073
49. R.K. Bhatia and A. Marwaha, *Int. J. Sci. Res.*, **9**, 127 (2020); https://doi.org/10.18203/2320-6012.ijrms20205830
50. R. Bussmann and A. Glenn, *Rev. Peru. Biol.*, **17**, 331 (2011); https://doi.org/10.15381/rpb.v17i3.8
51. S. Dasaroju and K.M. Gottumukkala, *Int. J. Pharm. Sci. Rev. Res.*, **24**, 150 (2014).
52. H. Soni, S. Sharma and J.K. Malik, *Asian J. Res. Dermatol. Sci.*, **3**, 21 (2020).
53. K. Rajagopal, G. Byran, S. Jupudi and R. Vadivelan, *Int. J. Health Allied Sci.*, **9**, 43 (2020); https://doi.org/10.4103/ijhas.IJHAS_55_20
54. K.K. Savera, P. Dastagiri and K.C. Muraleedharan, *Int. J. Hom.*, **4**, 160 (2020); https://doi.org/10.33545/26164485.2020.v4.i3c.206
55. S. Prajapati and N.G.V. Kumar, *Int. J. Complement Alt. Med.*, **13**, 103 (2020); https://doi.org/10.15406/ijcam.2020.13.00502
56. M.F. Kulyar, R. Li, K. Mehmood, M. Waqas, K. Li and J. Li, *Phytomedicine*, **10**, 153277 (2020); https://doi.org/10.1016/j.phymed.2020.153277
57. F.A. Mohammed, S.S. Razvi, W.M. Abdul, K. Mohammed, K.R. Hakeem, B. Banaganapalli, N. Shaik and A.I. Elkady, eds.: M. Ozturk and K.R. Hakeem, Plant and Human Health, Springer, vol. 3, pp. 181-194 (2019);
58. M. Dimri, R.S. Pawar, V.S. Rajwar and L. Kush, *Asian J. Pharmaceut. Res. Develop.*, **8**, 111 (2020); https://doi.org/10.22270/ajprd.v8i3.731
59. M.S. Butt, M.T. Sultan, M.S. Butt and J. Iqbal, *Crit. Rev. Food Sci. Nutr.*, **49**, 538 (2009); https://doi.org/10.1080/10408390802145344
60. A.B. Sharangi, *Food Res. Int.*, **42**, 529 (2009); https://doi.org/10.1016/j.foodres.2009.01.007
61. K.S. Hossain, M.G. Hossain, A. Moni, M.M. Rahman, U.H. Rahman, M. Alam, S. Kundu, M. Masudur-Rahman, M.A. Hannan and M.J. Uddin, *OSF Preprints* (2020); https://doi.org/10.31219/osf.io/w3hqu
62. M.Z. Mustafa, S.H. Shamsuddin, S.A. Sulaiman and J.M. Abdullah, *Malays. J. Med. Sci.*, **27**, 165 (2020); https://doi.org/10.21315/mjms2020.27.2.17
63. R.P. Rajkumar, *Brain Behav. Immun.*, **87**, 8 (2020); https://doi.org/10.1016/j.bbi.2020.04.056
64. T. Tanveer, *J. Ayu. Her. Med.*, **6**, 40 (2020).
65. S.N. Upadhyay, S. Dhawan, S. Garg and G.P. Talwar, *Int. J. Immunopharmacol.*, **14**, 1187 (1992); https://doi.org/10.1016/0192-0561(92)90054-O
66. M. Mukhtar, M. Arshad, M. Ahmad, R.J. Pomerantz, B. Wigdahl and Z. Parveen, *Virus Res.*, **131**, 111 (2008); https://doi.org/10.1016/j.virusres.2007.09.008
67. C.G. Slatore, A.J. Littman, D.H. Au, J.A. Satia and E. White, *Am. J. Respir. Crit. Care Med.*, **177**, 524 (2008); https://doi.org/10.1164/rccm.200709-1398OC
68. C.L. Rock, R.A. Jacob and P.E. Bowen, *J. Am. Diet. Assoc.*, **96**, 693 (1996); https://doi.org/10.1016/S0002-8223(96)00190-3
69. R. García-Closas, A. Berenguer, M.J. Tormo, M.J. Sánchez, J.R. Quirós, C. Navarro, R. Arnaud, M. Dorronsoro, M.D. Chirlaque, A. Barricarte, E. Ardanaz, P. Amiano, C. Martinez, A. Agudo and C.A. González, *Br. J. Nutr.*, **91**, 1005 (2005); https://doi.org/10.1079/BJN20041130
70. P. Mekala and T.R.G. Krishnamurthy, *J. Pharmacogn. Phytochem.*, **9**, 1031 (2020); https://doi.org/10.22271/phyto.2020.v9.i3q.11428
71. P. Kumar M, K.M. Sundaram and M.S. Ramasamy, *Asian J. Pharm. Res. Health Care*, **1**, 20 (2020); https://doi.org/10.18311/ajprhc/2020/25103

72. G. Kiran, L. Karthik, M.S. Shree Devi, P. Sathiyarajeswaran, K.M. Kumar, K. Kanakavalli, and D. Ramesh Kumar, *J. Ayurveda Integr. Med.*, (2020); https://doi.org/10.1016/j.jaim.2020.05.009
73. K. Kavitha, *GIS Business*, **15**, 420 (2020).
74. C. O'Neil, E. Shevill and A.B. Chang, *Cochrane Database Syst. Rev.*, **1**, CD006751 (2008); https://doi.org/10.1002/14651858.CD006751.pub2
75. A.D. Ashok, J. Ravivarman and K. Kayalvizhi, *Int. J. Chem. Stud.*, **8**, 105 (2020); https://doi.org/10.22271/chemi.2020.v8.i4b.9675
76. E. Abdollahi, A.A. Momtazi, T.P. Johnston and A. Sahebkar, *J. Cell. Physiol.*, **233**, 830 (2018); https://doi.org/10.1002/jcp.25778
77. M.R. Suchitra and S. Parthasarathy, *Int. J. Res. Pharm. Sci.*, **11**, 110 (2020); https://doi.org/10.26452/ijrps.v11iSPL1.2241
78. T. Nazli and A. Heena, *Epidem. Int.*, **5**, 10 (2020); https://doi.org/10.24321/2455.7048.202011
79. C.D. Mills and K. Ley, *J. Innate Immun.*, **6**, 716 (2014); https://doi.org/10.1159/000364945
80. https://www.mdlinx.com/article/boost-your-immune-system-with-these-foods/4UZzvffk76b5qJUU49iH52
81. D. Love, E. Allison, F. Asche, B. Belton, R. Cottrell, H. Froelich, J.A. Gephart, C.C. Hicks, D.C. Little, E.M. Nussbaumer, P.P. da Silva, F. Poulain, A. Rubio, J.S. Stoll, M.F. Tlusty, A.L. Thorne-Lyman, M. Troell and W. Zhang, *SocArXiv*., (2020). https://doi.org/10.31235/osf.io/x8aew
82. A.T. Borchers, C.L. Keen and M.E. Gershwin, *Exp. Biol. Med.*, **229**, 393 (2004); https://doi.org/10.1177/153537020422900507
83. E.J. Murphy, C. Masterson, E. Rezoagli, D. O'Toole, I. Major, G.D. Stack, M. Lynch, J.G. Laffey and N.J. Rowan, *Sci. Total Environ.*, **732**, 139330 (2020); https://doi.org/10.1016/j.scitotenv.2020.139330
84. A.G. Guggenheim, K.M. Wright and H.L. Zwickey, *Integr. Med.*, **13**, 32 (2014).
85. D. Baud, V. Dimopoulou Agri, G.R. Gibson, G. Reid and E. Giannoni, *Front. Public Health*, **8**, 186 (2020); https://doi.org/10.3389/fpubh.2020.00186