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Chapter

Natural Antioxidants to the Rescue?

Cenk Aydin and Nilay Seyidoglu

Abstract

Natural antioxidant compounds have different mechanisms of treatment and prevention against various diseases due to their richest ingredients. There are several antioxidants used today, such as phytogenic ingredients, flavonoids, capsaicin, spirulina, beta-glucan, polyphenol etc. Besides the outbreak of diseases, the ability to scavenge oxidative conditions of the natural antioxidants have been notably important. Thereby, therapeutic strategies of diseases have been interested by researchers. Try to seek a kind of effects of natural antioxidants to various diseases, especially viral or pandemic diseases are being important nowadays. This chapter we'll mention about how to viral or pandemic disease's effects on oxidative status in both animals and humans, and what kind of phytochemical ingredients would be a positive effect on. At the same time, the latest advances about these natural antioxidant compounds and pharmaceuticals will be critically highlighted and discussed with newest literatures.

Keywords: natural antioxidants, phytogenic ingredients, essential oils, pandemic, vitamins

1. Introduction

Antioxidants either endogenous or exogenous are essential substances to regulate the oxidative process. The endogenous antioxidants known as glutathione, glutathione peroxidase (GPx), catalase (CAT), and superoxide dismutase (SOD), have an inhibition role on free radicals during oxidation [1]. Nevertheless, either these antioxidant mechanisms are inadequate or for a better healthy life, exogenous antioxidants should be preferred [2]. The exogenous antioxidants which are especially called natural antioxidants such as vitamins, flavonoids, polyphenols, minerals, plants and phytochemicals, are derived from foods and medicinal plants. Over the years, the relationship between natural antioxidants and health has been discussed due to their important efficiencies. Generally, natural antioxidants have a wide range of effects especially antioxidant, antimicrobial, anticancer, immunomodulatory, and antiviral [3–5]. Belong these, natural antioxidants have been drawing great attention for scientific studies.

There are several multidisciplinary studies with natural antioxidants that have focused on human and animal experiments. The researchers have examined to understand the mechanisms of antioxidants on oxidative stress. They have been widely documented the knowledge of free radicals with antioxidants by identifying the oxidative stress pathway, cellular efficiencies and general health impact [6, 7].

Besides, although higher clinical complications have been observed in diseases, the mechanisms for the use of natural antioxidants are still not fully understood.

Since the past century, there have been essential diseases needed to determine how diseases progress and how the world could control them. Environmental factors, insufficient water, climate changes or new viruses influence the spread of contagious disease, and thereby cause epidemics. Nevertheless, The World Health Organization (WHO) has been still working on epidemiological studies to identify the possible sources of outbreaks, and to observe the pathogens spread from one region to different regions of the world [8]. Throughout history, there have been many significant pandemics recorded in human history. Some examples of the most up to date are Influenza virus (H1N1), Severe Acute Respiratory Syndrome (SARS), the Middle East Respiratory Syndrome (MERS), Ebola, Zika, Yellow Fever, Cholera, Malaria, and Tuberculosis [9].

Today, in response to pandemics, people have been transformed into plants and phytochemicals to protect their health. Also, researchers have advocated that these natural foods could meet antioxidant protection. However, studies are still ongoing. This chapter aims to summarize the essential natural antioxidants, their mechanism, and their effects on pandemic diseases.

2. The reality of diseases in the 21st century

In recent years, climate change, lack of safe drinking water, poor living conditions and food insecurity have been the main causes of illness, epidemics and pandemics. Besides, there are also many chemicals or toxins, which can contaminate food, drink, and medicines that cause death, injury or harm to organs. The WHO reported that besides environmental changes, many diseases can occur in animals and can be transmitted if animals and people come into close contact, for example, animal husbandry, wildlife trade, etc. Also, urbanization and air travel are essential factors for outbreaks nowadays. First and foremost, flights across the world can cause illness in other countries. This means that the pathogen has a new home, and a pandemic is realized within hours [8].

The WHO indexed the 21st century's serious diseases, which threaten public health and have no therapeutic strategies, especially vaccines or new medicines, in 2018. Some important as follows: Influenza virus (H1N1), Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), Ebola, Zika, Yellow Fever, Cholera, Malaria, Tuberculosis. It was also reported that in the 21st century, epidemics can spread faster and farther than ever. Besides that, the last announced one, coronavirus-disease 2019 (COVID-19), was accepted as a pandemic disease by the WHO.

The global strategy is to eliminate and eradicate these illnesses through vaccines or medical investments. The WHO also recommends fresh foods and healthy nutrition during pandemics, which positively affect immunity [10]. The key vision of the relationship between nutrition, their role in immunity, and stress management was highlighted. Recent advances are also being critically demonstrated in antioxidant compounds, herbal ingredients, and pharmaceutical products with literature. The coronavirus diseases such as MERS, SARS, and COVID-19, it was reviewed that vitamin C, D and E, have an important role in the regulation of T cell differentiation in immunity [11]. Also, Leite Diniz et al. [12] reviewed that several natural antioxidants can have antiviral properties on metabolic modulation, and can treat the clinical symptoms in SARS, MERS, and COVID-19.

Nevertheless, it was reviewed that some herbal remedies such as geranium, green tea, pomegranate or Echinacea may be safer than drugs against influenza

infections due to the anti-inflammatory, antibacterial and antioxidant activities of herbs and their extracts [13]. Also, it was showed that all these herbs and extracts have potential effects on respiratory complications and pro-inflammatory cytokines. Kaihatsu et al. [14] reported that natural phenolic compounds and coffee ingredients can inhibit the influenza virus by possessing radical scavenging activity. Moreover, flavonoids in citrus fruits have anti-inflammatory and antioxidant activities on the pulmonary system which showed by a bronchial epithelium model study [15].

The effect of thyme and its volatile oils may affect the penetration of the virus into the host cell or block viral proteins that are necessary for the virus to enter the host cells. Thyme may also act as an antiviral against intracellular viruses. In the meantime, evidence shows that natural compounds have plays a key role in alternative treatments to fight SARS-CoV-2. Recently determined that SARS-CoV-2 has spike glycoprotein consisted of two units. The first unit initiating virus attachment to the host cell surface and the second unit responsible for the virus-host membrane. Subunits are of great clinical importance as inhibition of the receptor binding domain which is the first step to hinder viral infections. Studies have shown that carvacrol, anethole, cinnamaldehyde, thymol, camphene, pulegone, ocimene and menthol showed good binding affinities and those natural compounds may contribute to the stability of the complex protein ligand [16, 17].

Furthermore, the potential effects of marine algal antioxidants on viral diseases has been reported [18]. Besides, some researchers reported that natural foods and natural compounds can have antibacterial and antiviral effects on cellular and molecular pathways, and thereby immunity is improved in several outbreaks such as Ebola, Cholera, Malaria and Tuberculosis [19–21].

Pandemics are old as humanity as well as natural antioxidants. Several natural foods and antioxidants have been used for healthy nutrition. However, the impact of several pandemics in the last century, there has been a growing interest between healthy food, nutrition, natural antioxidants and disease. Researchers studied the new therapeutic possibilities of the natural antioxidant for this purpose.

3. Life related to free radicals, oxidative stress and antioxidants

A healthy life is associated with the oxidative status of the organism. In a cellular mechanism, the oxidative process starts with oxygen generation to energy. Thereby, free radicals occur as a consequence of energy in mitochondria. The rest products are reactive oxygen species (ROS) and reactive nitrogen species (RNS) which have a role in toxicological and pathological conditions. On the contrary, both ROS and RNS positively affect the cellular mechanism and immune system when they are at low levels, which means a normal metabolic process. Free radicals produce against stress conditions and antioxidants during the normal healthy condition, which is also called homeostasis. So, the body tries to maintain the oxidant and antioxidant balance.

Oxidative stress markers, ROS and RNS, produce homeostasis through enzymatic and non-enzymatic reactions. Enzymatic reactions include cellular oxidase system like peroxidase, NADPH oxidase, hydrogen peroxidase. On the other side, the non-enzymatic process is based on organic compounds of the organism; for example, oxidative phosphorylation in mitochondria [22, 23]. ROS and RNS are formed from endogenous and exogenous sources that belong to several physiological and psychological mechanisms. Endogenous sources are generally occurring by immune cell activation, infection, excessive exercise, aging, or mental stress. However, environmental pollutants, drugs, heavy metals or radiation are exogenous sources, and are metabolized in free radical processes [22, 24].

The oxidative mechanism interacts with the antioxidant, endogenous, or exogenous mechanism. Both antioxidant mechanisms are capable of neutralizing free radicals and protecting the body. Endogenous antioxidant activity is the organism's first defensive system against free radicals. SOD, GPx, glutathione reductase, and CAT are the most important endogenous antioxidant in a healthy organism. Exogenous antioxidants are nutrients produced from foods and supplements, particularly vitamins E and C, flavonoids, phytochemicals, and certain essential plant-based antioxidants. These compounds can inactivate oxidizing agents and also inhibit inflammatory activation. They can modulate the enzymatic process and inflammatory mediators, including cytokines and peptides [25].

4. Oxidative stress in diseases

Oxidative stress, which includes significant bodily activities, is an imbalance between the oxidizing and antioxidant processes. If the oxidative stress cannot be regulated, several damages occur in an organism. While free radicals and oxidants are in excess production, antioxidant reactions are limited, thereby oxidative stress is generated. Several membranes or cellular structures and systems are also adversely affected by this status. Cellular proteins, lipids, lipoproteins, DNA or RNA, and oxidizing compounds, and also critical systems such as cardiovascular, neurological, or immunity, are damaged. For instance, the chains of free radicals react, and the peroxidation of lipids exists. Besides, protein damage affects the structure of the cell membrane as well as the lower antibody output. Also, enzyme activity is reduced due to proteins and occurs in several molecular and cellular mutations. These changes reflect body systems, and diseases can be occur [25].

There are several significant diseases reviewed for oxidative stress in both humans and animals (**Figure 1**). Cancer is one of the most important one, creates complex changes in an organism such as chromosomal defects or induced free radicals activation. Another critical disease is cardiovascular disease related to stress, hypertension, hypercholesterolemia, diabetes, etc. Studies showed that cardiac structure changes, especially heart failure, hypertrophy, ischemia, or atherosclerosis, generate oxidative stress [26, 27]. Nevertheless, oxidative status and its generation have been described for neurological, pulmonary, and other diseases. It was reported that loss of neuron production and progression stimulates the oxidative process, thereby neurological diseases are presented [28]. The pulmonary diseases

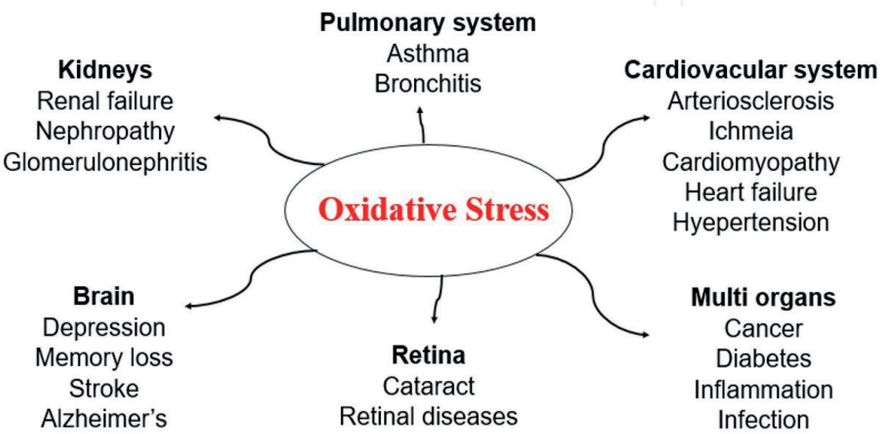

Figure 1.
Oxidative stress related diseases.

are qualified by inflammation and activation of redox transcript factors [29]. Also, researchers have been studied the generation of ROS and RNS in autoimmune and renal diseases, or several other diseases [30–32]. The importance of the immune system is interested in low antibody production and low protein which concluded in increasing the risks of diseases. Besides that, macrophages' infiltration of activated immune cells causes inflammation and oxidative damage [30]. Nevertheless, some drugs, heavy metals, or lipid peroxidation molecules are accepted as strong free radicals inducers [33]. The fact that oxidative stress has a large place during inflammation and diseases is inevitable.

Oxidative stress has a crucial role in disease onset and development. During viral infections, there may be an increase in the production of oxidizing species not neutralized by the antioxidant system, causing oxidative stress that promotes cell damage [34–36]. However, it was reviewed that in viral diseases, viruses can control oxidative stress on their benefits in cellular replication [37]. Viruses especially can change the activation of the immune system signaling pathway in oxidative status [38, 39]. ROS and RNS production are triggered by cytokines, and thereby, cell death occurs due to the imbalance between the production of reactive species and the host's anti-oxidative status. Also, RNA viruses bring about changes in the body's antioxidant defense system. Viruses are responsible for this by affecting enzymes like SOD and CAT, as well as lowering ascorbic acid, carotenoids and reduced glutathione [40–42]. Recently, in a pandemic disease COVID-19, lung damage occurs due to the release of pro-inflammatory cytokines, which alter the oxidative stress [43]. Zhao [44] also determined that another immune response of pro-inflammatory cytokines against oxidative stress is activated phagocytes cells in COVID-19. Nevertheless, generated oxidative stress is also associated with nucleic acid damage in viral mutations. It was reported that human coronavirus disease (HCoVs) and SARS are identified by genetic mutations, and also mutations in spike protein [45]. Nevertheless, influenza viruses have been demonstrated with induced oxidative stress with the activation of the Nrf2 pathway in nuclear translocation, and expression in alveolar epithelial cells [46]. Similarly, the hepatitis C virus (HCV) has been linked with genes and phosphorylation of Nrf2 [47]. It was reviewed that the Nrf2 pathway has a critical inhibition role of viral genes [37].

Management of pathogenic effects of viral diseases can be described by the mutual interaction between oxidant and antioxidant status control. Therefore this interaction is also associated with a healthy environment, balanced nutrition, and exogenous antioxidants.

5. The truth regarding antioxidants

The antioxidant process begins with oxidation when it damages a free radical compound, and then it follows by attempting to restore the body. An antioxidant may act as a pro-oxidant, which has generated ROS and RNS into two ways; breaking the chain and preventing it [48]. A chain breaking antioxidant may stabilize the formation of free radicals in the oxidative state, e.g., lipid peroxidation. Vitamins C and E, or carrots may be accepted in these anti-oxidants that break the chain. On the other hand, endogenous antioxidant enzymes such as glutathione, GPx, CAT, and SOD, may inhibit the initiation and propagation steps, consequently delaying the oxidant process.

Along with current literature, there have been several natural antioxidants reviewed for diseases or pandemic diseases [12, 49]. Each of these antioxidant properties is the neutralization capability of oxidative stress (**Table 1**).

Natural Antioxidants			
Vitamins	**Minerals**	**Plants**	**Phtyochemicals**
Vitamin E	Selenium	Garclic	Polyphenols
Vitamin C	Zinc	Ginger	Flavonoids
Beta carotene	Copper	Thyme	Carotenoids
Lycopene	Iron	Echinacea	
		Spirulina	
		Liquorice	

Table 1.
Natural antioxidants.

5.1 Vitamins

Vitamins, C, E and beta-carotene, which also called as primary antioxidants, have the beneficial effect either in health or diseases. Nevertheless, excessive doses of vitamins can be harmful rather than safe. So there has been ongoing research on nutritional antioxidants. WHO recommends antioxidants for malnutrition, disease, and pandemic-related needs [10]. Besides, nutritionists have endorsed antioxidant foods for humans first, while they have also pointed out that supplements may help.

Vitamins E and C have a higher antioxidative capacity among vitamins. Vitamin E (also known as tocopherol or alpha-tocopherol) has been reported to protect cellular membranes from lipid peroxide. Studies have suggested that vitamin E may be used in breast cancer, arthritis, some cardiovascular and neurological diseases. Besides, it was determined that the long-term use of vitamin E is acceptable as being available. Sources of vitamin E include vegetable oils, walnuts, cereals, eggs, poultry, and meat [50].

Nonetheless, vitamin C, called ascorbic acid, is essential for carnitine, neurotransmitter biosynthesis, and collagen. This vitamin has antioxidant, anti-carcinogenic, and immunomodulatory effects, which has also reduced the incidence of cancers. Also, vitamin C acts alongside vitamin E to quench free radicals. Vitamin C is found throughout natural sources such as fruits, vegetables, and tomatoes [51].

Beta-carotene, which is an active ingredient of pro-vitamin A, is a powerful antioxidant. Beta-carotene has the potential to quench oxygen during oxidative stress. This pro-vitamin has an antioxidant effect on cardiovascular diseases and cancer in particular. Beta-carotene comprises many foods, mainly green plants, spinach, carrots, oils, mangoes, apricots, and a watermelon [52, 53]. Another essential carotenoid, lycopene, is a vegetable nutrient that has protective effects on pulmonary cells and cancer. Lycopene was shown to be capable of balancing free radicals. The best source of lycopene is cooked tomato, juice, and sauce [54]. What are more, more red and pink fruits have this vitamin, like watermelon, grapefruit.

High doses of vitamins are recommended for using safely during pandemics. It was reported that especially Vitamin C has used for the treatment of cardiovascular, pulmonary disease as well as sepsis or nephropathy. It was evaluated that vitamin C can improve the mechanical ventilation of patients [55].

5.2 Minerals

There are several antioxidant minerals, in particular, selenium, zinc, copper, and iron. Selenium is an essential mineral in several vegetables, mushrooms, meat, and

seafood, with anticarcinogenic and immunomodulatory effects. Selenium also plays a crucial role in thyroid function, gastrointestinal, cardiovascular, and pulmonary diseases [48]. Selenium contains about 35 antioxidant proteins, which reduce free radicals and allow cytoprotective antioxidant genes [56]. The mineral targets hydrogen peroxide and transforms it into water.

The other minerals Mn, Cu, Zn, and Fe, can maintain the endogenous antioxidants. Fe and Cu can suppress free radicals' formation by keeping bound to transport proteins. A high dose of Fe may negatively affect Zn′s absorption to damage the immune system. It was reported that the increase of Zn in the cell has an antiviral effect in COVID-19 [57]. Also, Te Velthuis et al. [58] determined that a low dose of Zn inhibits replicating the virus in SARS.

Nevertheless, Cu is an essential mineral for cellular respiration, iron metabolism, and reducing oxidative stress. It was observed that Cu has an antiviral effect in some diseases such as COVID-19, human immunodeficiency virus (HIV), or bronchitis [59, 60]. On the other hand, according to some kinds of literature, Fe and Cu may be toxic due to an increase of viral replication and mortality in diseases, for example, HIV or COVID-19 [60]. Therefore, it was accepted that Cu and Fe must be taken in sufficient doses for the biological mechanism [61].

As the pandemic diseases continuing, humans should boost their immune system by taking sufficient minerals. Optimal nutrition can exist with dietary nutrient intake including especially vitamins and minerals.

5.3 Plants and phytochemicals

Earlier scientific studies have shown that commonly used wild edible plants, spices and herbal teas have high antiviral activity against a variety of viruses. There is also evidence that some of these drugs are used for various types of coronavirus diseases as potential phyto antiviral agents [62].

Natural antioxidants can alternate the multiple pathological processes in oxidative stress, primarily oxidative damage, inflammation, genetic changes, growth factors, etc. It was reviewed that natural antioxidants, mostly plants, and phytochemicals, can improve either oxidant status or antioxidant capacity [12]. Several plants are alternative medicines, such as ginger, garlic, curcumin, thyme, licorice, *Echinacea purpurea* or Spirulina, etc. These plants are recommended to strengthen immunity and reduce oxidative status. It was reported that these medicinal plants have essential roles in pandemic diseases, especially HIV, SARS and, COVID-19 [62–64].

Garlic, which is the most crucial spice worldwide, has a remarkably enhanced immune system booster. It may boost the activity of natural killer cells during immune deficiency. This medicinal herb has been approved as a therapeutic agent for homeostasis [65]. Furthermore, garlic has been used against cancer and cardiovascular disease [66]. This interesting spice, which has been used as a seasoning herb and traditional medicine in immunity and viral diseases, has several compounds such as saponin, cardio glycoside, and flavonoids [67–69]. Antiviral effects in garlic depend on inhibition of viral replication effects, viral protein synthesis, and viral DNA polymerization [70]. Also, garlic and its extracts have been shown to improve CAT and GPx enzymes and act as a collector of hydroxyl radicals [71]. It was reviewed that garlic and its extracts may be an alternative medicinal herbs against COVID-19 [72].

Ginger is a well-known herb with several effects such as treating sickness, colic, and appetite, controlling gastrointestinal problems, and respiratory infections. It is also accepted as a neuroprotectant, antidiabetic, anti-inflammatory, antioxidant, antiviral, and anticancer [73, 74]. This herb can maintain homeostasis by cooling the body, and reduce high fever. It was also reported that ginger shows its effect by

inhibiting productions of nitric oxide and superoxide [75, 76]. Chang et al. [77] reported that ginger can block the viral attachment in respiratory epithelium, and is effective in human respiratory syncytial virus.

A blue-green microalga named Spirulina is a popular superfood with several beneficial effects such as antioxidant, antiviral, immunomodulatory, etc. [5]. It was reported that Spirulina could inhibit viral replication by blocking replication [78]. Hernández-Corona et al. [79] found that Spirulina inhibited the viral cell penetration and replication in a virus disease named herpes simplex virus type-1 (HSV-1). It was reviewed that the antiviral features of Spirulina are belonged to acidic polysaccharides extract such as calcium spirulina. Moreover, studies suggested that Spirulina may be safe for managing influenza outbreaks, however, additional investigations are needed [80–82].

Essential oils are aromatic oily liquids derived from plant material. These natural products have been widely used, in particular fragrances, cosmetics, aromatherapy, and herbal medicine, spices, nutrition, and agriculture. Essential oils have a known biological activity, including antibacterial, antiviral, anti-fungal, and anti-inflammatory effects [83].

Echinacea purpurea, a popular natural food worldwide, includes essential oils, flavonoids, tannin, saponin, betain, etc. According to studies, this herbal medicine can reduce the symptoms of respiratory diseases. Antiviral and immunomodulatory effects in SARS and COVID-19 have been reported [84, 85].

Thyme, curcumin, and licorice have been used for decades safely for both therapeutic and treatments. The ingredients of the essential oils of the origanum species were linalol, γ terpinene, p-cymenon, thymol and myrcene. Thymus's essential oil consists primarily of thymol. Other components found other than thymol are carvacrol, linalyl acetate, linalool, γ-terpinene, p-cymene and geraniol. Numerous studies have been carried out over the application of detected phenolic compounds as an antioxidant and antiviral activities have been tested, and it shows the antiviral effects against respiratory syncytial virus, Coxsackie virus, and herpes simplex virus type 1 [86]. Zhang et al. [86] reported that a significant ingredient of thyme has antiviral and antioxidant features. Curcumin is an active supplement to inhibit the activation of cytokines and neutrophils in the lungs. Many clinical studies have evaluated its effect on inflammation, immunity, microbial, and viral conditions [87]. It was also reported that curcumin could induce the glutathione level as a scavenger of free radicals [37]. On the other hand, an exciting herb named licorice can grow in many geographical structures worldwide. It was reported that licorice could reduce hepatocellular damage in hepatitis B and C. Nevertheless, it has an antiviral effect on HIV and SARS virus [88]. Also, licorice has an immunomodulatory effect, and it can induce respiratory activity [89]. It was determined that licorice shows these activities by its extracts named triterpene, saponins, and flavonoids [90].

Scientific studies on different species of cistus have shown that different species of the plant contain useful phytochemical products. Plant-derived polyphenols have been shown to be strong antioxidant, antibacterial, antifungal, anti-inflammatory, anti-viral, cytotoxic and anti-cancer properties with potential health benefits [91]. *Cistus creticus* is a naturally occurring plant native to Turkey with phenolic substances and flavonoids. Plant-derived polyphenols are strong antioxidants, and have protective effects on DNA. Various reports have appeared on the antiviral and antibacterial potential, including several reports describing the antiviral activity of polyphenols against the parainfluenza 3 virus [92].

Begun to be remembered with the existence of human beings, the olive was the symbol of peace and healthy life in every period of life from antiquity. Olive leaf traditionally used against hypertension, diuretic, antipyretic, appetizing and against constipation [93]. The olive leaf contains much more oleuropein than other

parts. It has demonstrated that it is a phytochemical active against numerous diseases. Principal active constituents of the olive leaf are oleanolic acid and calcium elenolate compounds. These compounds have been shown to have anti-viral activity against many viruses such as parainfluenza, herpes simplex, pseudorabies, polioviruses (type-1, –2, and – 3), rhinoviruses, mycoviruses, coxsackievirus [94].

Phytochemicals are produced in plants, which are also referred to as naturally occurring plant chemicals. Several studies have demonstrated that flavonoids or phytochemicals may block these diseases' enzymatic activities [12, 95]. The most significant phytochemical compounds, polyphenols, flavonoids, and carotenoids, have been identified as antioxidants [96]. Polyphenols referred to as resveratrol and ellagic acid, are natural compounds in green tea, red wine, whole grains, grapes, and berries. They have potent antioxidants, metabolic, and cardiovascular effects. They can inhibit the proliferation of lung cancer cells by increasing autophagy [97, 98]. Resveratrol and ellagic acid may also help protect DNA and balance cell cycles. Also, it was reported that there is insufficient information on side effects and efficacy. Hence, traditional treatments need to be discussed before treatment.

Nevertheless, it was reported that flavonoids have an inhibition role in macrophages against inflammatory cytokines production in viral diseases [99]. There are some crucial plants included flavonoids, such as green tea, grapes, apples, and *Ginkgo biloba*. Also, the richest flavonoids, catechin and quercetin, are found in green tea. Catechin in green tea has anti-inflammatory features, which increases the glucocorticoids in pulmonary diseases, especially in the lung [100]. Quercetin is extracted from some plants such as *Rubus fruticosus*, *Passiflora subpeltata*, *Hypericum perforatum*, or Lagerstroemia. It was reported that quercetin could inhibit oxidative stress by increased endogenous antioxidants SOD, CAT, and GPx, and decreased lipid peroxidation. This flavonoid can also improve the function of non-enzymatic antioxidants such as vitamin C and E, and glutathione [101–103]. It was reported that another green tea metabolite named gallocatechin could reduce nitric oxide synthesis and oxidative status, and increase antioxidant capacity, especially catalase level [104, 105]. *Ginkgo biloba*, another popular herb, is a bioflavonoid compound, and also its extract named amentoflavone has a high antioxidant capacity, especially for lung diseases due to its improvement effect on SOD and glutathione [106]. Besides, some foods such as carrots, cabbage, and apple, which has luteolin, causes an increase in glutathione, SOD, and CAT. Luteolin also can improve lipid peroxidation during oxidative status in cancer and lung diseases [107].

Plant carotenoids were considered in terms of their role as mediators of free radicals through oxidation or oxygenation [108]. Furthermore, carotenoids act as chemical quench, which is necessary for the antioxidant function. They may reduce the risk of disease, in particular cancer and cardiovascular disease. The most important carotenoids are lycopene, lutein, zeaxanthine, beta-carotene found in tomatoes, carrots and watermelon.

Traditional medicinal herbs are rich compounds used in the development of medicines. They have centuries of experience with the use of herbal remedies for prevention and treatment. There are many medicinal herbs scattered geographically throughout the world. As such, further investigations are necessary to identify differences.

6. Future perspectives

Several clinical approaches have been agreed upon to deal with oxidative stress. Lately, for healthy living, the use of antioxidant supplements has been targeted to provide adequate homeostasis for humans and animals in many diseases or pandemics. Besides the prevention strategies such as isolation, hygiene, and control,

nutrition, mostly natural antioxidants, is essential for improving antiviral activity against viral and pandemic diseases such as SARS, COVID-19 and, HIV etc.

Natural antioxidants have been used in many therapeutic practices because of their enzyme inhibition and their inhibitory effect on viral protein receptors. In addition, natural antioxidants may enhance immunity during diseases. As well, they have been the subject of multidisciplinary studies [109]. The WHO also acknowledged that there was insufficient evidence of herbal medicines for the treatment or treatment of viral diseases in humans, especially COVID-19 [110].

7. Conclusion

Throughout history, there have been significant pandemic diseases such as the 1918 influenza pandemic (H1N1 virus), HIV and COVID-19. During pandemics, nutrition is as important as health, hygiene, or self-isolation standards. To that end, predominantly natural antioxidants have been used in therapeutic practices. Many herbal medicines, plants, and their extracts have inhibitory effects on pandemic diseases or their symptoms. These nutrients have been investigating their immune-modulating, antiviral, and antioxidant effects for decades. However, all these effects of natural antioxidants are not equal. Research into the health performance of these nutrients is therefore necessary.

Conflict of interest

The authors declare no conflict of interest.

Acronyms and abbreviations

WHO	The World Health Organization
H1N1	Influenza virus
SARS	Severe Acute Respiratory Syndrome
Mers-Cov	Middle East Respiratory Syndrome Coronavirus
COVID-2019	Coronavirus-disease 2019
hCoVs	Human coronavirus disease
SARS-CoV-2	Severe acute respiratory syndrome coronavirus
HIV	Human immunodeficiency virus
ROS	Reactive oxygen species
RNS	Reactive nitrogen species
GPx	Glutathione peroxidase
CAT	Catalase
SOD	Superoxide dismutase
HCV	Hepatitis C Virus
Cu	Copper
Fe	Ferrous
Zn	Zinc

Appendices and nomenclature

Ascorbic acid	Vitamin C
Tocopherol	Vitamin E

Beta carotene	provitamin A
Blue-green algae	Spirulina
Thymus	Thymol
Olive leaf	Oleanolic acid and calcium elenolate compounds
Green tea	Gallocatechin
Ginkgo biloba	Bioflavonoid compound
Phytochemical compounds	Polyphenols, flavonoids, carotenoids
Essential oils	Linalol, γ terpinene, p-cymenon, thymol, myrcene
Endogenous antioxidant	Superoxide dismutase, glutathione peroxidase, glutathione reductase, catalase
Cistus creticus	Polyphenols
Flavonoids	Catechin, quercetin

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References

[1] Birben E, Sahiner UM, Sackesen C, Erzurum S, Kalayci O. Oxidative stress and antioxidant defense. World Allergy Organ J. 2012;5(1):9-19. doi: 10.1097/WOX.0b013e3182439613.

[2] WHO/ FAO Report 2002. Dietary antioxidants: a consideration of factors influencing requirements. In: Human Vitamin and Mineral Requirements. Rome, 2002 Report of a joint FAO/ WHO expert consultation Bangkok, Thailand. Avaliable from: http://www.fao.org/3/Y2809E/y2809e0n.htm

[3] Chehue Romero A, Olvera Hernández EG, Flores Cerón T, Álvarez-Chávez A. The exogenous antioxidants. In: Morales-González JA, editor. Oxidative Stress and Chronic Degenerative Diseases—A Role for Antioxidants. Croatia: InTechOpen; 2013. p. 33.

[4] Zheng J, Zhou Y, Li, Y, Xu DP, Li S, Li HB. Spices for prevention and treatment of cancers. Nutrients. 2016;8:495. DOI: 10.3390/nu8080495

[5] Seyidoglu N, Aydin C. 2020. Stress, Natural Antioxidants and Future Perspectives. In: Salanta CL, editor. The Health Benefits of Foods - Current Knowledge and Further Development. London: Intechopen; 2020. p. 149-165.

[6] Lobo V, Patil A, Phatak A, Chandra N. Free radicals, antioxidants and functional foods: Impact on human health. Pharmacogn Rev. 2010;4(8):118-126. DOI: 10.4103/0973-7847.70902.

[7] Huang D. Dietary Antioxidants and Health Promotion. Antioxidants (Basel). 2018;7(1):9. DOI: 10.3390/antiox7010009.

[8] WHO (World Health Organization, Food and Agricultural Organization of the United Nations). Managing epidemics [Internet]. 2018. Available from: https://www.who.int/emergencies/diseases/managing-epidemics-interactive.pdf [Accessed: 2020-12-12]

[9] WHO (World Health Organization, Food and Agricultural Organization of the United Nations). [Internet]. 2020a. Available from: https:// https://www.who.int/emergencies/diseases/en/ [Accessed: 2020-12-30]

[10] WHO (World Health Organization, Food and Agricultural Organization of the United Nations). [Internet]. 2004. Available from: https://www.who.int/nutrition/publications/micronutrients/9241546123/en/ [Accessed: 2020-12-30]

[11] Fernandes IG, de Brito CA, Silva dos Reis VM, Sato MN, Pereira NZ. SARS-CoV-2 and Other Respiratory Viruses: What Does Oxidative Stress Have to Do with It?. Oxidative Medicine and Cellular Longevity. 2020;ID 8844280:13. DOI: 10.1155/2020/8844280

[12] Leite Diniz LR, Bezerra Filho CSM, Fielding BC, de Sousa DP. Natural Antioxidants: A Review of Studies on Human and Animal Coronavirus. Oxid Med & Cellular Longevity. 2020;Id3173281:14pages. DOI: 10.1155/2020/3173281

[13] Hudson JB. The use of herbal extracts in the control of influenza. Review. Journal of Medicinal Plants Research. 2009;3(13):1189-1195

[14] Kaihatsu K, Kawakami C, Kato N. Potential Anti-Influenza Virus Agents Based on Coffee Ingredients and Natural Flavonols. Nat Prod Chem Res. 2014;2:2. DOI: 10.4172/2329-6836.1000129

[15] Liu X, Wang N, Fan S, Zheng X, Yang Y, Zhu Y, Lu Y, Chen Q, Zhou H, Zheng J. The citrus flavonoid naringenin confers protection in a murine

endotoxaemia model through AMPK-ATF3-dependent negative regulation of the TLR4 signaling pathway. Scientific Reports. 2016;6:39735. DOI: 10.1038/srep39735.

[16] Zhang Y, Kutateladze TG. Molecular structure analyses suggest strategies to therapeutically target SARS-CoV-2. Nat. Commun. 2020;11(1):2920. doi: 10.1038/s41467-020-16779-4.

[17] Kulkarni SA, Nagarajan SK, Ramesh V, Palaniyandi V, Selvam SP, Madhavan T. Computational evaluation of major components from plant essential oils as potent inhibitors of SARS-CoV-2 spike protein. J. Mol. Struct. 2020:1221:128823. DOI: 10.1016/j.molstruc.2020.128823

[18] Sansone C, Brunet C, Noonan DM, Albini A. Marine Algal Antioxidants as Potential Vectors for Controlling Viral Diseases. Antioxidants (Basel). 2020;9(5):392. DOI: 10.3390/antiox9050392.

[19] Qui X, Kroeker A, He S, Kozak R. Prophylactic Efficacy of Quercetin 3-β-O-d-Glucoside against Ebola Virus Infection. Antimicrobial Agents and Chemotherapy. 2016;60(9):AAC.00307-16. DOI: 10.1128/AAC.00307-16

[20] Khalil A, Tazeddinova D. The upshot of Polyphenolic compounds on immunity amid COVID-19 pandemic and other emerging communicable diseases: An appraisal. Natural Products and Bioprospecting. 2020;10:411-429. DOI: 10.1007/s13659-020-00271-z

[21] Garcia S. Pandemics and Traditional Plant-Based Remedies. A Historical-Botanical Review in the Era of COVID19. Front. Plant Sci. 2020;11:571042. DOI: 10.3389/fpls.2020.571042

[22] Valko M, Leibfritz D, Moncola J, Cronin MD, Mazur M, Telser J. Free radicals andantioxidants in normal physiological functions and human disease. Review. Int J Biochem Cell Biol. 2007;39:44-84. DOI: 10.1016/j.biocel.2006.07.001

[23] Dröge W. Free radicals in the physiological control of cell function. Review. Physiol Rev. 2002;82:47-95. DOI: 10.1152/physrev.00018.2001

[24] Halliwell B. Biochemistry of oxidative stress. Biochem Soc Trans. 2007;35:1147-1150. DOI: 10.1042/BST0351147

[25] Pham-Huy LA, He H, Pham-Huy C. Free Radicals, Antioxidants in Disease and Health. Int J Biomed Sci. 2008;4(2):89-96. PMCID: PMC3614697

[26] Bahorun T, Soobrattee MA, Luximon-Ramma V, Aruoma OI. Free radicals and antioxidants in cardiovascular health and disease. Internet J Med. 2006;1(2):1-17. DOI: 10.4314/ijmu.v1i2.39839

[27] Ceriello A. Possible role of oxidative stress in the pathogenesis of hypertension. Review. Diabetes Care. 2008;31 (Suppl 2):S181–S184. DOI: 10.2337/dc08-s245

[28] Butterfield DA. Amyloid beta-peptide (1-42)-induced oxidative stress and neurotoxicity: implications for neurodegeneration in Alzheimer's disease brain. A review. Free Radic Res. 2002;36:1307-1313. DOI: 10.1080/1071576021000049890

[29] MacNee W. Oxidative stress and lung inflammation in airways disease. Eur J Pharmacol. 2001;429:195-207. DOI: 10.1016/s0014-2999(01)01320-6

[30] Walston J, Xue Q, Semba RD, Ferrucci L, Cappola AR, Ricks M, Guralnik J, Fried LP. Serum antioxidants, inflammation, and total mortality in older women. Am J Epidemiol. 2006;163:18-26. DOI: 10.1093/aje/kwj007

[31] Meyer CH, Sekundo W. Nutritional supplementation to prevent cataract formation. Dev Ophthalmol. 2005;38:103-119. DOI: 10.1159/000082771

[32] Braekke K, Harsem NK, Staff AC. Oxidative stress and antioxidant status in fetal circulation in preeclampsia. Pediatr Res. 2006;60:560-564. DOI: 10.1203/01.pdr.0000242299.01219.6a

[33] Galle J. Oxidative stress in chronic renal failure. Nephrol Dial Transplant. 2001;16:2135-2142. DOI: 10.1093/ndt/16.11.2135

[34] Sies H. Oxidative stress: a concept in redox biology and medicine. Redox Biology. 2015;4:180-183. DOI: 10.1016/j.redox.2015.01.002.

[35] Gravier-Hernández R, Gil-del Valle L, Valdes-Alonso L, Hernández-AyalaN, Bermúdez-AlfonsoY, Hernández-Requejo D, Rosell-Guerra T, Hernández-González-Abreu MC. Oxidative stress in hepatitis C virus–human immunodeficiency virus co-infected patients. Annals of Hepatology. 2020;19(1):92-98. DOI: 10.1016/j.aohep.2019.05.009

[36] Zhang Z, Rong L, Li YP. Flaviviridae Viruses and Oxidative Stress: Implications for Viral Pathogenesis. Oxid Med Cell Longev. 2019:1409582. DOI: 10.1155/2019/1409582.

[37] Lee W, Loo C, Bebawy M, Luk F, Mason R, Rohanizadeh R. Curcumin and its derivatives: Their application in neuropharmacology and neuroscience in the 21st century. Curr Neuropharmacol. 2013;11:338-378. DOI: 10.2174/1570159X11311040002

[38] Rehermann B, Nascimbeni M. Immunology of hepatitis B virus and hepatitis C virus infection. Nature Reviews Immunology. 2005;5(3):215-229. DOI: 10.1038/nri1573

[39] Imai Y, Kuba K, Greg Neely G, Yaghubian Malhami R, Perkmann T, van Loo G, Ermolaeva M, Veldhuizen R, Leuing YHC, Wang H, Liu H, Sun Y, Pasparakis M, Kopf M, Mech C, Bavari S, Perisi JSM, Slutsky AS, Akira S, Hultqvist M, Holmdahl R, NichollsJ, JiangC, BinderCJ, PenningerJM. Identification of oxidative stress and Toll-like receptor 4 signaling as a key pathway of acute lung injury. Cell. 2008;133(2):235-249.

[40] Bogden JD, Baker H, Frank O, Perez G, Kemp F, Bruening K, Louria D. Micronutrient status and human immunodeficiency virus (HIV) infection. Ann N Y Acad Sci. 1990;587:189-195. DOI: 10.1111/j.1749-6632.1990.tb00146.x

[41] Chrobot AM, Szaflarska-Szczepanik A, Drewa G. Antioxidant defense in children with chronic viral hepatitis B and C. Med Sci Monit. 2000;6(4):713-718.

[42] Reshi ML, Su YC, Hong JR. RNA Viruses: ROS-Mediated Cell Death. Int J Cell Biol. 2014;2014:467452. DOI: 10.1155/2014/467452

[43] Xiaowei Li, Manman G, Yizhao P, Liesu M, Shemin L. Molecular immune pathogenesis and diagnosis of COVID-19. J Pharm Anal. 2020;10(2):102-108. DOI: 10.1016/j.jpha.2020.03.001

[44] Zhao M. Cytokine storm and immunomodulatory therapy in COVID-19: role of chloroquine and anti-IL-6 monoclonal antibodies, Int. J. Antimicrob. Agents. 2020;55(6):105982. DOI: 10.1016/j.ijantimicag.2020.105982.

[45] Xu D, Zhang Z, Chu F, Li Y, Jin L, Zhang L, Gao GF, Wang FS. Genetic variation of SARS coronavirus in Beijing hospital, Emerg. Infect. Dis. 2004;10:789-794. DOI: 10.3201/eid1005.030875

[46] Kosmider B, Messier EM, Janssen WJ, Nahreini P, Wang J, Hartshorn KL, Mason RJ. Nrf 2 protects human alveolar epithelial cells against injury induced by influenza A virus. Respiratory Research. 2012;13(1):43. DOI: 10.1186/1465-9921-13-43

[47] Burdette D, Olivarez M, Waris G. Activation of transcription factor Nrf2 by hepatitis C virus induces the cell-survival pathway. J Gen Virol. 2010;91(Pt 3):681-690. DOI: 10.1099/vir.0.014340-0

[48] Young I, Woodside J. Antioxidants in health and disease. J. Clin.Pathol. 2001;54:176-186. DOI: 10.1136/jcp.54.3.176

[49] Derouiche S. Oxidative Stress Associated with SARS-Cov-2 (COVID-19) Increases the Severity of the Lung Disease - A Systematic Review. Infect Dis Epidemiol. 2020;6(3):1-6. DOI: 10.23937/2474-3658/1510121

[50] Zhou Z, Xi W, Hu Y, Nie C, Zhou Z. Antioxidant activity of citrus fruits, review. Food Chemistry. 2016;196:885-896. DOI: 10.1016/j.foodchem.2015.09.072

[51] Coulter ID, Hardy ML, Morton SC, Hilton LG, Tu W, Valentine D, Shekelle PG. Antioxidants vitamin C and vitamin E for the prevention and treatment of cancer. Journal of General Internal Medicine. 2006;21(7):735-744. DOI: 10.1111/j.1525-1497.2006.00483.x

[52] Gaziano JM, Hennekens CH. The role of beta-carotene in the prevention of cardiovascular disease. Annals of the New York Academy of Sciences. 1993;691:148-155. DOI: 10.1111/j.1749-6632.1993.tb26166.x

[53] Ozsoy N, Candoken E, Akev N.Implications for degenerative disorders: Anti oxidative activity, total phenols, flavonoids, ascorbic acid, beta-carotene and beta-tocopherol in Aloe vera. Oxidative Medicine and Cellular Longevity. 2009;2:99-106. DOI: 10.4161/oxim.2.2.8493

[54] Donaldson MS. Nutrition and cancer: A review of the evidence for an anti-cancer diet. Nutr. J. 2004;3:19-25. DOI: 10.1186/1475-2891-3-19

[55] Hemilä H, Chalker E. Vitamin C can shorten the length of stay in the ICU: a meta-analysis. Nutrients. 2019;11(4):708. DOI: 10.3390/nu11040708

[56] Nakamura H. Thioredoxin and its related molecules: Updated 2005. Antioxidants and Redox Singaling. 2005;7(5-6):823. DOI: 10.1089/ars.2005.7.823

[57] Skalny AV, Rink L, Ajsuvakova OP, Aschner M, Gritsenko VA, Alekseenko SI, Svistunov AA, Petrakis D, Spandidos DA, Aaseth J, Tsatsakis A, Tinkov AA. Zinc and respiratory tract infections: Perspectives for COVID-19 (Review). International Journal of Molecular Medicine. 2020;46:17-26. DOI: 10.3892/ijmm.2020.4575

[58] te Velthuis AJW, van den Worm SHE, Sims AC, Baric RS, Snijder EJ, van Hemert MJ. Zn2+ inhibits coronavirus and arterivirus RNA polymerase activity in vitro and zinc ionophores block the replication of these viruses in cell culture. PLOS Pathogens. 2010;4;6(11):e1001176. DOI: 10.1371/journal.ppat.1001176

[59] Raha S, Mallick R, Basak S, Duttaroy AK. Is copper beneficial for COVID-19 patients? Medical Hypotheses. 2020;142:109814. DOI: 10.1016/j.mehy.2020.109814

[60] Dalamaga M, Karampela I, Mantzoros CS. Commentary: Could iron chelators prove to be useful as

an adjunct to COVID-19 treatment regimens? Metabolism Clinical and Experimental. 2020;108:154260. DOI: 10.1016/j.metabol.2020.154260

[61] Li C, Li Y, Ding C. The role of copper homeostasis at the host-pathogen axis: From bacteria to fungi. International Journal of Molecular Sciences. 2019;20(1):175. DOI: 10.3390/ijms20010175

[62] Sekeroglu N, Gezici S. Coronavirus Pandemic and Some Turkish Medicinal Plants. Anadolu Kliniği Tıp Bilimleri Dergisi. 2020;25(1):163-182. DOI: 10.21673/anadoluklin.724210 (Turkish)

[63] Vellingiri B, Jayaramayy K, Iyer M, Narayanasamy A, Govindasamy V, Giridharane B, Ganesan S, Venugopal A, Venkatesan D, Ganesan H, Rajagopalan K, Rahman PKSM, Cho SG, Kumar NS, Subramaniam MD. COVID-19: A promising cure for the global panic. Sci. Total Environ. 2020;725:138277. DOI: 10.1016/j.scitotenv.2020.138277

[64] Babich O, Sukhikh S, Prosekov A, Asyakina L, Ivanova S. Medicinal Plants to Strengthen Immunity during a Pandemic. Pharmaceuticals. 2020;13:313. DOI: 10.3390/ph13100313

[65] Kyo E, Uda N, Kasuga S, Itakura Y. Immunmodulator effects of agedgarlic extract. J. Nutr. 2001;131(3s):1075S–1079S. DOI: 10.1093/jn/131.3.1075S

[66] Amagese H. Clarifying the real bioactive cconstituents of garlic. J. Nutr. 2006;136:716S–725S. DOI: 10.1093/jn/136.3.716S

[67] Kun S. Seetaha S, Pongsanarakul S, Hannongbua Si Shoowongkomon K. Anti HIV-1 reverse tanscriptase activities of hexane etracts from some Asian medicinal plants. Journal of Medicinal Plants Research. 2011;5(19):4899-4960. DOI: 10.5897/JMPR.9000098

[68] Rehman R, Saif S, Hanif MA, Riaz M. Garlic. In: Hanif M, Nawaz H, Khan M, Byrne H, editors. Medicinal plants of South Asia. Amsterdam: Elsevier BV; 2019. p. 301-315. DOI: 10.1016/B978-0-08-102659-5.00023-9

[69] Rouf R, Uddin SJ, Sarker DK, Islam MT, Ali ES, Shilpi JA, Nahar L, Tiralongo E, Sarker SD. Antiviral potential of garlic (Allium sativum) and its organosulfur compounds: A systematic update of pre-clinical and clinical data. Trends in Food Science & Technology. 2020;104 (2020):219-234. DOI: 10.1016/j.tifs.2020.08.006

[70] Mehrbood P, Ideris A, Amini E, Eslami T, Bande F, Kheiri M. Assessment of direct immınofluoresence assay in detection of antiviral effect of grlic extract on influenca virus. Africa Journal of microbiology research. 2013;7:2608-2612. DOI: 10.5897/AJMR12.2329

[71] Prasad K, Haxdal A, Yu M, Raney BL. Antioxidant activity of allicin, an active principle in garlic. Mol Cell Biochem. 1995;148:183-189. DOI: 10.1007/BF00928155

[72] Oladele JO, Ajayi EI, Oyeleke OM, Oladele OT, Olowookere BD, Adeniyi BM, Oyewole OI, Oladiji AT. A systematic review on COVID-19 pandemic with special emphasis on curative potentials of Nigeria based medicinal plants. Heliyon. 2020;6(9):e04897. DOI: 10.1016/j.heliyon.2020.e04897

[73] Sornpet B, Potha T, Tragoolpua Y, Pringproa K. Antiviral activity of five Asian medicinal pant crude extracts against highly pathogenic H5N1 avian influenza virus. Asian Pac J Trop Med. 2017;10:871-876. DOI: 10.1016/j.apjtm.2017.08.010

[74] Abiyana S, Gayatri Devi R, Lakshmanan G. Knowledge and awareness about ginger and turmeric as a herbal cure for COVID-19. Int. J.

Pharm. Res. 2020;(12): 768-777. DOI: 10.31838/ijpr/2020.SP2.093

[75] Ippoushi K, Azuma K, Ito H, Horie H, Higashio H. [6]-Gingerol inhibits nitric oxide synthesis in activated J774.1 mouse macrophages and prevents peroxynitrite-induced oxidation and nitration reactions. Life Sci. 2003;14;73(26):3427-37. doi: 10.1016/j.lfs.2003.06.022

[76] Rahmani AH, Al Sharbrmi FM, Aly SM. Active ingredients of ginger as potential candidates in the prevention and treatment of diseases via modulation of biological activities. Int J Physiol Pathophysiol Pharmacol. 2014;6(2):125-136. PMCID: PMC4106649

[77] Chang JS, Wang KC, Yeh CF, Shieh DE, Chiang LC. Fresh ginger (Zingiber officinale) has anti-viral activity against human respiratory syncytial virus in human respiratory tract cell lines. J Ethnopharmacol. 2013;145(1):146-151. DOI: 10.1016/j.jep.2012.10.043

[78] Hayashi K., Hayashi T., Kojima I. A natural sulfated polysaccharide, calcium spirulan, isolated from Spirulina platensis: in vitro and ex vivo evaluation of anti-Herpes simplex virus and anti-human immunodeficiency virus activities. AIDS Research and Human Retroviruses. 1996;12:1463-1471. DOI: 10.1089/aid.1996.12.1463

[79] Hernández-Corona A, Nieves I, Meckes M, Chamorro G, Barron BL. Antiviral activity of Spirulina maxima against herpes simplex virus type 2. Antiviral Res. 2002;56(3):279-285. DOI: 10.1016/S0166-3542(02)00132-8

[80] Singh S, Dwivedi V, Sanyal D, Dasgupta S. Therapeutic and Nutritional Potential of Spirulina in Combating COVID-19 Infection. AIJR prints. 2020;49(1). DOI: 10.13140/RG.2.2.16527.41127

[81] Deng F, Lu JJ, Liu HY, Lin LP, Ding J. Zhang JS. Synthesis and antitumor activity of novel salvicine analogues. Chin Chem Lett. 2011;22:25-28. DOI: 10.1016/j.cclet.2010.07.009

[82] Chen YH, Chang GK, Kuo SM, Huang SY, Yu IC, Lo YL, Shih SR. Well-tolerated Spirulina extract inhibits influenza virus replication and reduces virus-induced mortality. Scientific Reports. 2016;6:24253. DOI: 10.1038/srep24253

[83] Sengezer E, Gungor T. Essential oils and their effects on animals. Lalahan Hay. Araşt. Enst. Derg. 2008;48(2):101-110 (Turkish). Avaliable from: Retrieved from https://dergipark.org.tr/tr/pub/lahaed/issue/39442/465209

[84] David S. Cunningham, R. Echinacea for the prevention and treatment of upper respiratory tract infections: A systematic review and meta-analysis. Complement. Ther. Med. 2019:44:18-26. DOI: 10.1016/j.ctim.2019.03.011

[85] Li SJ, Wang YL, Xue J, Zhao N, Zhu TS. The impact of COVID-19 epidemic declaration on psychological consequences: A study on active Weibo users. Int. J. Environ. Res. Public Health. 2020;17(6):2032. DOI: 10.3390/ijerph17062032

[86] Zhang XL, Guo YS, Wang CH, Li GQ, Xu JJ, Chung HY, Ye WC, Li YL, Wang GC. Phenolic compounds from Origanum vulgare and their antioxidant and antiviral activities. Food Chem. 2014; 152:300-306. DOI: 10.1016/j.foodchem.2013.11.153

[87] Boskabady MH, Shakeri F, Naghdi F. The effects of Curcuma Longa L. and its constituents in respiratory disorders andmolecular mechanisms of their action. In: Rahman A, editor. Studies in Natural Products Chemistry. Oxford, UK: Elsevier; 2020;65:239-269. DOI: 10.1016/B978-0-12-817905-5.00007-X

[88] Fiore C, Eisenhut M, Krausse R, Ragazzi E, Pellati D, Armanini D, Bielenberg J. Antiviral effects of Glycyrrhiza species. Phytother Res. 2008;22(2):141-148. DOI: 10.1002/ptr.2295

[89] Fiore C, Eisenhut M, Ragazzi E, Zanchin G, Armanini D. A history of the therapeutic use of liquorice in Europe. J Ethnopharm. 2005;99(3):317-324. DOI: 10.1016/j.jep.2005.04.015

[90] Wang C, Chen L, Xu C, Shi J, Chen S, Tan M, Chen J, Zou L, Chen C, Liu Z, A Comprehensive Review for Phytochemical, Pharmacological, and Biosynthesis Studies on Glycyrrhiza spp. (Review). Am. J. Chin. Med. 2020;48:17-45. DOI: 10.1142/S0192415X20500020

[91] Stępień A, Aebisher D, Bartusik-Aebisher D. Biological properties of "Cistus species". Eur J Clin Exp Med. 2018; 16(2):127-132. DOI: 10.15584/ejcem.2018.2.8

[92] Kilic DD, Siriken B, Erturk O, Tanrikulu G, Gül M, Başkan C. Antibacterial, Antioxidant and DNA Interaction Properties of Cistus creticus L. Extracts. J Int Environ Appl Sci. 2019; 14(3):110-115.

[93] Wyk BE, Wink M. Medicinal Plants of the World: An Illustrated Scientific Guide to Important Medicinal Plants and Their Uses. 1st ed. Portland, Oregon. USA: Timber Press; 2004. 480 p.

[94] AMR. Alternative Medicine Review. Olive Leaf Monograph-Foundational Med Rev. 2009;14(1):62-66. Available from: https://www.foundationalmedicinereview.com/wp-content/uploads/2019/02/v14-1-62.pdf [Accessed:2020-12-10]

[95] Jo S, Kim S, Shin DH, Kim MS. Inhibition of SARSCoV 3CL protease by flavonoids. Journal of Enzyme Inhibition and Medicinal Chemistry. 2020;35(1):145-151. DOI: 10.1080/14756366.2019.1690480

[96] Miller AL. Antioxidant Flavonoids: Structure, Function and Clinical Usage. Alt. Med. Rev. 1996;1:103-111.

[97] Han DH, Lee MJ, Kim JH. Antioxidant and Apoptosis-inducing Activities of Ellagic Acid. Anticancer Research. 2006;26:3601-3606. DOI: 10.1007/s11356-019-07352-8

[98] Duan J, Zhan JC, Wang GZ, Zhao XC, Huang WD, Zhou GB. The red wine component ellagic acid induces autophagy and exhibits anti-lung cancer activity in vitro and in vivo. Journal of Cellular and Molecular Medicine. 2018;23(1):143-154. DOI: 10.1111/jcmm.13899

[99] Yahfoufi N, Alsadi N, Jambi M, Matar C. The immunomodulatory and anti-inflammatory role of polyphenols. Nutrients. 2018;10:1618. DOI: 10.3390/nu10111618

[100] Lugt T, Weseler AR, Vrolijk MF, Opperhuizen A, Aalt B. Dietary advanced glycation endproducts decrease glucocorticoid sensitivity in vitro. Nutrients. 2020;12:441. DOI: 10.3390/nu12020441

[101] Kucharíková A, Kusari S, Sezgin S, Spiteller M, Čellárová E. Occurrence and distribution of phytochemicals in the leaves of 17 in vitro cultured Hypericum spp. adapted to outdoor Conditions. Frontiers in Plant Science. 2016;27;7:1616. DOI: 10.3389/fpls.2016.01616

[102] Meng LQ, Yang FY, Wang MS. Shi BK, Chen DX, Chen D, Zhou Q, He QB, Ma LX, Cheng WL, Xing NZ. Quercetin protects against chronic prostatitis in rat model through NF-κB and MAPK signaling pathways. Prostate. 2018;78(11):790-800. DOI: 10.1002/pros.23536

[103] Zahoor M, Shah AB, Naz S, Ullah R, Bari A, Mahmood HM. Isolation of quercetin from rubus fruticosus, their concentration through nf/ro membranes, and recovery through carbon nanocomposite. a pilot plant study. BioMed Research International. 2020;2020(11):1-7. DOI: 10.1155/2020/8216435

[104] Pan Y, Long X, Yi R, Zhao X. Polyphenols in Liubao tea can prevent CCl4-induced hepatic damage in mice through its antioxidant capacities. Nutrients. 2018;10;10(9):1280. DOI: 10.3390/nu10091280

[105] Bulboaca AE, Boarescu PM, Porfire AS, Dogaru G, Barbalata C, Valeanu M, Munteanu C, Râjnoveanu RM, Nicula CA, Stanescu IC. The effect of nano-epigallocatechin-gallate on oxidative stress and matrix metalloproteinases in experimental diabetes mellitus. Antioxidants. 2020;9(2):172. DOI: 10.3390/antiox9020172

[106] Bajpai VK, Park IW, Lee JI, Shukla S, Nile SH, Chun HS, Khan I, Oh SY, Lee H, Huh YS, Na MK, Han YK. Antioxidant and antimicrobial efficacy of a biflavonoid, amentoflavone from Nandina domestica in vitro and in minced chicken meat and apple juice food models. Food Chemistry. 2019;271:239-247. DOI: 10.1016/j.foodchem.2018.07.159

[107] Kang KA, Piao MJ, Ryu YS, Hyun YJ, Park JE, Shilnikova K, Zhen AX, Kang HK, Koh YS, Jeong YJ, Hyun JW. Luteolin induces apoptotic cell death via antioxidant activity in human colon cancer cells. International Journal of Oncology. 2017;51(4):1169-1178. DOI: 10.3892/ijo.2017.4091

[108] Fiedor J, Burda K. Potential Role of Carotenoids as Antioxidants in Human Health and Disease. Nutrients. 2014;6:466-488. DOI: 10.3390/nu6020466

[109] Thomford NE, Dzobo K, Chimusa E, Andrae-Marobela K, Chirikure S, Wonkam A, Dandara C. Personalized herbal medicine? a roadmap for convergence of herbal and precision medicine biomarker innovations. OMICS: A J Integrative Biology. 2018;22(6):375-391. DOI: 10.1089/omi.2018.0074.

[110] WHO (World Health Organization, Food and Agricultural Organization of the United Nations). Myth busters. [Internet]. 2020b. Available from: https://www.who.int/westernpacific/emergencies/covid-19/information/mythbusters [Accessed: 2020-12-25]