Обзор / Review

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Potential medicinal plants used in the treatment of COVID-19: a review

ABSTRACT

Novel coronavirus COVID-19 (SARS-CoV-2), the unexpected pandemic that been caused severe fright worldwide. It has presented the world with one of the most difficult global public health crises and the arrival of COVID-19 has kept the whole world on their toes. The spread of COVID-19 has become a health emergency and attention has been raised worldwide to design prevention and management strategy. Although several clinical trials are ongoing, no approved medications from Food and Drug Administration are available at a time, after while some preventative vaccines have been developed, manufactured and deployed depending on variant of COVID-19. As situation warrants for the exploration of a successful antiviral, there should be a search for the remedies in nature medicine. Medicinal plants and their metabolites have long been used as a treatment option for various life-threatening diseases with minimal side effects. Thus this review aims to summarize previous outcomes concerning the role of medicinal plants in treating several life-threatening diseases for the potential medicinal plants used in the case of COVID-19 treatment. Some of these includes Turmeric (*Curcuma longa* Linn.), Black Cumin (*Nigella sativa* L.), Garlic (*Allium sativum* L.), and Ginger (*Zingiber officinale* Rosc.). These are important traditional herbal medicines to cure many complicated health ailments. However, further extensive researches and trials are suggested to discover the role of medicinal plants for management of the pandemic. Moreover, the use of potential medicinal plants for specific variant of COVID-19 and others life-threatening diseases has to be investigated.

KEYWORDS:

COVID-19, medicinal plants, pandemic, worldwide

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Потенциальные лекарственные растения, используемые при лечении COVID-19. Обзор

РЕЗЮМЕ

Новый коронавирус COVID-19 (SARS-CoV-2), неожиданная пандемия, которая вызвала сильный испуг во всем мире. Вирус дал миру один из самых сложных глобальных кризисов общественного здравоохранения, а появление COVID-19 держало весь мир в напряжении. Распространение COVID-19 стало чрезвычайной ситуацией в области здравоохранения, и во всем мире было повышено внимание к разработке стратегии профилактики и лечения. Были разработаны, изготовлены и внедрены некоторые профилактические вакцины в зависимости от варианта COVID-19. Хотя некоторые клинические испытания продолжаются, поскольку ситуация требует исследования успешного противовирусного препарата, следует искать средства в природной медицине. Лекарственные растения и их метаболиты уже давно используются в качестве варианта лечения различных опасных для жизни заболеваний с минимальными побочными эффектами. Таким образом, этот обзор направлен на обобщение предыдущих результатов, касающихся роли лекарственных растений в лечении опасных для жизни заболеваний, в том числе потенциальных лекарственных растений, используемых в случае лечения COVID-19. Некоторые из них включают куркуму (*Curcuma longa* Linn.), черный тмин (*Nigella sativa* L.), чеснок (*Allium sativum* L.) и имбирь (*Zingiber officinale* Rosc.). Это важные традиционные растительные лекарственные средства для лечения многих сложных заболеваний. Однако предлагаются дальнейшие обширные исследования и испытания, чтобы выяснить роль лекарственных растений в борьбе с пандемией. Кроме того, необходимо изучить использование потенциальных лекарственных растений для лечения определенных вариантов COVID-19 и других опасных для жизни заболеваний.

КЛЮЧЕВЫЕ СЛОВА:

COVID-19, лекарственные растения, пандемия

INTRODUCTION

Infectious diseases are one of the leading causes of morbidity and mortality around the world. Ebola, SARS-CoV (severe acute respiratory syndrome coronavirus), MERS-CoV (middle east respiratory syndrome coronavirus), Malaria, AIDS (Acquired immuno-deficiency syndrome), influenza, tuberculosis, and most recently coronavirus COVID-19 are among the major infectious diseases that have killed a large number of people worldwide as epidemics or pandemics [1]. These diseases have inflicted a heavy socioeconomic burden on the people of the world, despite enormous efforts to control them at both local and international levels.

Coronavirus disease 2019 (COVID-19), a highly contagious viral illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the unexpected pandemic that caused fear among people worldwide and has presented the world with one of the most difficult global public health crises. The arrival of COVID-19 has kept the whole world on their toes and all countries are maximizing their efforts to fight the virus and minimize infection [2]. In the race to contain this highly contagious coronavirus that rapidly spread through direct (sneeze or cough droplets in the air) and indirect transmissions (nasal, and oral mucosal excretions on surfaces), various strategies are being implemented from social distancing, selective mask using, sanitizer, quarantine and lockdown were established to avoid social interactive, testing and tracing to research and development of drugs and vaccines [3, 4]. Even if several clinical trials underway, there are no approved medications from Food and Drug Administration are available at a time. After while some vaccines have been developed, manufactured and deployed to combat this pandemic, but delivery remains a barrier, particularly in underdeveloped or developing nations [5]. Due to the urgency of the situation, some investigations focuses on the repurposing possibilities of already existing antiviral medications and the exploration of various complementary traditional medicines for prevention and treatment of COVID-19 [6, 7]. Particularly traditional herbal medicines are being extensively explored as potential COVID-19 management medication with fair share of applause and criticisms [8]. Some investigators have returned to plant-based medicinal approaches as a result of the lack of specific, viable treatments for SARSCoV-2. This is due to numerous medications are derived from plant materials or their bioactive herbal ingredients [9]. The Chinese National Health Commission has approved various commendations on the herbal therapy and allowed the use of herb-based medications in conjunction with Western medicine as an alternative treatment for COVID-19 [9, 10].

Traditional natural medicine are effectively used in treating and managing various diseases for over hundreds and thousands of years for it contains phytochemical compounds that exhibit anti-bacterial, antiviral, immuno-modulatory, anti-cancer, and anti-inflammatory properties [11, 12], and its efficacy and effectiveness have been further confirmed scientifically through several studies. Even if natural products are a major source of inspiration for modern drug discovery and development, the traditional medicinal practices began getting shadowed over time and even became extinct in some cases with the advent of new technologies for modern drug development for their ease of production, standardization, quality control, and quick effects. Even so, there is still a significant reliance on complementary medicine, particularly in developing nations, on natural products or traditional medicine [13]. The traditional natural medicines are important to treat many complicated health ailments from the past experience and present evidence for their low cost, fewer side effects, and accessibility [14, 4].

The aim of this review is to highlight for the roles and potential medicinal plants that used in the case of COVID-19 treatment. Some of these are Turmeric (*Curcuma longa* Linn.), Black Cumin (*Nigella sativa* L.), Garlic (*Allium sativum* L.), and Ginger (*Zingiber officinale* Rosc.). The constituents presented in medicinal plants possess excellent metabolic properties, including significant antiviral and antimicrobial potential. Therefore, undoubtedly these medicinal plants are used in reducing the suffering from illness through the COVID-19 in boosting immunity and a need for possible management option against COVID-19.

MEDICINAL PLANTS AND ITS POTENTIALS TO TREAT COVID-19

Exploration of natural medicinal plants

Traditional natural medicine has a long history of treating and managing various infectious diseases. Traditional medicine is the "sum total of the knowledge, skills, and practices based on the theories, beliefs, and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health as well as in the prevention, diagnosis, improvement, or treatment of physical and mental illness" [15]. Since traditional medicine has been used safely and effectively for hundreds of years to treat a wide range of illnesses, developing nations rely on it for alternative healthcare facilities [16]. The primary health care system's traditional medication is still the most effective and straightforward form of treatment in underprivileged areas [17]. Several species of medicinal plants are widely used as a medical mediator to treat a variety of communicable diseases worldwide. Collectively, about ¼ of existing approved medications have been derived from sources of botanical origins [18].

Natural products are a rich source of medicinally active ingredients that have been used for centuries to treat and prevent a wide range of illnesses. Medicinal plants are essential sources of new pharmaceutical targets, because of their inexhaustible array of relevant molecular entities like secondary metabolites, enzymes and skeletons [19, 20]. Medicinal plants are effective against a multitude of diseases because of it contains phytochemical compounds that exhibit anti-bacterial, antiviral, immuno-modulatory, anti-cancer, and anti-inflammatory properties [11, 12].

Traditional and complementary medicine (TCM) has regained momentum into the "mainstream" medicine and incorporated in the national policies of 96 WHO member states [21] were in line with traditional natural medicinal practices such as indigenous traditional medicine as it became extinct over time. African traditional natural medicines are very older and highly dependent on cultural, religious, and spiritual belief; and still in existence even after the introduction of science-based medicine by the Europeans [22].

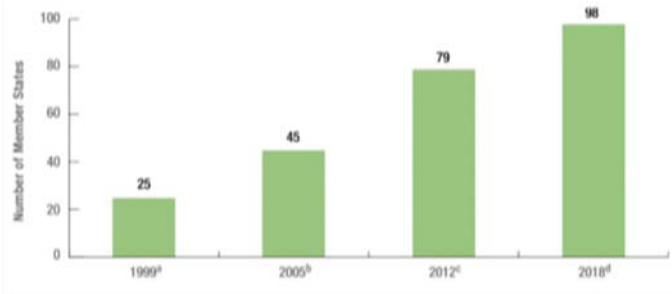

Figure 1. Growth in the number of member states with a national policy on traditional and complementary medicine in 1999-2018 [21]

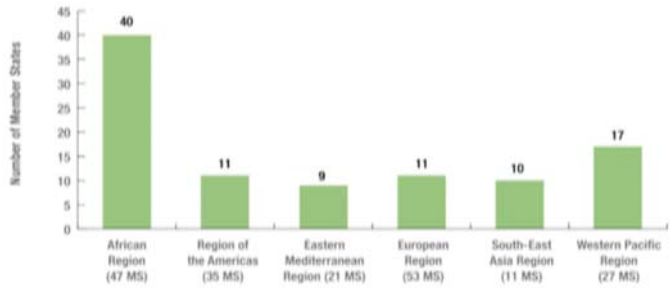

Figure 2. Regional distribution of member states on TCM at 2018 [21]

Historical significances and medicinal values of natural remedies for a variety of illnesses

The lengthy and tedious history demonstrates how long people have been using plants to treat a variety of ailments. Due to their diversified range of phytochemicals, which are important for their therapeutic use against a variety of ailments, plant species offer an extensive amount of medicinal promise in herbal medicine [5]. Its significant efficacy evidence is provided by immunomodulatory, antiviral, anti-inflammatory, and mixed-effect medications [5]. In April 2009, the extremely harmful Influenza A (H1N1) virus was first noted in the United States and Mexico. It quickly spread to other region of the world, and resulted as the first influenza pandemic since 1968 occurred. According to World Health Organization data, the pandemic had reached nearly every country by March 2010 and claimed 17,700 lives [23]. The antiviral oseltamivir was widely utilized to manage the H1N1 influenza pandemic, and advised by the World Health Organization [23]. While no direct comparative data was presented to clarify the role of oseltamivir in H1N1 influenza was reported, certain isolated cases of H1N1 virus resistance to oseltamivir were detected [24]. Because of the high price and shortage of oseltamivir, Traditional Chinese medicine (TCM) was employed in low cost as an alternative treatment in areas with low resources, such as rural China, where oseltamivir supplies were frequently insufficient [24]. TCM has demonstrated efficacy in treating coronavirus pneumonia caused by the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and severe acute respiratory syndrome (SARS) [25, 26]. During the 2003 SARS outbreak, TCM achieved impressive therapeutic results. The TCM program participated in the COVID-19 analysis and treatment recommendations during the retrieval era, and TCM experts were employed throughout the entire rescue process [9, 27].

According to contemporary pharmacological research, seasonal influenza has been treated with Traditional Chinese Medicine (TCM) for thousands of years [28]. Wang et al. [29] conducted a clinical trial using the TCM formulation Maxingshigan-Yinqiaosan (MY), which is made up of 12 herbs from 11 medical sites across 4 provinces in China during the 2009 H1N1 influenza epidemic. Both oseltamivir and MY, alone and in combination has a capacity to shortened the time it took for H1N1 patients to recover from their fevers without causing any negative side effects, indicating that MY might be a viable choice for treating fever in H1N1 influenza patients. Additionally, the cost of Maxingshigan-Yinqiaosan treatment was 70% less than that of oseltamivir [29, 30]. Similarly, WHO recommended artemisinin-based combination therapy (ACT) for the treatment of malaria by combine an artemisinin derivative like that of artemether, artesunate or dihydroartemisinin with an effective antimalarial medicine [31]. Although using as an alternative or in combination with contemporary medications, traditional herbal remedies, such as those for influenza and malaria, have demonstrated great promise in lowering the long-term problems associated with infectious diseases, such as drug resistance, availability, cost, and socioeconomic burden. Since nearly all highly contagious diseases are affected by these issues, it is imperative to expand the selection of antiviral medications by incorporating traditional herbal remedies in order to better prepare for infectious disease-related public health emergencies like COVID-19 [13].

Role and potentials of natural products in the case of COVID-19 treatment

Boosting immunity, antiviral and phytochemical potential

The active ingredients found in herbal medications can help minimize the risk of infection and its symptoms. Additionally, herbal therapy strengthens the body, boosts immunity, and enhances overall health and well-being [5]. For the treatment of respiratory infections, numerous natural items and herbal remedies have received approval as medications or food additives, and it can prevent or slow down the SARSCoV-2 infection [5]. Maximizing the natural immunity of the body is critically important as the host environment is supposed to be a governing factor for the attacking organism. The novel coronavirus COVID-19 has offered mode of infection similar to SARS, which affects elderly and immune-compromised people as well as those with diabetes (high blood sugar) and chronic heart conditions. Therefore, several immune-boosting drugs are also being explored for COVID-19 therapy [13]. There are many protein domains in viruses such as spike protein and nucleocapsid protein that helps viruses to develop the capsid, replicate and attach to the host cells [20]. The intervention includes inhibition of viral spike protein attachment to host receptors or preventing viral replication and assembly could be strategies to cure COVID-19 infection [7].

The importance of traditional medicinal plants in emerging pandemics was made evident when it was effectively partnered with conventional medicine in the management of the SARS outbreak in 2003 [32]. There is a lot of evidence that viruses mainly target the body's immune system. No Food and Drug Administration (FDA) approved drugs are available to cure the COVID-19 at a time. However, some published studies on Ayurvedic and TCM

have shown that the herbs employed in these practices are useful in inhibiting viral replication, preventing entry and attachment of virus to the host cell along with boosting the immune system of a person [9]. TCM has shown encouraging results in reducing the overall death rate, the rate of mild and/or severe cases, and the overall length of the disease. Combining herbal medicine with contemporary biomedicine may have direct antiviral, immunomodulatory, and anti-inflammatory benefits in addition to alleviating hypoxemia and chronic obstructive pulmonary disease [9, 27]. Certain herbs like Ashwagandha (*Withania somnifera*), Giziewa in Amharic, has been shown in numerous studies and suggested as the effective medication in boosting immune response, and inhibiting viral replication [33].

Several studies are being conducted to screen for possible plant-based drugs that can inhibit important COVID-19 proteins. To develop a remedy for COVID-19 infection, a wide range of phytochemicals and antiviral herbs including black cumin, ginger, cloves, cardamom, garlic, turmeric, lemon and ashwagandha were examined in a recent study by Sharma and Maurya, [20]. To investigate the antiviral effect of phytochemicals at various stages of infection, the phytochemical component and bio-active compounds found in herbs were docked with several coronavirus target proteins, mainly viral capsid spike and protease. According to this study's findings, certain phytochemical substances used in traditional medicine have a high affinity for viral proteins, which makes them ideal candidates for target medication development. The other study's deployed molecular docking methods effectively screen 83 chemical structures from TCM compounds and found that theaflavin and its derivatives, which are derived from black tea, can inhibit the activity of the SARS-CoV 3CL (3-chymotrypsin-like cysteine) protease, making it a potent inhibitory compound against COVID-19 infection [19]. Traditional Chinese Medicine (TCM) has indicated a great scientific knowledge, effective and applicable inhibition and treatment of respiratory disorders in herbal formulations. The 1st patient with clinical features of COVID-19 pneumonia was recovered from the hospital on 24 January 2020 after management with TCM medicine [34, 35]. The National Health Commission (NHC) of China employed TCM in the COVID-19 treatment guidelines for their notable contributions [36]. At a press conference held on February 17, an official reported that 60,107 COVID-19 cases (85.2% of total cases at the time) were treated with TCM [8].

Similarly, Khan et al. [37] conducted a computational chemistry approach to perform a molecular docking analysis of seven SARS-CoV-2 proteins that contain eighteen active constituents that have been identified as antiviral or anti-SARS-CoV medicines in the past. Remdesivir and chloroquine, two FDA-approved medications that are used to treat COVID-19 were compared to these 18 candidate compounds. The findings showed that green tea's main ingredient, epigallocatechin gallate (EGCG), could fit well into the docked proteins of SARS-CoV-2, indicating that it is a promising therapy option against COVID-19. Epigallocatechin-3-O-gallate (EGCG) is known to inhibit a variety of DNA and RNA viruses. The plant metabolite quercetin inhibits viral entry into target cells via interaction with viral protein, and turmeric (*Curcuma longa*) are reported that contain quercetin [38]. Garlic (*Allium cepa*) contains Allicin metabolite that exhibits antiviral, antifungal, and antiparasitic activities [39].

According to Tefera Belachew [40] report on narrative review, Most of the spices including turmeric, ginger, lemon, garlic, Cinnamon, black pepper, clove, coriander, green paper, mustard, thyme, oregano, white cumin, and chilli used in Ethiopia have antiviral, antibacterial, antioxidant, anti-inflammatory and immune boosting effects. Combining spices like turmeric and black pepper enhances the bioavailability of curcumin, which is strong antiviral and antioxidant. Having balanced a healthy diet that has micro and macro nutrients, moderate physical activity, managing stress, and getting enough sleep are critical to keep immune system strong and withstand acute infections, but there is no empirical evidence on specific dietary recommendations that can reduce risk of COVID-19 and related mortality. Finally, the findings indicated that there is a scientific basis for the use of spices and herbs in preventing and fighting acute viral infections and encourage the public on the use of such spices in their normal diet. The public should also be advised to be cautious in the use of some spices and herbs in large doses especially in pregnant women. Further clinical trials should elucidate the effect of these spices on COVID-19 using direct empirical data.

Potential medicinal plants that used in the case of Covid-19

Herbal medicinal plants and their derivatives can be used for the treatment of COVID-19. The botanical detoxifiers, immune boosting remedies, natural antioxidants, plant haematinics and different spices can be used for the treatment of COVID-19 [13]. In this review, some summarized potential medicinal plants which can be used against different viruses as well as against COVID-19 due to their active constituents against to different viruses. So, some describe here medicinal plants are having antioxidants, antiviral, blood purifier, immune boosters and haematinic potentials.

Ginger (*Zingiber officinale* Rosc.)

Ginger (*Zingiber officinale* Rosc.) belongs to the family Zingiberaceae. *Zingiber officinale* is a rhizomatous, perennial, herbaceous flowering plant which originates from Southeast Asia and now extensively cultivated in most tropical and subtropical countries including African countries. All parts of the plant, especially the rhizome are used in African traditional medicine for the treatment of various conditions such as indigestion, gastric ulcerations, constipation, nausea, vomiting, arthritis, rheumatism, pains, fever, cough and cold, sore throats, lung diseases, cramps, hypertension, infectious diseases, asthma, and diabetes [41, 42]. Several studies on *Zingiber officinale* was reported as a potential inhibitor of infections from coronaviruses. *Zingiber officinale* possesses high medicinal activities such as antioxidant, anti-microbial, antiinflammatory, anti-arthritic, anti-platelet, anti-rhinoviral, cardiovascular protection, glucose lowering, and anticancer activities [43, 44]. *Zingiber officinale* was strengthening the body's defense mechanism by improving the antioxidant property will undoubtedly cure many chronic diseases and disorders.

Bioactive constituents include in the ginger are Zingiberene, Zingerone, Gingerol, Gingerdiol, Shogaol, Paradols, Curcumene [43, 45, and 46].

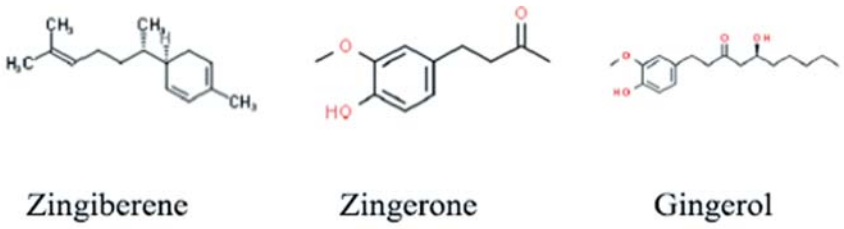

Figure 3. The structure of some bioactive compounds includes in the Nigella sativa

Shogaol obtained from *Zingiber officinale* are the important compound aids in relieving the patients from respiratory issues [47]. Prasad *et al.* [48] and Laksmiani *et al.* [49] were suggested *Zingiber officinale* as a component of a formulation for the treatment of COVID-19. The alakaloid irritant taste from ginger also aids in clearing respiratory issues, so it also help preventing from COVID-19 [14]. Gingerol and curcumene modulate immune responses against SARS-CoV-2 [4].

Turmeric (*Curcuma longa* Linn.)

Curcuma longa are from Zingiberaceae family and the common names are Turmeric. *Curcuma longa* is a rhizomatous, perennial, small flowering herbaceous plant indigenous to South Asia. Widely cultivated East and West part of Africa for it's culinary spicy and medicinal values. The rhizome is the most commonly used part in Africa for the traditional treatment of some ailments like that of headache, skin diseases, jaundice, smallpox, microbial infections, diarrhea, diabetes, arthritis, anorexia, cough, sinusitis, conjunctivitis, and diabetic wounds [50].

The medicinal activities of *Curcuma longa* has been widely found to possess anti-inflammatory, anti-ulcer, antioxidant, antidiabetic, anti-coagulant, anti-fertility, anti-neoplastic, antimicrobial, anti-viral, wound healing, cardiovascular protective, hepatoprotective, and immunostimulant activity[53, 54]. The bioactive constituents include in the *Curcuma longa* are Curcumin, Quercetin, Curcuminoids [51, 52]. Among major bioactive compounds of *Curcuma longa* extracts curcumin had the highest binding affinity to SARS-CoV-2 main protease [56]. Curcumin, the primary phytochemical of *Curcuma longa* L., is a strong antioxidant that also promotes the synthesis of interferons, which activates the host's innate immunity. It also possesses anti-SARS-CoV-2 actions and can enhance immunity [57, 58].

Several studies show that as *Curcuma longa* has a potential activity for coronavirus treatment and management. Curcumin's has a significant antiviral properties have been shown by its high affinity for binding SARS-CoV-2 proteins [59]. Wen et al. [55] and Zahedipour et al. [60] reported *Curcuma longa* as a plant with potent anti-viral activity against SARS coronaviruses, so it could be effective in the treatment of SARS CoV-2. Liu and Ying [61] employed the antioxidant and anti-inflammatory properties of curcumin to treat pneumonia in patients infected with COVID-19 infection. The plant bioactive quercetin inhibits viral entering into target cells via interaction with the viral protein [38]. The derivative curcumin has an excellent candidate for supplementary therapy in the treatment of patients with COVID-19 because of its multiple therapeutic properties [4], binding proteins of COVID-19 [62], and inhibits viral binding to ACE2 receptors and by hindering spike proteins [63, 64].

Black Cumin (*Nigella sativa* L.)

Black seed, black cumin, fennel flower are its common names; the Ranunculaceae family, Tikur azmud, and Abasuuda guaracha (Amharic and Oromic) are its local names in Ethopia. The annual flowering plant *Nigella sativa* is indigenous to North Africa, Eastern Mediterranean, Indian subcontinent, and Southwest Asia.

For over 2,000 years, seeds and oil have been widely utilized as a traditional heals to treat a variety of health conditions. In the long history "Prophet Muhammad (PBUH) mentioned the name of black cumin as a treatment for all diseases except death" [65]. It is also specified within the list of natural medication of 'Tibb-e-Nabavi', or "Medicine of the Prophet (Muhammad PBUH)" [66]. Traditionally widely used for treating asthma, cough, bronchitis, rheumatoid arthritis, diabetes, hypertension, and boosting immune system [67]. It has anti-inflammatory, anti-cancer, analgesic, antioxidant, antimicrobial, anti-parasitic, and anti-viral properties [68]. Based on several finding evidences, Black cumin is suggested strongly for combating the coronavirus disease and its remedial capabilities against autophagy dysfunction, immune disturbance, and cardiovascular disease, viral and bacterial infections [69].

Bioactive compounds include in *Nigella sativa* are Thymoquinone (TQ), Cymene, Carvacrol, Dihydrothymoquinone (DTQ), thymol [70, 46].

Thymoquinone is the primary bioactive compound obtained from black cumin seed volatile oil. It has a significant antioxidant, anti-histaminic, anti-inflammatory, anti-microbial, anticancer, and cardioprotective activities with low or no side effects [71]. Thymoquinone encourages autophagy in human body and autophagy is considered as a promising therapeutic way to the management of the coronavirus disease [72, 73]. *Nigella sativa* was found helpful against various viruses including coronavirus that are; avian influenza [74], HIV [75], Newcastle disease virus [76]. Eldeeb and Belal [77] and Rahman [78] were reported that *Nigella sativa* possesses

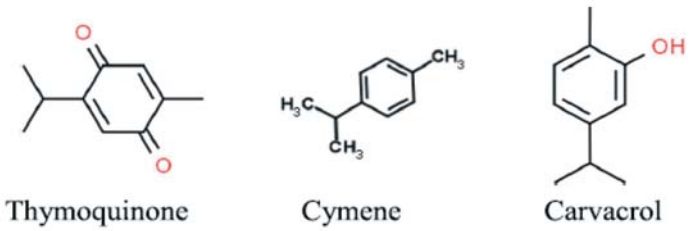

Figure 4. The structure of some bioactive compounds includes in the Nigella sativa

potential anti-coronavirus activity. The derivative DTQ has a high binding affinity targeting SARS-CoV-2 and also TQ has a high to moderate affinity target [79, 80].

Garlic (*Allium sativum* L.)

The monocotyledonous flowering plant *Allium sativum* is indigenous to central Asia. Nowadays, the plant is grown and dispersed widely worldwide. The bulb is the component of the plant that is most commonly used in traditional medicine in Africa and other nations. In the past, it was used as a treatment for respiratory diseases, bacterial infections, worm infestation, amoebic dysentery, cholera, diphtheria, tuberculosis, and influenza [81, 82]. Garlic possesses anti-diabetic, anti-inflammatory, antioxidant, hepatoprotective, cardiovascular protective, antibacterial, antifungal, antiviral, and anticancer properties [83].

The bioactive constituents that includes in the *Allium sativum* are Ajoene, Allicin, Diallyl disulfide, Vinyldithiins [84, 46]. Organo-sulfur compounds (OSG) present in garlic, including allicin, ajoene, and garlicin are shown the effective anti-viral properties [4].

Allicin is a good source of *Allium sativum* phytochemical compounds that exhibits antiviral, antifungal, and antiparasitic properties [39]. According to Keyaerts *et al.* [85], *Allium sativum* exhibits strong antiviral properties against coronaviruses. Thuy *et al.* [86] suggested as *Allium sativum* that have a valuable source of anti-SARS-CoV-2. Clinical research showed that giving individuals with moderate to severe COVID-19 symptoms 24 grams of garlic daily for three days significantly reduced the majority of their symptoms, including fever and headaches, within the second day of medication [87, 4]. Garlic (*Allium sativum* L.) can enhances immune cells system and inhibits the production and secretion of proinflammatory cytokines, and it was suggested as a beneficial preventive measure prior to SARS-CoV-2 infection [88, 58].

CONCLUSION

As epidemics or pandemics, infectious diseases such as Ebola, SARS-CoV (severe acute respiratory syndrome coronavirus), MERS-CoV (Middle East respiratory syndrome coronavirus), malaria, AIDS (acquired immunodeficiency syndrome), influenza, tuberculosis, and most recently, COVID-19 have claimed numerous lives worldwide. The world has been suffered recently as a result of the emergence of COVID-19 (SARS-CoV-2), an unexpected pandemic that has caused widespread panic and presented as one of the most difficult global public health issues. Early diagnosis and quarantining

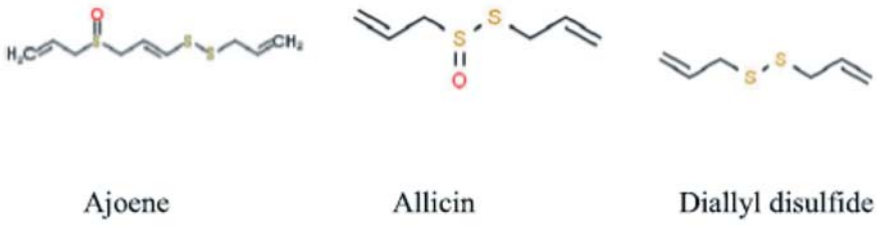

Figure 5. The structure of some bioactive compounds includes in the Allium sativum

Figure 6. The pictures of described potential herbs for the management of various diseases including Covid-19

infected individuals with supportive therapies is the minimum measure to prevent the outbreak in the absence of specific medicines that have been shown to be effective at a time. In relation to the similarity of the diseases symptoms, some treatment approaches against coronaviruses have been used globally in the previous times for fighting the SARS-CoV and MERS-CoV outbreaks. These approaches rely on medicinal plants and herbs to address the patients' primary healthcare needs in utilizing indigenous knowledge about various kinds of medicinal plants. Additionally, it is undeniable that the human body needs a strong and flexible immune system from plant source in order to protect against COVID-19.

In this review, the highlighted potential medicinal plants have a wide range of derivatives that can be used to treat COVID-19 by improving the host immune responses, reducing the virus replication and having antiviral properties that inhibits further infection. They can also have the pharmacological potential. Because of the natural derivatives' high quality, low cost, and fewer or no side effects than synthetic medications, medicinal plants can open up the paths for drug development to combat pandemics like COVID-19. Furthermore, investigation is necessary to determine the safety, efficacy, and identifying potential lead medicine plant candidates are important before making any extrapolated claims. In-depth studies and experiments have been suggested to determine the role of medicinal plants in preventing a pandemic. Moreover, the use of medicinal plants for specific variant of COVID-19 has to be investigated.

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