

ACCLAIMED MEDICINAL PLANTS USED FOR THE PREVENTION AND TREATMENT OF CORONAVIRUS DISEASE 2019: CONCERNS ON SAFETY LEVELS

RITA MANEJU SUNDAY*

Department of Medical Biotechnology, National Biotechnology Development Agency, Lugbe, Abuja, Nigeria. Email: reetersun@gmail.com

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ABSTRACT

Medicinal plants are being used all over the world for the prevention, treatment, and management of diseases. Most consumers assume that medicinal plants have no toxic effect because they are plant natural products. Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 which originated from Wuhan in China, is a current pandemic that is spreading globally. This disease has led to mortality of humans all over the world. There are reports from research that plants with antiviral, antioxidant, anti-inflammatory, or immunostimulatory activity might help in the treatment and prevention of this disease; and these have led to the increase in intake of medicinal plants with these activities all over the world. However, preclinical and clinical studies have not been carried out on some of these plants to confirm their use in prevention and treatment of COVID-19. Furthermore, the actual dose of some of these plant products for the prevention of the disease is unknown. This review discusses the use of medicinal plants including turmeric, garlic, and ginger for the treatment and prevention of COVID-19 and their possible toxic effects. In conclusion, medicinal plants should be taken in moderation in order to prevent adverse effects which include inflammation, nausea, vomiting, fever, and mortality.

Keywords: Severe acute respiratory syndrome coronavirus 2, Ginger, Garlic, Turmeric, Immunostimulators.

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INTRODUCTION

Traditional systems of medicine have become a topic of global importance. The World Health Organization (WHO) reported that 80% of the world population use herbal medicine for their primary health care [1]. Although orthodox may be available in many developing and developed countries, people are still turning to traditional medicine practices that has to do with use of medicinal plants as herbs for the treatment of diseases [2]. This is due to the belief that medicinal plants have little or no side effects [3,4]. Plants with therapeutic effect have been used from ancient times for the treatment of diseases [5]. There are reports from the previous studies showing that medicinal plants have therapeutic properties which include anti-oxidant, anti-viral, anti-cancer, and anti-inflammatory effects [6-10]. Medicinal plants exert these effects due to the presence of bioactive compounds which include gingerol, quercetin, and curcumin [11-13]. Emphasis has been placed on the use of medicinal plants for the treatment of diseases rather than prevention. However, there are reports from literature that medicinal plants can also be used for the prevention of diseases [6,7].

The novel coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [14] which is a member of beta coronavirus family [15]. The outbreak of this virus occurred in December, 2019 in Wuhan, China [16]. This led to the rapid spread of COVID-19 into a pandemic that is responsible for the recent health crisis globally [17]. SARS-CoV-2 is the seventh known virus of the *Coronaviridae* family that infects humans [18]. As at April 10, 2021, there have been 135,568,565 confirmed cases of COVID-19 and 2,932,845 deaths worldwide as reported by the WHO [11]. The United States of America has the highest number of COVID-19 cases (31,805,293 cases), followed by Brazil (13,375,414 cases) and India (13,261,376 cases) [19]. This disease spread fast by close contact with infected individuals through respiratory droplets from either coughing or sneezing [20]. COVID-19 exerts various symptoms which range from mild to severe among infected patients. The frequent manifestations of the disease reported by patients include fever (98%), cough (76%), fatigue (44%), sputum production (28%), and headache (8%) [21]. COVID-19 symptoms might also be accompanied by nasal

congestion, runny nose, diarrhea, or sore throat. Fatal cases have also been reported by patients experiencing progressive respiratory failure due to SARS-CoV-2 attacking the alveolar epithelial cells [22,23]. This damage is caused by the receptor-binding domain attachment of the virus to the receptor on the respiratory tract in humans known as the angiotensin-converting enzyme-2 receptor [22] and transmembrane protease, serine 2 [23]. COVID-19 disease causes mortality in some cases due to acute respiratory distress syndrome and severe cytokine release syndrome [24]. The release of numerous pro-inflammatory cytokines in the blood is also responsible for the clinical appearance of inflammation in humans [21].

Researchers are trying to find a medicine for the treatment and prevention of COVID-19 because up to date there is no specific drug for the cure of the disease. There are reports that the immune status of patients plays an important role in COVID-19 infection [25]. Thus, studies are carried out on medicinal plants with immunostimulatory activities. There are reports from the literature that some plants with anti-viral effect also have the ability to boost the immune system [26]. Furthermore, there is a recent increase in the consumption of medicinal plants that have anti-viral, immunostimulatory, and anti-inflammatory effects by humans because of believe that plants with these activities have the ability to prevent or cure COVID-19 [11].

There is this believe by consumers that medicinal plants have no toxic effect or adverse effects because they are natural products. There are concerns regarding the use of medicinal plants and their ability to cause adverse effects which include nausea, vomiting, body itching, skin irritation, fever, and in severe cases death [27,28]. The WHO encourages the use of medicinal plants as supplements for health-care provided they are confirmed to be nontoxic [29]. Most medicinal plants consumers are ignorant of factors which include dosage and drug interactions that might lead to toxicity after intake of plants with medicinal activities [27,30].

This review highlights medicinal plants with immunostimulatory activity used for the prevention and treatment of COVID-19. The factors that might make medicinal plants to exert a toxic effect are also mentioned.

ACCLAIMED MEDICINAL PLANTS USED FOR THE PREVENTION AND TREATMENT OF COVID-19

Curcuma longa (turmeric)

It is a medicinal plant that belongs to the *Zingiberaceae* family and the genus *Curcuma* [31]. The rhizomes of *C. longa* are mostly used as spice, food flavor, and natural food coloring [32]. The plant is cultivated in all parts of the world. Turmeric is also used traditionally as food supplement and medicine [33]. There are reports from studies that turmeric has antioxidant, anti-inflammatory, antiviral, anticancer, and immunostimulatory activities [34]. *C. longa* is used as medicine for the treatment of diseases which include neurodegenerative diseases, diabetes, cardiovascular disease, asthma, inflammatory bowel disease, and high blood pressure [33,35]. Turmeric exerts these effects due to the presence of a bioactive compound known as curcumin [11]. Consuming high doses of turmeric over long period of time may cause stomach upset, skin rash, diarrhea, headache, and it might trigger miscarriage in women [36,37].

Allium sativum (garlic)

A. sativum commonly known as garlic belongs to the family Liliaceae and the genus *Allium*. The part of the plant used as spice and for medicinal purpose is the bulb. *A. sativum* is found all over the world. Studies have reported that garlic have anti-inflammatory, antioxidant, anti-fungal, antiviral, hypoglycemic, and immunostimulatory activities [38,39]. Garlic has also been used as spice in food and also in traditional medicine for the treatment of cough, cold, diabetes, hypertension, and asthma [38]. Allicin; a sulfur containing bioactive compound present in garlic is mainly responsible for the medicinal properties of garlic [40]. High doses of garlic have the ability to cause nausea, vomiting, diarrhea, and liver damage [41].

Zingiber officinale (GINGER)

The medicinal plant ginger with the botanical name *Z. officinale* also belongs to the family *Zingiberaceae*, genus *Zingiber*, and species *officinale*. The part of the plant used for medicinal purpose is the rhizome. Ginger is also found in all parts of the world. There are reports that ginger has antioxidant, anti-inflammatory, antiviral, immunostimulatory, and analgesic activities [42-44]. Ginger is used as food additive and for the treatment and prevention of diseases which include cancer, diabetes, cardiovascular diseases, asthma, cough, and inflammations due to the presence of a bioactive compound known as gingerol [13,45-48]. Ginger is generally considered to be safe [49]. However, the lack of complete understanding of its mechanism of action suggests caution when using it for therapeutic purpose [50]. More so, caution when taking ginger and other medicinal products needs to be taken because of apparent association of ginger with reported cases of increased risk of bleeding during surgery [51,52] or when taken with anticoagulant drugs such as warfarin [53].

Cuminum cyminum (cumin seed)

C. cyminum commonly known as cumin belongs to the family *Apiaceae* and the genus *Cuminum*. The seed of the plant is used as food additives/spice and for medicinal purpose. Cumin is cultivated in India, China, Middle East, and Mediterranean countries [54]. *C. cyminum* is reported to have antimicrobial [55], antidiabetic [56], anticancer [57], antioxidant [58], analgesic, anti-inflammatory [59], anti-hypertensive [60], and immunostimulatory [61] effects. In traditional medicine, cumin seeds are used for the treatment of diarrhea, headache, and stomach ache [62]. The bioactive compounds present in cumin are flavonoids, terpenes, and phenols [63]. These compounds provide the wide range of therapeutic benefits. Side effects of *C. cyminum* have not reported.

Allium cepa (onions)

A. cepa commonly known as onion is a vegetable crop that belongs to the family Liliaceae and genus *Allium* [64]. However, in recent taxonomic schemes, the *A. cepa* belongs to the family *Amaryllidaceae* [65]. It is grown in all parts of the world. The bulb is the part of the plant used for

medicinal purpose and it is mostly included in food preparations. Onion has been reported to have several medicinal properties which include antioxidant, anti-inflammatory, antiviral, antifungal, and antiparasitic effects [66,67]. Bioactive compounds such as quercetin, myricetin, isorhamnetin, and kaempferol present in onion are reported to be responsible for the antiviral activity [68]. There are reports that onion is used for the treatment of diabetes, hypertension, and cardiovascular diseases [69-71]. Health risk of onions has not been reported.

CONCLUSION

Medicinal plants have great potential to be used for the treatment and prevention of COVID-19; however, there is a need for pre-clinical and clinical investigations of promising medicinal plants for their safety and efficacy.

REFERENCES

- Davidson-Hunt I. Ecological ethnobotany: Stumbling toward new practices and paradigms. *MASAJ* 2000;16:1-13.
- Maqbool M, Dar MA, Gani I, Mir SA, Khan M. Herbal Medicines as an alternative source of therapy: A review. *World J Pharm Pharm Sci* 2019;8:374-80.
- Philomena G. Concerns regarding the safety and toxicity of medicinal plants an overview. *J Appl Pharm Sci* 2011;1:40-4.
- Raghavendra HL, Kekuda TR. Ethnobotanical uses, phytochemistry and pharmacological activities of *Peperomia pellucid* (L.) Kunth (Piperaceae) a review. *Int J Pharm Pharm Sci* 2018;10:1-7.
- Newman DJ, Cragg GM. Natural products as sources of new drugs over the last 25 years. *J Nat Prod* 2007;70:461-77.
- Cai YZ, Luo Q, Sun M, Corker H. Antioxidant activity and phenolic compounds of 112 traditional Chinese medicinal plants associated with anticancer. *Life Sci* 2004;74:2157-84.
- Sen A. Acute rheumatic cardiac associated with Schoenlein-Henoch vasculitis. *Anadolu Kardiol Derg* 2012;10:465-6.
- Paul R, Prasad M, Sah NK. Anticancer biology of *Azadirachta indica* L (Neem): A mini review. *Cancer Biol Ther* 2011;12:467-76.
- Liu HY, Qui NX, Ding HH, Yao RQ. Polyphenols content and antioxidant capacity of 68 Chinese herbals suitable for medical or food uses. *Food Res Intern* 2008;41:363-70.
- Webster D, Taschereau P, Lee TD, Jurgens T. Immunostimulant properties of *Heracleum maximum*. *Bartr. J. Ethnopharmacol* 2006;106:360-3.
- Kocaadam B, Sanlie N. Curcumin, an active component of turmeric (*Curcuma longa*), and its effects on health. *Crit Rev Food Sci Nutr* 2017;57:2889-95.
- Nuutila AM, Puupponen-Pimiä R, Aarni M, Oksman-Caldentey KM. Comparison of antioxidant activities of onion and garlic extracts by inhibition of lipid peroxidation and radical scavenging activity. *Food Chem* 2003;81:485-93.
- Jolad SD, Lantz RC, Chen GJ, Bates RB, Timmermann BN. Commercially processed dry ginger (*Zingiber officinale*): Composition and effects on LPS-stimulated PGE2 production. *Phytochemistry* 2005;66:1614-35.
- Murugan S, Prathiba S, Abhaya M, Fujita AA. COVID-19: An update on the epidemiological status of South India. *Int J Pharm Pharm Sci* 2020;12:15-8.
- Walls AC, Park YJ, Tortorici MA, Wall A, McGuire AT, Veesler D. Structure, function and antigenicity of the sars-cov-2 spike glycoprotein. *Cell* 2020;181:281-92.e6.
- Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak of global health concern. *Lancet* 2020;395:470-3.
- Bedford J, Enria D, Giesecke J, Heymann DL, Ihekweazu C, Kobinger G, *et al.* For the WHO strategic and technical advisory group for infectious hazards. COVID-19: Towards controlling of a pandemic. *Lancet* 2020;395:1015-8.
- Cheepsattayakorn A, Cheepsattayakorn R. Proximal origin and phylogenetic analysis of COVID-19 (2019-nCoV or SARS-CoV-2). *EC Microbiology* 2020;19:9-12.
- World Health Organization. Available from: <https://www.covid.who.int>. [Last accessed on 2021 April 10].
- Adhikari SP, Meng S, Wu Y, Mao YP, Ye RX, Wang QZ, *et al.* Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: As coping review. *Infect Dis Poverty* 2020;9:1-12.
- Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, *et al.* Clinical features of

- patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395:497-506.
22. Ren Y, Shang J, Graham R, Baric RS, Li F. Receptor recognition by the novel coronavirus from Wuhan: An analysis based on decade-long structural studies of SARS coronavirus. *J Virol* 2020;94:1-9.
 23. Hoffmann M, Kleine-Weber H, Schroeder S, Kruger N, Herrler T, Erichsen S, *et al.* SARS-CoV-2 cell entry depend on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell* 2020;181:271-80.e8.
 24. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ, *et al.* COVID-19: Consider cytokine storm syndromes and immunosuppression. *Lancet* 2020;395:1033-4.
 25. Zhang L, Liu Y. Potential interventions for novel corona virus in China: A systematic review. *J Med Virol* 2020;92:479-90.
 26. Barak V, Halperin T, Kalickman I. The effect of Sambucol, a black elderberry-based, natural product, on the production of human cytokines: I. Inflammatory cytokines. *Eur. Cytokine Netw* 2001;12:290-6.
 27. Pawar HA, Pawar S, Pawar PA. A review on benefits and toxicities of some popular herbs. *Int J Res Ayurveda Pharm* 2011;2:1068-72.
 28. Sunday RM, Ilesanmi OR, Obuotor EM. Acute and sub-chronic oral toxicity of *Anthocleista vogelii* (Cabbage tree) root hydroethanolic extract in Albino rats. *Br J Pharm Res* 2016;12:1-9.
 29. World Health Organization. The WHO traditional medicine programme: Policy and implementation. *Int Tradit Med Newsl* 1985;1:1-5.
 30. Engdal S, Klepp O, Nilsen OG. Identification and exploration of herb-drug combinations used by cancer patients. *Integr Cancer Ther* 2009;8:29-36.
 31. Hewlings S, Kalman D. Curcumin: A review of its' effects on human health. *Foods* 2017;6:1-11.
 32. Nwaekpe JO, Anyaegbunam HN, Okoye BC, Asumugha GN. Promotion of turmeric for the food/pharmaceutical industry in Nigeria. *Am J Exp Agric* 2015;8:335-41.
 33. Lekshmi PC, Arimboor R, Nisha VM, Menon AN, Raghu KG. *In vitro* antidiabetic and inhibitory potential of turmeric (*Curcuma longa* L) rhizome against cellular and LDL oxidation and angiotensin converting enzyme. *J Food Sci Technol* 2014;51:3910-7.
 34. Dony CM, Wei-Li H. Antiviral potential of curcumin. *J Funct Foods* 2018;40:692-9.
 35. Araujo CC, Leon LL. Biological activities of *Curcuma longa* L. *Mem Inst Oswaldo Cruz* 2001;96:723-8.
 36. Christopher D, Lao TR, Mack N, Daniel DH, Sandra IM, *et al.* Dose escalation of a curcuminoid formulation. *BMC Complement Altern Med* 2006;6:10.
 37. Chauhan PS, Satti NK, Suri KA, Amina M, Bani S. Stimulatory effects of *Cuminum cyminum* and flavonoid glycoside on cyclosporine-A and restraint stress induced immune-suppression in Swiss Albino mice. *Chem Biol Interact* 2010;185:66-72.
 38. Gaber EB, Beshbishy AM, Lamiaa GW, Yaser HA, Ahmed AA, Mohamed EA, *et al.* Chemical constituents and pharmacological activities of garlic (*Allium sativum* L.): A review. *Nutrients* 2020;12:872.
 39. Mehrbod P, Amini E, Tavassoti-Kheiri M. Antiviral activity of garlic extract on Influenza virus. *Iran J Virol* 2009;2:8-15.
 40. Ikpa CBC, Tochukwu OD, Christian EE, Ikezu UJ. Potential plants for treatment and management of COVID-19. *Acad J Chem* 2020;5:2521.
 41. Rana SV, Pal R, Vaiphei K, Singh K. Garlic hepatotoxicity: Safe dose of garlic. *Trop Gastroenterol* 2006;27:26-30.
 42. Ahmad N, Katiyar SK, Mukhtar H. Antioxidants in chemoprevention of skin cancer. *Curr Probl Dermatol* 2001;29:128-39.
 43. Young HY, Luo YL, Cheng HY, Hsieh WC, Liao JC, Peng WH. Analgesic and anti-inflammatory activities of [6]-gingerol. *J Ethnopharmacol* 2005;96:207-10.
 44. Jung SC, Kuo CW, Chia FY, Den ES, Lien CC. Fresh ginger (*Zingiber officinale*) has anti-viral activity against human respiratory syncytial virus in human respiratory tract celllines. *J Ethnopharmacol* 2013;145:146-51.
 45. Islam MS, Choi H. Comparative effects of dietary ginger (*Zingiber officinale*) and garlic (*Allium sativum*) investigated in a Type 2 diabetes model of rats. *J Med Food* 2008;11:152-9.
 46. Nicoll R, Henein MY. Ginger (*Zingiber officinale* Roscoe): A hot remedy for cardiovascular disease? *Int J Cardiol* 2009;131:408-9.
 47. Aggarwal BB, Kunnumakkara AB, Harikumar KB, Tharakan ST, Sung B, Anand P. Potential of spice-derived phytochemicals for cancer prevention. *Plant Med* 2008;74:1560-9.
 48. Thirumalaisamy R, Murugan P, Srinivasan P, Arjunan S, Selvankumar T. Phytochemical 6-gingerol a promising drug of choice for COVID. *Int J Adv Sci Eng* 2020;6:1482-9.
 49. Kaul PN, Joshi BS. Alternative medicine: Herbal drugs and their critical appraisal-part II. *Prog Drug Res* 2001;57:1-75.
 50. Wilkinson JM. Effect of ginger tea on the fetal development of Sprague-Dawley rats. *Reprod Toxicol* 2000;14:507-12.
 51. Chang LK, Whitaker DC. The impact of herbal medicines on dermatologic surgery. *Dermatol Surg* 2001;27:759-63.
 52. Pribitkin ED, Boger G. Herbal therapy: What every facial plastic surgeon must know. *Arch Facial Plast Surg* 2001;3:127-32.
 53. Heck AM, De Witt BA, Lukes AL. Potential interactions between alternative therapies and warfarin. *Am J Health Syst Pharm* 2000;57:1221-7.
 54. Shivakumar SI, Shahapurkar AA, Kalmath KV, Shivakumar B. Antiinflammatory activity of fruits of *Cuminum cyminum* Linn. *Pharm Lett* 2010;2:22-4.
 55. Bameri Z, Amini-Boroujeni N, Saeidi S, Bazi S. Antimicrobial activity of *Cuminum cyminum* against biofilm *E. coli*. *Int Res J Appl Basic Sci* 2013;5:1232-4.
 56. Willatgamuva SA, Platel K, Sarawathi G, Srinivasan K. Antidiabetic influence of dietary cumin seeds (*Cuminum cyminum*) in streptozotocin induced diabetic rats. *Nutr Res* 1998;18:131-42.
 57. Allahghadri T, Rasooli I, Owlia P, Nadooshan MJ, Ghazanfari T, Taghizadeh M, *et al.* Antimicrobial property, antioxidant capacity, and cytotoxicity of essential oil from cumin produced in Iran. *J Food Sci* 2010;75:H54-61.
 58. Vallverdú-Queralt A, Regueiro J, Martínez-Huélamo M, Alvarenga JF, Leal LN, Lamuela-Raventos RM. A comprehensive study on the phenolic profile of widely used culinary herbs and spices: Rosemary, thyme, oregano, cinnamon, cumin and bay. *Food Chem* 2014;154:299-307.
 59. Bhat SP, Rizvi W, Kumar A. Effect of *Cuminum cyminum* L seed extracts on pain and inflammation. *J Nat Remedies* 2014;14:186-92.
 60. Kalaivani P, Saranya RB, Ramakrishnan G, Ranju V, Sathya S, Gayathri V, *et al.* *Cuminum cyminum*, a dietary spice, attenuates hypertension via endothelial nitric oxide synthase and NO pathway in renovascular hypertensive rats. *Clin Exp Hypertens* 2013;35:534-42.
 61. Boskabadhy MH, Kiani S, Azizi H. Relaxant effect of *Cuminum cyminum* on guinea pig tracheal chains and its possible mechanism(s). *Indian J Pharmacol* 2005;37:111-5.
 62. Parthasarathy VA, Chempakam B, Zachariah TJ. Chemistry of spices. *CAB Int* 2008;2008:211226.
 63. Rai N, Yadav S, Verma AK, Tiwari L, Sharma RK. A monographic profile on quality specifications for a herbal drug and spice of commerce *Cuminum cyminum* L. *Int J Adv Herb Sci Technol* 2012;1:1-12.
 64. Breu W. *Allium cepa* L. (onion) Part 1: Chemistry and analysis. *Phytomedicine* 1996;3:293-306.
 65. Yoshinari O, Shiojima Y, Igarashi K. Angiosperm phylogeny group an update of the angiosperm phylogeny group classification for the orders and families of flowering plants: APG III. *Bot J Linn Soc* 2009;161:105-21.
 66. Prakash D, Singh BN, Upadhyay G. Antioxidant and free radical scavenging activities of phenols from onion (*Allium cepa*) *Food Chem* 2007;102:1389-93.
 67. Saba A, Zolfaghar R, Mehdi VM. Evaluation of the antiviral effects of aqueous extracts of red and yellow onions (*Allium cepa*) against avian influenza virus subtype H9N2. *Iran J Vet Sci Technol* 2018;2:1-11.
 68. Neha S. Efficacy of Garlic and Onion against virus. *J Res Pharm Sci* 2019;10:3578-86.
 69. Kender BS. Garlic (*Allium sativum*) and onion (*Allium cepa*): A review of their relationship to cardiovascular disease. *Prev Med* 1987;16:670-85.
 70. Akash MS, Rehman K, Chen S. Spice plant *Allium cepa*: Dietary supplement for treatment of Type 2 diabetes mellitus. *Nutrition* 2014;30:1128-37.
 71. Brüll V, Burak C, Stoffel-Wagner B, Wolfram S, Nickenig G, Müller C, *et al.* Effects of a quercetin-rich onion skin extract on 24 h ambulatory blood pressure and endothelial function in overweight-to-obese patients with (pre-) hypertension: A randomised double-blind placebo-controlled cross-over trial. *Br J Nutr* 2015;114:1263-77.