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Chapter

The Therapeutic and Phytopharmacological Potential of Ginger (*Zingiber officinale*)

Madonna Ngwatshipane Mashabela and Wilfred Otang-Mbeng

Abstract

Ginger (*Zingiber officinale*), a Zingiberaceae family member, is a popular spice all around the world. This perennial creeping plant has long leaves, vivid green flowers, and a strong tuberous rhizome. Throughout history, several cultures and civilizations have recognized the potential of ginger in the treatment and prevention of disease. Various research with ginger and its extract support the potential effect in a variety of applications. Ginger has been used medicinally for over 2000 years and is regarded as one of the most versatile medicinal herbs, with a wide range of biological properties. Since ancient times, ginger has been used to cure a variety of conditions including heart problems, menstrual disorders, food poisoning, osteoarthritis, epilepsy, nausea, inflammation, cough and cold, motion sickness, menstrual cramps, cancer, and many others. Apart from that, it has antibacterial and antioxidant properties. The presence of gingerol and paradol, as well as shogaols and other chemicals, is responsible for ginger's medicinal properties. The medical benefits of ginger and current knowledge provide a solid platform for future research into how it can protect humans from a number of diseases.

Keywords: medicinal uses, gingerol, COVID-19, antioxidants, nausea

1. Introduction

Medicinal plants are the “backbone” of traditional medicine, which means people in the less developed countries utilize medicinal plants on a regular basis. These medicinal plants are thought to be a rich source of components for medication discovery and synthesis. Furthermore, these plants are important in the evolution of human cultures all around the world. Plants have formed the foundations of conventional traditional medical systems for thousands of years. Plants will continue to provide us with new remedies. Some of the beneficial benefits attributed to plants have been proven to be false, and medical plant therapy is based on hundreds to thousands of years of experimental research [1]. Many cultures around the world rely on traditional medicine since it is conveniently accessible from a local plant. According to a WHO (World Health Organization) estimate, the medicinal plant is used by over 3.5 billion people in underdeveloped nations for health care [2–4]. Traditional

medicine is still prescribed by African doctors, i.e. (70–80%). Traditional medicine is used to treat human and livestock ailments in almost every part of the world [5]. A lot of attention has been paid to various areas of ginger's activities in reviews. For example, Grzanna et al. [6] focused on the use of ginger as an anti-inflammatory agent, whereas Shukla and Singh [7] focused on the cancer prevention properties of the crude drug. Chaiyakunapruk et al. [8] published a review on the effects of ginger as a post-operative anti-emetic drug. As a result, the goal of this chapter was to present an overview of the medicinal and phytopharmacological potential of ginger (*Zingiber officinale*).

2. Description of ginger

Z. officinale belongs to the Zingiberaceae plant family, which includes 1300 species and 49 genera, with 80–90 Zingiber species. It is native to East and Southern Asia. Its common name, Zingiber, derives from the Greek word zingiberis from the Sanskrit word singabera, which means “spice.” The Latin word, Zingiber, means “horn-shaped,” and refers to the roots' antler-like appearance. Ginger is a weedy perennial herbaceous plant that grows to a height of 2 meters and thrives in humid environment [9]. Some of the names given to ginger are Zenzero in Italian, Jeung or Sang Keong in Chinese, Aliah in Indonesia, Adrack in Urdu, Gember in Dutch, Jengibre in Spanish, Ingwar in German, and Gingembre in French [10]. Ginger was one of the first eastern spices introduced to Europe, and it is still in high demand today [10]. Zingiberaceae species typically have thickened rhizomes with secretory cells producing essential oil [11].

Ginger is traded in three basic forms - green (fresh), pickled or preserved and dry. Only dry ginger (whole, peeled, or sliced) is considered a spice; green or fresh ginger is primarily used as a vegetable, while pickled or preserved ginger is primarily used in the Chinese and Japanese culinary industries. In addition, ginger oil and oleoresins are also available for purchase. Despite the fact that ginger is grown in many countries, India and China are the top two exporters of dry ginger, followed by Nigeria, Sierra Leone, Australia, Fiji, Bangladesh, Jamaica, Nepal and Indonesia.

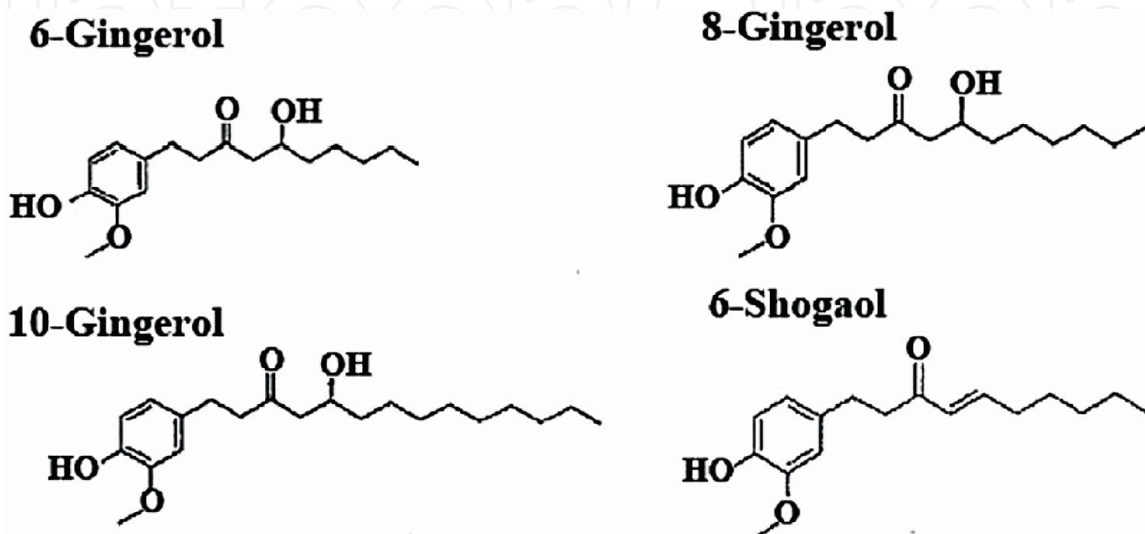


Figure 1. Structure of 8-gingerol, 6-gingerol, 6-shogaol and 10-gingerol [14].

2.1 Ginger's active ingredients

Ginger has over 60 constituents, all of which are considered active compounds [12]. Alantolacton, inulin and certain essential oils are key components found in this plant root [12]. The powdered rhizome is made up of 9% protein, 3–8% crude fiber, 3–6% fatty oil, 60–70% carbohydrates, 9–12% water, roughly 8% ash and 2–3% volatile oil [13]. Gingerols, Ingenol, gingerdiols, zingerone, paradols, and shogaol are just a few of the therapeutic substances found in ginger. Gingerols are the most important of these chemicals because of their active pharmacological characteristics. Gingerols and shogaol are chemically composed of 6-, 8- and 10-structural analogs (**Figure 1**) [15].

3. Discussion

3.1 Therapeutic and Phytopharmacological potential of ginger

The most important therapeutic properties of *Z. officinale* (ginger) are given below:

3.1.1 Evidence of ginger's anti-COVID-19 properties

SARS-CoV-2-related papain-like protease (PLpro) cleaves polyprotein a/b (PP a/b) at different sites yielding several proteins needing for viral survival and replication (**Figure 2**) [17]. SARS-CoV-2-related PLpro also interferes with type I IFN anti-virus response [17]. In order to successfully suppress virus multiplication and survival, anti-SARS-CoV-2 medications should target PLpro. [18]. According to the findings of a study conducted in Saudi Arabia, COVID-19 patients' consumption of ginger increased from 36.2% prior to infection to 57.6% after infection. The proportion of patients admitted to the hospital for COVID 19 treatment was also lower (28.0%) among ginger users than among nonusers (38.0%) [19]. A few examples of cured COVID-19 patients were recorded in a Bangladesh study, who drank home medicines using ginger in blends of various herbs with or without further treatments [20]. A few cases of COVID-19 were treated with home remedies including ginger in combination with other herbs improved disease symptoms, according to the findings of a Tunisian study [21]. In certain African countries, renowned treatments involving ginger in combinations with other herbs were also utilized to treat COVID-19 [22]. In compared to those treated with a normal protocol using hydroxy-chloroquine alone, the results of an Iranian clinical trial study show that combining outpatients with probable COVID-19, ginger and Echinacea alleviated some of their clinical symptoms (breath shortness, coughing, and muscular discomfort) [23]. Ginger may help patients with pulmonary problems such ARDS (Acute respiratory distress syndrome), fibrosis, lung and pneumonia, as well as sepsis, which are all indications seen in COVID-19. Overall, the evidence suggests that more high-quality controlled trials are needed to validate ginger's benefit and safety in COVID-19 patients. In Iran, a clinical investigation is underway in which 84 COVID-19 patients were randomly assigned to two groups, each with 42 participants, including intervention and control groups [24]. The intervention group will receive standard treatment plus 1000 mg ginger three times daily for seven days, whereas the control group will receive normal treatment plus placebo tablets at the same dose and schedule for seven days [16].

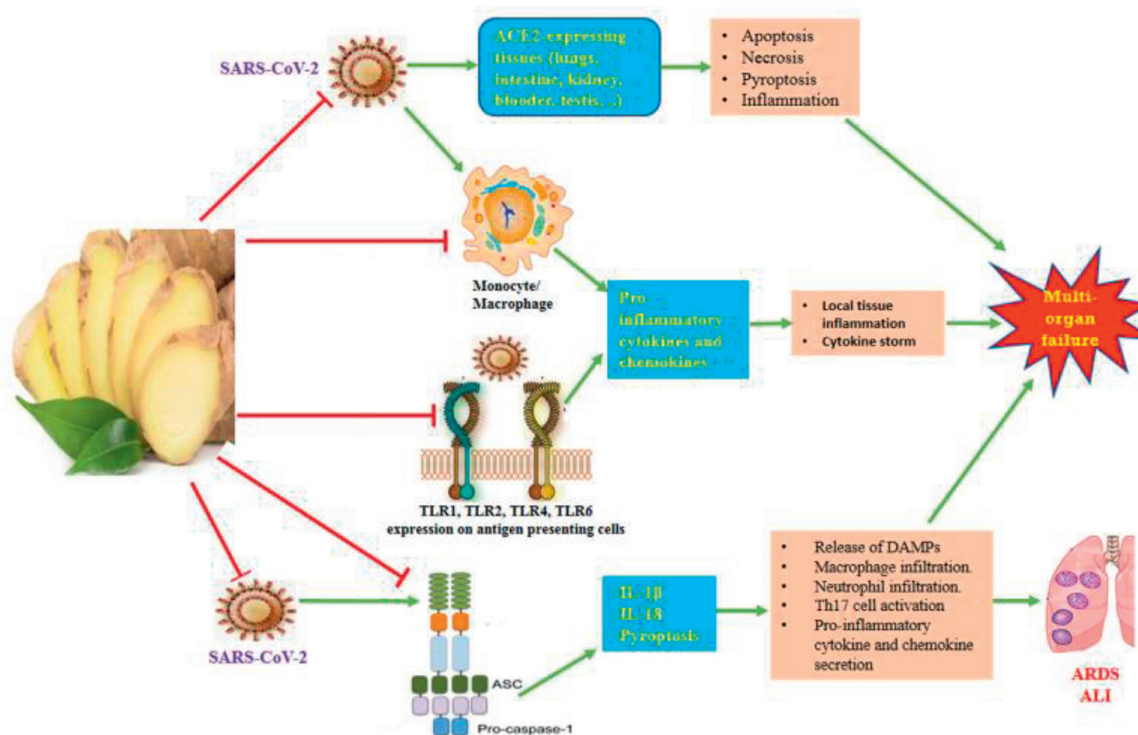


Figure 2.

COVID-19 pathogenesis is influenced by SARS-CoV-2 and inflammation. SARS-CoV-2 infects tissues that express ACE2, causing necrosis, pyroptosis and apoptosis, as well as inflammation. Infected macrophages with SARS-CoV-2 release a variety of cytokines and chemokines, causing tissue inflammation and a cytokine storm. TLRs and inflammasomes can be activated by SARS-CoV-2, resulting in an increase in inflammatory responses and tissue damage. Ginger can enhance antiviral immune responses and have direct anti-SARS-CoV-2 effects, as well as interfere with inflammatory responses mediated by macrophages, TLRs, and inflammasomes. Abbreviations: ALI: Acute lung injury; ACE2: Angiotensin-converting enzyme 2; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; ARDS: Acute respiratory distress syndrome; TLR: Toll-like receptor; IL: Interleukin [16].

4. Medicinal uses and potential health benefits in traditional medicine

Ginger has direct antimicrobial properties and can thus be used to treat bacterial infections [25]. It is used as a stimulant in Traditional Chinese Medicine to treat colic and atonic dyspepsia [26–28]. Ginger is a Yang plant that might help to reduce Yin and nourish the body [29]. Ginger is described as spicy and hot in Traditional Chinese Medicine, and it is said to treat cold extremities and warm up the body, enhance a slow and erratic heartbeat, a pale appearance on skin, and strengthen the body after blood loss [30]. Ginger is used as a herbal treatment for a variety of cardiovascular conditions [31]. Other researchers emphasized that ginger is used to treat inflammation, nausea, headaches, arthritis, muscular discomfort, rheumatism, and colds in Ayurvedic, Chinese, Arabic, and African traditional remedies (Figure 3) [32, 33]. The rhizomes of ginger have recently been utilized in Traditional Medicine to treat a variety of cardiovascular disorders, including hypertension [34]. Ginger has been used as an anti-edema drug in Iranian Traditional Medicine as a therapy for a variety of diseases, such as athero-sclerosis, gastric ulcer, respiratory disorders, gastrointestinal disorders, migraine, cholesterol; depression and nausea, other benefits of ginger include pain relief, anti-inflammatory, rheumatoid arthritis and antioxidant effects [35]. This is one of India's most popular spices, and it has long been used in traditional oriental medicine to treat common colds, stomach problems, and rheumatism [36]. The primary components of ginger include 10-gingerol, 8-gingerol, 6-shogaol, and

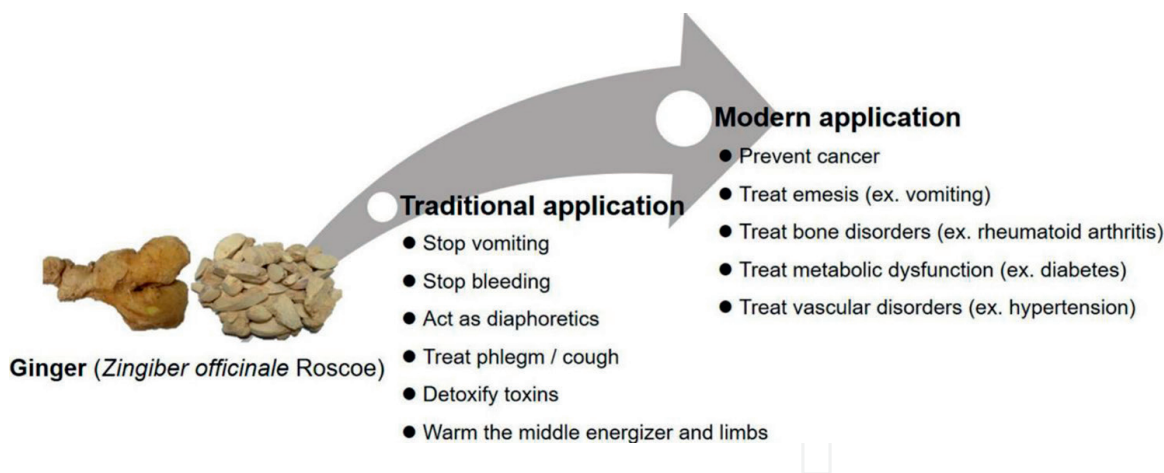


Figure 3.
 Traditional and modern pharmacological applications of ginger. In both traditional and modern medicine, ginger has been used to treat a variety of symptoms and disorders [32].

Phenols	Volatile Sesquiterpenes	Others
Shogaols and Gingerols	Sesquiphellandrene, Bisapolene, Zingiberene, Zingiberol, Curcurnene	Zingerone, 6-dehydrogingerdione, Galanolactone, Gingesulfonic acid, Neral, Geraniol, Gingerglycolipids, Monoacyldigalactosylglycerols,

Table 1.
 Ginger's active chemical components [41].

6-gingerol, all of which have been demonstrated to have significant antioxidant activity [37]. Ginger's most prevalent bioactive ingredient, 6-gingerol, has a wide range of pharmacological actions, including antipyretic activities, antioxidant, anti-inflammatory and analgesic [38, 39]. After being digested and absorbed by the digestive system, shogaols can be partially changed to paradols by cooking or metabolized to paradols in the animals' bodies [40]. Anti-inflammatory and antioxidant activities are known to exist in Shogaol and Gingerol in particular (**Table 1**) (**Figure 1**) [42].

5. Medicinal uses and potential health benefits in modern medicine industry

As a powerful anti-oxidant, ginger extract can treat illnesses induced by oxidative stress. Extant anthocyanins and phenolic compounds, such as sugevals and gingerols, have been shown to have neuroprotective qualities, such as memory enhancement, analgesic effects, and learning induced by aging [43]. Ginger can be used in a variety of dishes, both sweet and savory, including drinks, puddings, apple pie, cakes, breads, sweets, and sauces, soups, savory puddings, grills, roasts, stews, and more [44]. Furthermore, heat had no influence on the active hypoglycaemic component of ginger, as a result, ginger consumption in both cooked and raw forms in a variety of cuisines could be an effective diabetes management strategy. Ginger contains anti nausea, antimicrobial, cardio tonic, antiemetic, antipyretic, anti-hypertensive,

analgesic, anti ulcer, hypoglycaemic, anti-inflammatory, and anti-platelet aggregation effects in both experimental animals and human patients [41]. Antibacterial agents, gingerols, phenylbutenoids, diterpenoids, shogaols, diarylheptanoids, sesquiterpenoids, and flavanoids, as well as phenylbutenoids, diarylheptanoids, flavonoids, and diterpenoids, were discovered in phytochemical examination of many species of ginger rhizomes [45, 46]. Because ginger leaves have more antioxidant activity than rhizomes and flowers, it has been proven in some studies that it has significant potential for development into functional foods and other health products [47]. An infusion of ginger rhizomes with brown sugar is used to cure common colds, according to Semwal et al. [15], while scrambled eggs with powdered ginger is used as a home remedy in China to relieve coughing. Ginger is used in the United States to treat motion sickness and morning sickness during pregnancy, as well as leg cramps [15]. Maghbooli et al. [48] confirmed the effectiveness of ginger powder in the treatment of common migraine attacks and its antiepileptic drug-like properties. Ginger has been found in numerous trials to help prevent cancer and to treat nausea and vomiting caused by pregnancy and chemotherapy [49–51].

Ginger has the ability to preserve DNA from harm caused by H₂O₂ and may be useful in improving sperm quality [52]. Ginger rhizome has long been used in Iran to improve male sexuality, control female menstrual cycles, and relieve painful periods [53]. Mahassni and Bukhari [54] revealed that the extract of ginger rhizome had varied effects on immune system cells and antibodies in smokers and non-smokers, despite the fact that both benefited from thyroid gland augmentation. Furthermore, ginger may help smokers with anemia, whereas it may help non-smokers have a higher humoral immunity or antibody response to infections. According to Atashak et al. [55], both ginger supplementation and progressive resistance training (PRT)

-
- Treats diarrhea
 - Relieves nausea
 - Prevents menstrual cramps
 - Prevents obesity
 - Treats cold and flu
 - Prevents infection
 - Improves cognition
 - Skin care
 - Aids in proper digestion
 - Reduces arthritis pain
 - Stomach ulcers
 - Detoxifies the body
 - Relieves asthma
 - Relieves muscle pain
 - Liver protection
 - Prevents cancer
 - Controls diabetes
 - Boosts heart health
 - Increases sexual activity
 - Improves brain function
 - Removes excess gas
 - Regulates blood sugar
 - Regulates blood sugar
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Table 2.
The most significant advantages of ginger.

protect against oxidative stress after 10 weeks, therefore both therapies can help obese persons. Future trials focused on the efficacy of *Z. officinale* in treating various forms of pain, as well as treatment duration, dosing methodologies, safety, and cost efficiency, will be built on the foundation laid by Gagnier et al. [56]. **Table 2** lists the most major health advantages of ginger [41].

5.1 Blood pressure-lowering effect

Ginger has been used for a long time to treat a variety of ailments, including hypertension. The crude extract of ginger induced a dose-dependent (0.3–3 mg/kg) fall in the arterial blood pressure of anesthetized rats and a cardio depressant activity in guinea pigs. The blood-pressure-lowering effect of ginger is mediated through blockade of voltage-dependent calcium channels [57]. Another study found that aqueous ginger extract reduces blood pressure by a dual inhibitory effect mediated by muscarinic receptor stimulation and Ca^{++} channel blocking, and this work provides a solid mechanistic basis for the use of ginger in hypertension and palpitations [57]. The effect of ginger tea on blood pressure of hypertensive individuals has been studied to determine and compare the mean arterial pressure, median number of hypertensive episodes of the respondents with and without intake of ginger tea. From the fifth to the eighth week, when the participants began drinking 10 g of ginger tea twice a day, their average mean arterial pressure dropped to 94.804 mmHg [58].

5.2 Other medicinal and toxicological properties

Muscular aches, indigestion, fever, hypertension, fever, rheumatism, pains, infectious diseases, sore throats, cramps, colds, vomiting, constipation, motion sickness, gastrointestinal diseases, arthritis, sprains, helminthiasis and dementia are just a few of the ailments that ginger has been used to treat in Chinese, Ayurvedic, Tibb-Unani, Sri Lankan, Arabic, and African traditional medicines. Ginger has been traditionally used from time immemorial for varied human ailments in different parts of the world, to aid digestion and treat stomach upset, diarrhea, nausea, and migraine. In a double-blind, randomized research involving 60 ladies who have undergone major gynecological surgery the group that got ginger root had much less reported instances of nausea and was comparable to the placebo group [59]. In a study of 100 persons with common migraine headaches, Maghbooli et al. [48], compared the efficiency of ginger (250 mg of ginger rhizome powder) to sumatriptan (50 mg, a synthetic migraine headache medication) (no aura). Both medicines resulted in a 44% reduction in pain 2 hours after treatment, though it is unclear how much of this was due to natural history and/or a placebo effect. Both medicines resulted in a 44% reduction in pain 2 hours after treatment, though it is unclear how much of this was due to natural history and/or a placebo effect.

6. Ginger's memory-boosting properties

As the population ages, aging-induced cognitive impairment is recognized as a prodromal stage of dementia that affects the quality of life of older people [60, 61]. Then, in order to slow the course of dementia, researchers may need to look into interventions that improve memory function. Ginger improved memory function in aging-related disorders, according to a clinical trial by Saenghong et al. [62]. They

tested middle-aged women's working memory and cognitive function after giving them ginger extract orally, and found that the ginger treatment increased scores in word recognition, digit vigilance, choice reaction, arithmetic working memory, and spatial working memory significantly. Ginger treatment improved memory in normal mice via increasing hippocampus levels of nerve growth factor (NGF), which activates extracellular signal-regulated kinases (ERK) and then cAMP response element-binding protein (CREB), resulting in increased synaptogenesis [63–65]. In these investigations, ginger was found to help with cognitive decline in the early stages of dementia in the elderly.

6.1 Effects of ginger and its compounds on stroke

Stroke incidence rates and bad outcomes both rise with age, indicating that more than 80% of strokes occur in those over the age of 65 [66]. After a stroke, brain damage is more severe in the elderly, and endogenous synthesis of antioxidant enzymes and neurotropic factors is lacking [67]. The loss of ovarian hormones with age, as well as the functional decline of brain supporting cells including astrocytes and endothelial cells, contribute to the severity of stroke outcomes in the aging brain [68]. Two separate studies looked into the pharmacological potential of ginger and found that it can help with memory loss and brain infarction caused by middle cerebral artery occlusion (MCAO) [29, 69].

6.2 Ginger's anti-epileptic properties

Ginger has been shown to have extraordinary effects on epilepsy patients who suffer from recurring seizures. When compared to younger individuals, epilepsy in the elderly has fewer pre-symptoms and a longer duration of postictal disorientation [70–72]. This effect could be linked to the substantial changes in brain anatomy that occur as a result of ventricular expansion speeding up as people get older [73]. Ginger extract was effective for reducing the duration and incidence of seizures induced by pentylenetetrazole (PTZ), which is a well-known inducer of epilepsy-like symptoms in an age-dependent manner [74, 75]. Another study conducted lately in mice found comparable benefits after treatment with ginger extract [76]. Ginger therapy significantly reduced myoclonic and clonic seizures, as well as forelimb tonic extension, in both investigations. These effects of ginger could be attributed to 6-gingerol's inhibitory effects on the synthesis of nitric oxide (NO), which activates the soluble guanylyl cyclase, which controls the seizure threshold [77].

7. Conclusion

Ginger is a popular condiment, cooking spice, and herbal remedy around the world, as well as a flavoring agent. Ginger contains over 60 active ingredients, which are classified as non-volatile or volatile. Hydrocarbons mostly monoterpenoid hydrocarbons and sesquiterpene include the volatile component of ginger and impart distinct aroma and taste to ginger. Paradols, gingerols, zingerone and shogaols, are examples of non-volatile chemicals. Ginger's active components, such as gingerols, shogaols, zingerone, and others, have antioxidant properties. 6-gingerol and 6-shogaol are the most pungent gingerols and shogaols found in the rhizome. The main ingredient in ginger, gingerol, has been extracted and tested for toxic and

pharmacological effects. Cold-induced disease, colic, dyspepsia, loss of appetite, swellings, heart palpitation, nausea, asthma, cough and rheumatism have all been treated with fresh ginger. Anti-inflammatory qualities, anti-thrombotic properties, cholesterol-lowering characteristics, blood pressure-lowering properties, anti-microbial properties, anti-oxidant properties, anti-tumor properties, and hypoglycaemic activities are all medicinal properties linked with ginger. Ginger can help with cancer, obesity, heart disease, osteoarthritis, hypertension, bacterial infections and diabetes among other things. Ginger is a herbal, readily available, low-cost treatment with a low risk profile that can be used in place of chemical, rare, and expensive pharmaceuticals. Ginger can alter critical fundamental processes involved in COVID-19 formation because of its antiviral, anti-inflammatory, immunomodulatory, and antioxidant properties. This study summarizes current understanding about the possibility of ginger and its components for the treatment of COVID-19. Ginger appears to have some promising health advantages, according to other scientific literature, and further data from additional clinical research will help confirm whether ginger's many health benefits can be realized in humans. Herbal remedies and other nutraceuticals are increasingly and extensively used by a substantial part of the population. To sum up, treatment with natural herbal medicine especially ginger, non-synthetic drug, is recommended. However, the majority of these pharmacological benefits of ginger must be confirmed in clinical research before the pharmacological usefulness of ginger and its ingredients may be endorsed.

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