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**Review Article**


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# Frugal Chemoprophylaxis against COVID-19: Possible preventive benefits for the populace

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## Abstract

Due to the outbreak of Covid-19 identified around December 2019 which is rapidly expanding with confirmed cases in over 210 countries. Global incidence is on a ravaging increase and with new cases reported daily of both symptomatic and asymptomatic cases which has imposed threat to global health and economy. Some of the notable symptoms include dry cough, cold, fever and respiratory distress alongside inflammation.

In order to curtail the community spread and reduce the incidence of new cases of Covid-19 we reviewed some medicinal foods, leafs and spices that has chemoprophylaxis and potent pharmacological activities which include anti-inflammatory, anti-viral, anti-bacterial, antioxidant, anti-pyretic and inhibition of viral replication properties against the SARS-COV-2 (Severe acute respiratory syndrome coronavirus 2) symptoms and elucidate their bioactive compounds with their mechanism of action and suggest possible preventive roles they play in the abating the spread of the Covid-19 and reduce the cases globally in a bid of raising the immune system function and possible abate the development of symptoms and general health function.

Frugal Chemoprophylaxis, using natural products and foods were considered due to some factors which include readily available, cost effective as well as economical provident due to the current state of the global economy and as such foods, herbs and spices that are already known globally are considered.

In this present review, we presented the preventive potentials of some medicinal foods, natural products and their role in mitigating as well as abating the community spread of Covid-19 globally and enhancing immune system function.

**Keywords:** Frugal Chemoprophylaxis; COVID-19; Medicinal foods; bioactive compounds; Pharmacological properties; Mechanism of action; Protective benefits.

## 1.0 Introduction

The outbreak of a novel coronavirus disease; a respiratory syndrome, referred to as COVID-19, was first recognized in Wuhan, China, in December 2019. The causative agent for this deadly viral infection is a coronavirus known as SARS-CoV-2. COVID-19 is demonstrated by fever, dry cough, persistent pressure in the chest, and shortness of breath (Huang *et al.*, 2020; CCDC, 2020) [1, 2]. There are several symptoms of coronavirus infection, such as sore throat, running nose, cough, sneezing, fever, viral conjunctivitis, loss of smell and taste and severe pneumonia (Chen *et al.*, 2020; Huang *et al.*, 2020; Li et al., 2020, Xia et al., 2020) [3,1,4,5]. Sneezing, runny nose, and symptoms similar to the common cold are observed in only 5% of patients. The novel coronavirus-related pneumonia COVID-19has continued to disseminate, with the current case count close to 7,039,918 cases, and more than 404,396 deaths according to the World Health Organization (WHO) as of 9 June, 2020 (WHO, 2020) [6].

The mortality rate of COVID-19 is about 7% which varies by countries and regions is less than that of SARS (severe acute respiratory syndrome), which has a mortality rate of 9.6%, and less than that of MERS (Middle East respiratory syndrome), up to 34.4% deaths. Individuals already suffering from cardiovascular disease, hypertension, respiratory disease, or diabetes are at a high risk of mortality. Age and gender-specific variations in the death rate have also been reported (WHO, 2020) [7]. The disease became pandemic within a few months of its emergence, indicating a high transmission ability as compared with SARS and MERS (Munster et al., 2020; Guan *et al.*, 2020) [8,9].

COVID-19 can last for up to 6 weeks depending upon the individual' s immunity and the disease intensity. A variable incubation period has been reported for the infection to establish completely; a second exposure to the viral inoculum may decrease the incubation time (Munster et al., 2020) [8].An incubation time of 3 to 27 days (average 14 days) has been reported by different sources (WHO, 2020, Bai *et al.*, 2020; Lauer *et al.*, 2020) [7,10,11].This incubation period is considerably longer than that required by SARS or MERS (Lessler *et al.*, 2009; Backer *et al.*, 2020) [12,13]. SARS-CoV-2has an airborne route of transmission, whereby small aerosols spread in the surrounding air by the coughing and sneezing of infected individuals. These fine airborne droplets, harboring viral particles, can be directly inhaled by nearby healthy individuals (Liu *et al.*, 2020) [14]. The viral particles can stick to the fingertips and invade the healthy individuals by contact of contaminated hands with the nose, eyes, or mouth. Hence, hand hygiene is an expedient precaution to reduce SARS-CoV-2 transmission (Yang, 2020) [15]. The infection mechanism of both the SARS and COVID-19 viruses involve an interaction with the angiotensin-converting enzyme 2 (ACE2) and cleavage of the viral spike protein by a serine protease (Zhao *et al.*, 2020; Prabakaran *et al.*, 2004) [16, 17].

To have a better understanding of respiratory infectious disease transmission for pathogenesis and epidemiological spread of disease, a model for respiratory emissions was established and it was found that droplets containing the virus can be as small as 1 micron and a multiphase turbulent gas cloud from a human sneeze exhibited the property to travel great distance (7–8 m) (Bourouiba, 2020) [18]. This suggests that the gas cloud with its pathogen payload can span a certain space in a few seconds. The pathophysiology of SARS-CoV-2 infection closely resembles that of SARS-CoV infection, with aggressive inflammatory responses strongly implicated in the resulting damage to the airways (Wong et al., 2004) [19]. Therefore, disease severity in patients is due to not only the viral infection but also the host response.

Giving a high rate of community spread, there is a need to change the public health policy from containment to mitigation of transmission amongst community, and determine the extent to which mild disease is contagious in the community, particularly among less vulnerable young adults for acquisition of SARS-CoV-2 infection (Spellberg *et al.*, 2020) [20]. The constant and rapid spread of novel coronavirus SARS-CoV-2 and its ability to disseminate from human to human has prompted researchers to identify existing medicinal foods that are frugal and could have suitable preventive benefits on the novel coronavirus-related pneumonia COVID-19.

Chemoprophylaxis refers to the administration of medication or natural substance for the purpose of preventing a disease or infection. The choice of chemoprophylaxis agent is dependent on if the benefits outweighs the potential harm and if it is cost effective.

Since these medicinal foods are having bioactive compounds with potent pharmacological activities which include anti-inflammatory, anti-viral, anti-bacterial, antioxidant, anti-pyretic and inhibition of viral replication properties against the SARS-COV-2 (Severe acute respiratory syndrome coronavirus 2) symptoms. In this review, we elucidated their various bioactive compounds with their mechanism of action and suggest possible preventive roles they play in the abating the spread of the Covid-19 and reduce the cases globally in a bid of raising the immune system function and possible abate the development of symptoms and general health function.

## 2.0 Medicinal foods, leafs and spices

These are foods that do not only provide nutrient for the body but also confers medicinal and health promoting benefits. There are many examples of these medicinal foods. In this review, we would be examining foods, leafs and spices like onion, bitter cola, bitter leaf, alligator pepper, turmeric, ginger, garlic and nutrients like zinc, ascorbic acid.

### 2.1 Onion (*Allium Liliaceae*)

Onions are members of the *Allium* genus of flowering plants that also includes garlic, shallots, leeks and chives. These vegetables contain various vitamins, minerals and potent plant compounds that have been shown to promote health in many ways. In fact, the medicinal properties of onions have been recognized since ancient times, when they were used to treat ailments like headaches, heart disease and mouth sores (Nemeth, 2007) [21].

#### 2.1.1 Biochemical composition of Onion

Onions contain 89% water, 1.5% protein, and vitamins $B_1$, $B_2$, and C, along with potassium and selenium. Polysaccharides such as fructosans, saccharose, and others are also present, as are peptides, flavonoids (mostly quercetin), and essential oil. Methods for the qualitative assessment of the flavonoids have been detailed, and quercetin glycosides have been shown to be heat stable and transferable to cooking water (Lanzotti, 2006) [22].

**Figure 1. Picture of Onion**

Onion contains numerous sulfur compounds, including thiosulfinates and thiosulfonates; cepaenes; S-oxides; S-dioxides; mono-, di-, and trisulfides; and sulfoxides. When the onion bulb is minced or crushed, cysteine sulfoxides are released from cellular compartments and make contact with the enzyme alliinase from the adjacent vacuoles. Hydrolysis results in the release of reactive intermediate sulfenic acid compounds and then the various sulfur compounds which can be utilized as a potential preventive property on the novel Covid-19 virus (Arnault, 2006, Blumenthal, 1998, Graefe, 2001).[23,24,25]

#### 2.1.2 Potential Mechanisms of Pharmacological Uses of Onion and its Potential Use as Chemoprophylaxis against Covid-19

1. Anti-inflammatory effects: Animal and *in vitro* data shows that compounds derived from onion have exerted anti-inflammatory and antihistamine effects *in vitro* and in animal models. (Griffiths, 2002 [26]
2. Antimicrobial effects: In vitro studies have shown onion possesses antibacterial (including against Helicobacter pylori), antiparasitic, and antifungal activity. (Elnima, 1983; Rose, 2005; Zohri,1995) [27,28,29]. Clinical applications for this activity have not been determined, and use as a food preservative is limited by the strong odor and instability of sulfur compounds. (Griffiths, 2002)[26].

### 2.1.3 Dosing

An average daily dose of 50 g of fresh onion, or 20 g of dried onion has been suggested for a variety of uses. (Blumenthal, 1998;WHO, 1999) [24, 30].

### 2.1.4 Possible Adverse Reactions of Onion

Ingestion of onion and onion extract appears to be relatively safe. (Blumenthal, 1998; WHO, 1999). [24, 30] Excessive consumption of onion has been associated with GI upset (burning sensation and diarrhea), flatulence, and changes in intestinal flora. (Suleria, 2015) [31]. Onion seeds have been reported as occupational allergens, but frequent contact with onion rarely causes allergic reaction. (Navarro, 1995) [32]. Certain sulfur compounds, such as propanethial-S-oxide, escape from onion in vapor form and hydrolyze to sulfuric acid when cut, causing eye irritation and lacrimation. (Chan, 1972) [33]

## 2.2 Bitter Kola (*Garcinia kola*)

*Garcinia kola* (bitter kola) is a dicotyledonous plant belonging to the family of plants called Guttiferae. It is a perennial crop growing in the forest, distributed throughout West and Central Africa (Iwu 1993) [34]. *G. kola* is also found distributed in the forest zone of Sierra Leone, Ghana, Cameroon and other West African countries. In Nigeria, it is common in the South Western States and Edo State (Otor, *et al.*, 2001) [35].

It is a medium sized evergreen tree, about 15-17m tall and with a fairly narrow crown. The leaves are simple, 6-14cm long and 2-6cm across, shiny on both surfaces and spotted with resin glands. The small flowers are covered with short, red hairs (Iwu, 1993) [34]. The fruit is a drupe of 5-10cm in diameter and weighs 30-50g. It is usually smooth and contains a yellow-red pulp. The fruit changes color during maturation from green to orange, and each fruit contains 1-4 seeds (Juliana *et al.*, 2006) [36].

**Figure 2. Picture of bitter kola**

*Garcinia kola* has been referred to as a "wonder plant" because every part of it has been found to be of medicinal importance (Dalziel, 1937) [37]. It is also called bitter cola**,** male kola due to the reported aphrodisiac properties. It is commonly called "Orogbo" in Yoruba language, Akuilu‟ in Igbo language and Namijingoro‟ in Hausa language (Dalziel, 1937) [37].

### 2.2.1 Biochemical constituents

The phytochemical compounds isolated from *G. kola* include tannins, saponins, alkaloids, cardiac glycosides (Ebana, *et al.*, 1991) [38]. Other phytochemical compounds isolated from *G. kola* seeds are biflavonoids such as kolaflavone and 2-hydroxybi-flavonols. Two new chromanols, garcioic and garcinal, together with tocotrienol were reported isolated from *G. kola* (Terashima, *et al.*, 2002). Morabandza, *et al.*, (2013) [39,40] had also determined the chemical composition of *Garcinia kola* Heckel (Clusiaceae) mesocarp.

### 2.2.2 Traditional Uses and Medicinal Values

*Garcinia kola* is chewed extensively in Southern Nigeria as a masticatory and it is readily served to visitors, especially among the Igbo tribe in Eastern Nigeria, as a sign of peace and acceptance of visitors. The root of the plant is used as favorite bitter chew-sticks in West Africa (Otor, *et al.*, 2001) [35].

The stem bark is used in folklore remedies as a purgative among the natives of Eastern Nigeria and the latex is externally applied to fresh wounds to prevent sepsis, thereby assisting in wound healing. It is also popular among the people of Nigeria for nervous alertness and induction of insomnia. *Garcinia kola* is highly valued for medicinal use. This plant has been referred to as a wonder plant‟ because every part of it has been found to be of medicinal importance (Dalziel, 1937) [37]. The seeds are chewed as an aphrodisiac or used to cure cough, dysentery, chest colds, liver disorders, diarrhoea, laryngitis, bronchitis, and gonorrhea (Adesina, *et al.,* 2005)[41]. The seed is used to prevent and relieve colic; it can also be used to treat headache, stomach ache and gastritis (Ayensu, 1978) [42]. It has also been reported for the treatment of jaundice, high fever, and as purgative (Iwu, 1989) [43]. In Sierra Leone, the roots and bark are taken as a tonic for sexual dysfunction in men.

The bark is also added into palm wine to improve its potency (Iwu, *et al.,* 1990) [44]. Traditional medicine practitioners in Nigeria, particularly in the Ogoni area use a decoction of *Garcinia kola* stem bark for the treatment of dysmenorrhoea, fever, inflammation and burns (Adesina, *et al., 200*5)[41]. "Bitter kola is anti-poison and helps to detoxify the system, it has the ability to repel evil men and spirits, it could sound superstitious but it works (Iwu,1989) [43].

### 2.2.3 Possible Mechanism of action of *Garcinia kola*as Chemoprophylaxis agent against Novel Covid-19

#### 2.2.3.1 Anti-microbial properties

Adegboye, *et al.* (2008) [45] had investigated the *in vitr*o antimicrobial activities of crude extract of *Garcinia kola* against some bacterial isolates comprising of both Gram-positive and Gram negative organisms. In another study, the antimicrobial interaction between *Garcinia kola* seed (GKS) and gatifloxacin (GAT), a fourth generation fluoroquinolone was evaluated by a modification of the checkerboard technique using *Bacillus subtilis* and *Staphylococcus aureus* as the test organisms (Ofokansi, *et al.,* 2008) [46]. The antimicrobial activity of five solvent extracts of *Garcinia kola* seeds had also been investigated against 30 clinical strains of *H. pylori* and a standard control strain, NCTC 11638, using standard microbiological techniques (Collise, *et al.,* 2011)[47]. *In vitro* anti-Vibrio activities of methanol and aqueous extracts of *Garcinia kola* seeds against 50 Vibrio isolates obtained from wastewater final effluents in the Eastern Cape Province, South Africa were also investigated (Penduka, *et al.,* 2011) [48]. The bioactivity of *G. kola* seeds was also assessed on *Streptococcus pyogenes*, *Staphylococcus aureus*, *Plesiomonas shigelloides* and *Salmonella typhimurium* (Christinah and Roland, 2012) [49]. Trichomonacidal effects of *G. kola nuts* were also investigated (Gabriel and Emmanuel, 2011) [50]. Esimone *et al.* 2002 [51] also investigated the effect of *Garcinia kola* seed extract (100 mg/kg) on the pharmacokinetic and antibacterial effects of ciprofloxacin hydrochloride (40 mg/kg).

#### 2.2.3.2 Hepatoprotective and Anti-oxidant activities

The hepatoprotective effect of *Garcinia kola* seed extract against paracetamol induced hepatotoxicity had been investigated in rats (Alade and Ani, 1990) [52]. The protective effects of *Garcinia kola* against a dose of Carbon-Tetrachloride (CC14)-induced liver damage in experimental rats were also investigated (Mathew and Blessing, 2007) [53]. Antioxidant potentials of five fractions (ME1–ME5) of methanolic extract of *Garcinia kola* seeds was also studied (Tebekeme, 2009)[54].

### 2.2.4 Other studies on *Garcinia kola* and its health benefits

Anti-ulcer potential and proton pump inhibitory activity of kolaviron (KV) isolated from *Garcinia kola.* Heckel had been evaluated using different ulcer models and was suggested to emerge as a potent anti-ulcer compound (Onasanwo, *et al.,* 2011)[55]. *Garcinia kola* (Heckel) seed extract evaluated in albino Wistar rats possess significant anti-pyretic activity, which justified its ethnomedicinal use (Kakjing, *et al.,* 2014) [56]. *Garcinia kola* 0.5% aqueous solution eye drop significantly reduces intraocular pressure (IOP) as compared to baseline (Adebukunola, *et al.,* 2010) [57]. Comparative study on the efficacy of *Garcinia kola* in reducing some heavy metal accumulation in liver of Wistar rats was also carried out. *Garcinia kola* has the highest hepatoprotective effect to Cd followed by Hg and least protection against Pb toxicity in rats and its administration was beneficial in reducing heavy metal accumulation in the liver (Nwokochaa, *et al.,* 2011) [58].

Administration of *Garcinia kola* for a period of six weeks in rabbits elicited no observable histo-pathological effects on the histology of the liver (Charity, *et al.,* 2012) [59]. *Garcinia kola* had been shown to enhance erythropoiesis in rabbits and rats and as well has no long term significant toxicological implication (Unigwe and Nwakpu, 2009; Esomonu, *et al.,* 2005) [60,61]. In another study, *Garcinia kola* significantly reduced tissue damage induced by lipopolysaccharide (LPS) (Okoko and Ndoni, 2009)[62]. Daily administration of *Garcinia kola* (G. kola) in growing Wistar rats for a period of 70 days showed a depressive effect on appetite and water intake with resultant poor feed utilization efficiency and mass gain of rats in a dosedependent manner. Plasma alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities were elevated ($P<0.05$) but histological examinations of liver, heart and lungs of experimental rats revealed no alterations. The extract enhanced sexual interest (libido) of the male rats but did not necessarily improve their fertility rate (Otor, *et al.,* 2001) [35].

## 2.3 Zinc

Zinc essentiality was established in 1869 for plants, in 1934 for experimental animals and in 1961 for humans (King, 2006) [63]. A syndrome of anemia, hypogonadism and dwarfism was reported in a 21-year-old Iranian farmer in 1961 who was subsisting on a diet of unrefined flat bread, potatoes, and milk.(Prasad,1963)[64].Shortly after, a similar syndrome was observed in Egyptian adolescents who had similar dietary history to that of the Iranians, mainly subsisting on bread and beans (Sandstead *et al.,* 1967) [65].

### 2.3.1 Biochemical and Physiologic Functions:

Although, zinc-dependent biochemical mechanisms in physiologic functions have received extensive study, clear relationships have not been fully established. Zinc is ubiquitous within cells in contrast to iron, which is contained in defined cellular components and has defined physiological roles. The role of zinc in biology can be grouped into three general functional classes, namely catalytic, structural and regulatory functions (Cousins, 1996) [66].

Zinc is released from food as free ions during digestion. These liberated ions may then bind to endogenously secreted ligands before their transport into the enterocytes in the duodenum and jejunum (Turnlund, 1984) [67]. Specific transport proteins may facilitate the passage of zinc across the cell membrane into the portal circulation. With high intakes, zinc is also absorbed through a passive paracellular route. The portal system carries absorbed zinc directly to the liver, and then released into systemic circulation for delivery to other tissues. About 70% of the zinc in circulation is bound to albumin, and any condition that alters serum albumin concentration can have a secondary effect on serum zinc levels. Although, serum zinc represents only 0.1% of the whole body zinc, the circulating zinc turns over rapidly to meet tissue needs (Tubek, 2007)[68].

### 2.3.2 Possible Mechanism of action of Zinc as Chemoprophylaxis agent against Novel Covid-19

**Diarrhea:** Diarrhea is characteristically, although not inevitably, a prominent feature of acrodermatitisenteropathica. (Hambidge, 1992) [69]. Plausible explanations for a link between zinc deficiency and diarrhea include impairment of the immune system and of intestinal mucosal cell transport (Ghishan, 1884) [70]. A causal relationship between zinc deficiency and diarrhea is indicated by the beneficial effects of zinc supplements and concurrent increase in growth velocity (Brown *et al.*, 1998) [71].

**Pneumonia:** Community zinc supplementation studies in children have demonstrated a substantial and statistically significant reduction in the prevalence of pneumonia in developing countries (Bhutta *et al.*, 1999)[72] this makes its effective in treatment of pneumonia complications which results from Covid-19.

**Malaria:** It is uncertain to what extent oral supplementation with zinc can reduce episodes of malaria in endemic areas. According to some studies, malaria also appears to be reduced by zinc supplementation (Shankar *et al.,* 2000)[73] However, there are studies showing no effect of zinc supplementation against malaria (Veenemans *et al.,* 2011)[74]. Further studies are required to establish this effect.

## 2.4 Alligator pepper (*Aframomum melegueta*)

This plant is a member of the ginger family (Zingiberaceae) and is wildly cultivated in tropical areas of Africa, mostly in West Africa. *Aframomum melegueta* (Grains of Paradise) has names such as grains of paradise, Atare (in Yoruba), chitta (Hausa),

is one seed with many healing power and of great benefits to mankind.

The seeds of the plant are used to flavor foods and as components of traditional African medicine. Alligator pepper has been reported to have anti-ulcer, anti-microbial, anti-nociceptive, anti-plasmodial, hepatoprotective and anticancer activities (El-Halawany *et al.*, 2014)[75].

**Figure 3.** *Aframomum melegueta* (Alligator pepper)

Traditionally, *Aframomum melegueta* is mixed with other herbs for the treatment of common ailments such as body pains, diarrhoea, sore throat, catarrh, congestion and rheumatism in West Africa, Nigeria (Ajaiyeoba & Ekundayo, 1999) [76]. Diabetes, a major underlying disease of people afflicted with covid-19 might also be combated by *Aframomum melegueta*. A myriad of compounds found in *Aframomum melegueta* such as 6-paradol, 6-shagaol, 6-gingerol, oleanolic acid and acarbose exert an anti-diabetic effect by inhibiting enzymes such as α-amylase and α-glucosidase. These enzymes are responsible for digestion and break down of carbohydrates and polysaccharides from food into simple sugars to increase blood glucose levels. Among the compounds, 6-gingerol and oleanolic acid are more effective in inhibiting the enzymes (Mohammed *et al.*, 2017)[77]. *Aframomum melegueta*is suitable for consumption by diabetic patients; its consumption will help a diabetic patient stay healthy (Venugopal, 2012) [78].

The ethanolic seed extract and stem bark of *Aframomum melegueta* contains phytochemicals such as tannins, saponins, flavonoids, steroids, terpernoids, cardiac glycosides and alkaloids that possess antimicrobial and anti-inflammatory effects (Doherty *et al.*, 2010; Okwu, 2004; Okoli*et al.*, 2007)[79,80,81]. These compounds which are natural antioxidant are believed to scavenge free radicals and offer protections against viruses, allergens, microbes, platelet aggregation, tumors, ulcers and hepatotoxins (chemical liver damage) in the body. To support this claim of anti-inflammatory properties of *Aframomum melegueta* Ilic *et al.* (2014) [82] reported that ethanolic *Aframomum melegueta* extract inhibited cyclooxygenase-2 (COX-2). Compounds that inhibit COX-2 activity are capable of reducing inflammatory responses. The most active COX-2 inhibitory compound in the *Aframomum melegueta* extract was [6]-paradol, while [6]-shogaol was found to inhibit expression of a pro-inflammatory gene, interleukin-1 beta (IL-1β) (Osuntokun *et al.*, 2017)[83].

### 2.5 Turmeric (*Curcuma longa*)

Turmeric (Curcuma longa L.) belongs to the family of ginger (Zingiberaceae) and natively grows in India and Southeast Asia. The plants rhizomes contain several secondary metabolites including curcuminoids, sesquiterpenes, and steroids (Omosa *et al.*, 2017)[84]; with the curcuminoid curcumin being the principal component of the yellow pigment and the major bioactive substance. It has been used as traditional medicine from ancient time, especially in Asian countries. Plants as a rich source of phytochemicals with different biological activities including antiviral

activities are in interest of scientists (Jassim and Naji, 2003) [85]. It has been demonstrated that curcumin as a plant derivative has a wide range of antiviral activity against different viruses. Inosine monophosphate dehydrogenase (IMPDH) enzyme due to rate-limiting activity in the *de novo* synthesis of guanine nucleotides is suggested as a therapeutic target for antiviral and anticancer compounds. Among the 15 different polyphenols, curcumin through inhibitory activity against IMPDH effect in either noncompetitive or competitive manner is suggested as a potent antiviral compound via this process (Dairaku *et al.*, 2010) [86].

Furthermore, protein molecules encoded by the SARS-CoV-2 genome are potential targets for chemotherapeutic inhibition of viral infection and its replication. These intriguing targets include the spike protein (S), which mediates the entry of the virus, the SARS-CoV-2 main protease (3CL protease), the NTPase/helicase, the RNA-dependent RNA polymerase, the membrane protein (M) required for virus budding; the envelope protein (E) which plays a role in coronavirus assembly (Stadler *et al.*, 2003; Lai, 2005; Holmes, 2003)[87,88,89] and the nucleocapsid phosphoprotein (N) that relates to viral RNA inside the virion and possibly other viral protein-mediated processes (Gallagher and Buchmeier, 2001) [90]. With such a drastic increase in molecular and biochemical information about various components of the SARS-CoV-2 and their cellular targets, it is important and timely to again evaluate anti-SARSCoV-2 activities of various turmeric phytocompounds. It is to be noted that *in vitro* studies have positively demonstrated effective antiviral properties of curcumin against enveloped viruses such as Dengue virus (DENV), influenza virus and emerging arboviruses like the Zika virus (ZIKV) or chikungunya virus (CHIKV) (Tzu-Yen *et al.*, 2013; Mounce *et al.*, 2017) [91,92] which are similar to the SARS-CoV-2 an enveloped virus.

### 2.6 Bitter leaf (*Vernonia amygdalina)*

Vernoniaamygdalina (Del.) commonly called bitter leaf is the most widely cultivated species of the genus Vernonia which has about 1,000 species of shrubs (Muanya, 2013)[93]. Bitter leaf is a seedless plant, green in colouration with a characteristic odour and bitter taste. It has different names such as 'Omjunso' in East Africa especially Tanzania, 'Ewuro' in yoruba, Etidot (Ibibio), Ityuna (Tiv), Oriwo (Edo), Chusa-dokiShiwaka (Hausa), and 'Omubirizi' in south-western Uganda.

*Vernonia amygdalina* is known as food and medicinal plants used in Asia and Africa (West Africa) due to its pharmacological effects which include antioxidant, anti-inflammatory, anti-diabetes, anticancer, anti-malaria etc. One major properties of considering *Vernonia amygdalina* in the management of covid-19 is its antioxidants property. Antioxidants inhibit deleterious effects of free radicals that are capable of deteriorating lipid biomembranes in the human body. Researchers in the field of medical sciences have observed free radical scavenging ability and antioxidant property in *Vernonia amygdalina*.

*Vernonia amygdalina* has been documented to possess antioxidant properties which correlates to its medicinal properties. Antioxidant activities of bioactive compounds isolated from *Vernonia amygdalina* leaves have been established from various studies (Igile *et al.*, 1994; Farombi and Owoeye, 2011; Ho*et al.*, 2012; Udochukwu *et al.*, 2015) [94,95,96,97]. Farombi and Owoeye (2011) [95] observes phytochemicals compounds such as saponins and alkaloids, terpenes, steroids, coumarins, flavonoids, phenolic acids, lignans, xanthones, anthraquinones, edotides, sesquiterpenes extracted and isolated from *Vernonia amygdalina* to elicit various biological effects in humans including cancer chemoprevention. The chemoprophylaxis properties of *Vernonia amygdalina* was attributed to their abilities to scavenge free radicals, induce detoxification, inhibit stress response proteins and interfere with DNA binding activities of some transcription factors.

### 2.7 Black seeds (*Nigella sativa*)

*Nigella sativa*, commonly known as black seed is native to Southern Europe, North Africa and Southwest Asia and it is cultivated in many countries in the world like Middle Eastern Mediterranean region, South Europe, India, Pakistan, Syria, Turkey, Saudi Arabia (Khare, 2004) [98].

N. sativa is regarded as a valuable remedy for various ailments, the seeds, oil and extracts have played an important role over the years in ancient Islamic system of herbal medicine. Bukhari reported that Holy Prophet Muhammad (peace be upon him) told "There exists, in the black grains, health care of all the diseases, except death" (Ghaznavi, 1988) [99].

Many studies have been carried out to affirm the acclaimed medicinal properties emphasized on different pharmacological effects of *N. sativa* seeds

such as antioxidant (Hosseinzadeh *et al.,* 2007),[100] anti-tussive (Hosseinzadeh *et al.,* 2008)[101], gastroprotective (El-Abhar *et al.,* 2003)[102], anti-anxiety (Bin-Sayeed *et al.,* 2014)[103], anti-inflammatory, anti-cancer, immunomodulatory and anti-tumor properties (Shafi *et al.,* 2009; Salem, 2005; Majdalawieh *et al.,* 2010)[104,105,106], hepatoprotective effect (Khan, 1999) [107], protective effects on lipid peroxidation (Hosseinzadeh *et al.,* 2007)[100], antibacterial activity (Hosseinzadeh *et al.,* 2007)[100], antiviral activity against cytomegalovirus have been reported for this medicinal plant.

**Figure 4**: *Nigella sativa* plant and seeds

It should be noted that the seeds of N. sativa are the source of the active ingredients of this plant. Thymoquinone (TQ), dithymquinone (DTQ), which is believed to be nigellone, thymohydroquinone (THQ), and thymol (THY), are considered the main phytochemicals of the seed (Omar *et al.,* 1999)[108]. N. sativa seeds contain other ingredients, including nutritional components such as carbohydrates, fats, vitamins, mineral elements, and proteins, including eight of the nine essential amino acids (Chun *et al.,* 2002; Correa *et al.,* 1986)[109,110]. The potential immunomodulatory and immunotherapeutic potentials of N. sativa seed active ingredients, most especially TQ will show a promising therapy in managing covid-19 virus.

### 2.8 Ginger (*Zingiber officinale Roscoe*)

Ginger, with the botanical name *ZingiberOfficinale Roscoe* a commonly used spice and belongs to the family Zingiberaceae (Singh and Singh, 2019)[111]. Its local names are Ata-ile, Jinja, and Cithar among the Yoruba, Igbo and Hausa folks of Nigeria (Nwauzoma and Dappa, 2013)[112]. Commonly, ginger can be found in subtropical and tropical Asia, Africa, Far East Asia, China, and India (Tanaka, *et al.,* 2015)[113]. It can be used as a component in curry powder, sauces, ginger bread, and ginger-flavoured carbonated drinks and also in the preparation of dietaries for its aroma and flavour (Durak, *et al.,* 2015)[114]. Investigations, reveal that ginger possesses several biological properties such as anti-inflammatory and anti-oxidative (Chung *et al.,* 2019)[115], antimicrobial (Beristain-Bauza, *et al.,* 2019)[116], neuroprotective (Sahin, *et al.,* 2019)[117], cardiovascular protective (Ilkhanizadeh, *et al.,* 2016)[118], antidiabetic and anti-nausea (Mele, *et al.,* 2019)[119], antiemetic activities and chemo-protective effects (Amar *et al.,* 2019)[120]. Its main bioactive components are 6-gingerol, 6-shogaol which is phenolics, thus accounting for its various bioactivities (Sahardi and Makpol, 2019) [121].

Till date, there are no antiviral therapeutics that specifically target human corona viruses, and thus completely eradicating the pandemic. Even though several potential vaccines have beendeveloped, such as recombinant attenuated viruses, live virus vectors, or individual viral proteins expressed from DNA plasmids (Fehr and Perlman, 2015)[122]. However, none have been yet approved for use. The limitation with the use of vaccines is a propensity of the viruses to recombine, thereby posing a problem of rendering the vaccine useless and potentially increasing the evolution and diversity of the virus into a more virulent form (Wang, *et al.,* 1993) [123]. It therefore implies that a preventive approach could be a better option.

### 2.8.1 Possible Mechanism of action of Ginger against Corona virus

Virus–receptor interactions play a key regulatory role in viral host range, tissue tropism, and viral pathogenesis (Maginnis, 2018)[124]. Many α-coronaviruses utilize amino-peptidase N (APN) as their receptor (Reguera, *et al.*, 2012)[125], SARS-CoV and HCoV-NL63 use angiotensin- converting enzyme 2 (ACE2) as their receptor (Li, *et al.*, 2020)[126], MHV enters through CEACAM1 (Li, 2015)[127], and the recently identified MERS-CoV binds to dipeptidyl-peptidase 4 (DPP4) to gain entry into human cells (Raj, *et al.*, 2013)[128]. Following receptor binding, the viruses then proceeds into the cytosol of the host. A possible mechanism of preventing access of the viruses into the host's cell could be the inhibition of microbial binding to cellular receptors. In the antimicrobial mechanism of ginger, inhibition of receptor binding has been identified as a major mechanism.

### 2.8.2 Angiotensin converting enzyme-2 (ACE-2) binding

Hitherto, ACE-2 has been associated with an obscure function, not until in recent times with the widespread of the corona virus disease (COVID-19). It is now established as a protein being recognized by various corona viruses to gain entry into hosts cell (Li, *et al.*, 2020) [126], suggesting it to be a therapeutic target in the treatment of the disease. We propose that both ACE receptor antagonism and agonism can be an effective mechanism of ginger in its chemopreventive strategy against corona viruses. This claims are supported by a recent report of Cava et al. (2020)[129] who demonstrated through computational methods that anti-ACE 2 compounds could be effective in blocking the replication of SARS-CoV variant. Moreover, Huentelman *et al.* (2004)[130] also used docking methods to predict the inhibitory ability of small molecules against ACE 2 enzymes, and possibly inhibiting SARS corona virus S protein mediated cell fusion, and high binding affinity was scored. In addition, different bioactive compounds in ginger have been shown to have different effects on ACE2. One mechanism is through ACE 2 inhibition. A study by Alu'datt *et al.* (2015)[131] in the bid to evaluate the anti-hypertensive activity of ginger, demonstrated that its methanolic extract has excellent inhibitory activity on ACE 2 at an extraction temperature and time of $40^0$C and 6 hours respectively. To further corroborate our hypothesis, 3-3'-digallate, a phenolic compound present in ginger was found to interact with ACE2 receptor in a recent computational modelling studies (Zhang *et al.*, 2019)[132]. Taken together, we suggest that the intake of ginger might be beneficial for both prevention and treatment of the pandemic COVID-19 corona virus. Below (Figure 5) is a proposed inhibitory mechanism of action of Ginger against ACE-2 in its chemoprophylaxis strategy.

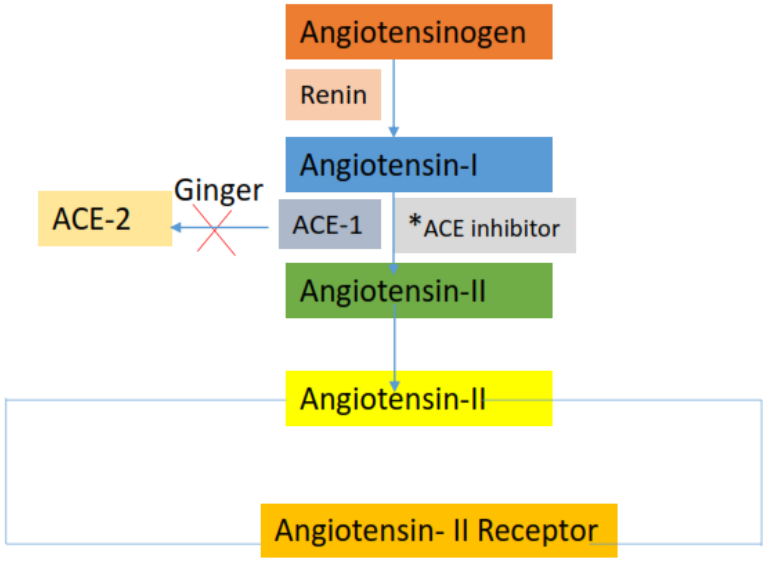


**Figure 5:** Ginger is able to inhibit ACE-2, thereby preventing the binding of the corona virus to the protein.

## 2.9 Garlic (*Allium sativum* L.)

Garlic (*Allium sativum* L.) is a widely consumed spice in the world, and it contains diverse phytochemicals such as organosulfur compounds (Diretto, *et al.*, 2017)[133], saponins (Szychowski, *et al.*, 2018)[134], phenolic compounds (Bradley, *et al.*, 2016)[135], and polysaccharides (Wang, *et al.*, 2018) [136]. However, its major bioactive compounds (figure 6) are the organosulfur compounds including allicin, alliin, diallylsulfide, diallyldisulfide, diallyltrisulfide, ajoene, and S-allyl-cysteine (Shang, *et al.*, 2019)[137]. It has been reported that garlic and its constituents exhibit different bioactivities such as anti-carcinogenic, antioxidant, anti-diabetic, renoprotective, anti-atherosclerotic, antibacterial, antifungal, and antihypertensive activities.

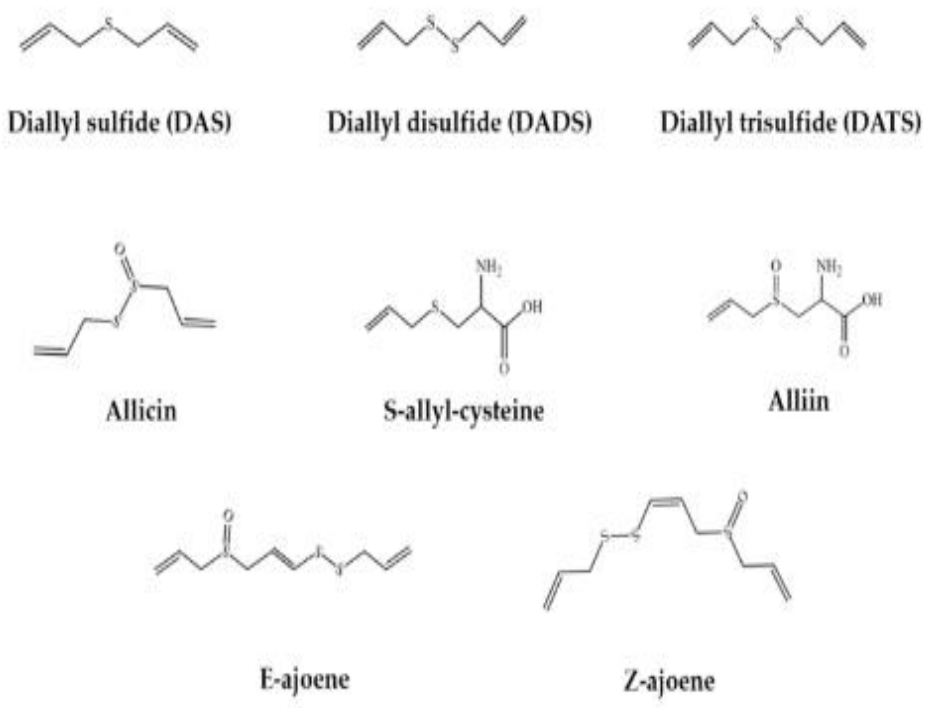


**Figure 6:** Structures of some bioactive compounds in garlicexcerpted from Shang et al. (2019)

From the foregoing, worthy of relevance to our subject matter among the bioactivities of garlic is its antiviral properties. We suggest that this could be due in part to its anti-inflammatory and antioxidative abilities. The antiviral potential of garlic extracts has been demonstrated against influenza virus and entero-virus (Sharma, 2019)[138], HIV virus (Bezerra, *et al.*, 2018)[139], herpes simplex type 2 (Weber *et al.*, 1992)[140], dengue virus (Hall, *et al.*, 2017)[141], Infectious Bronchitis virus (Shojai, *et al.*, 2016)[142], Newcastle Disease virus (Harazem, *et al.*, 2019)[143] etc.

### 2.9.1 Possible Mechanisms of action of Garlic against Corona virus

Major challenges in treating viral diseases are the development of resistance in the virus against the antiviral drugs, due to the high mutation rate of the viral RNA Polymerase (Elena and Sanjuan, 2005) [144] and some of the antiviral drugs can also induce negative side effects in the body (Bindu and Anusha, 2011)[145]. Therefore, it is necessary to find alternative therapies in natural plants and their products, out of which garlic stands out significantly, because of its robust pharmacological bioactive components as stated above. Below is a possible mechanism of action of garlic for the prevention and treatment of the human corona virus.

#### 2.9.1.1 Blocking of the attachment of the virus with cell membranes through protein inhibition

Following receptor binding, the corona virus then fuses with the cell membrane (Fehr and Perlman, 2015)[122]. Coronaviruses are enveloped positive-stranded RNA viruses that replicate in the cytoplasm. To deliver their nucleocapsid into the host cell, they rely on the fusion of their envelope with the host cell membrane, which is mediated by the spike (S) glycoprotein, a class I fusion protein (Belouzard, *et al.,* 2012)[146]. Inhibition of this protein by peptide inhibitors is an important mechanism of antiviral drugs. These molecules could stabilize the viral envelope protein or alter its conformation, thereby blocking oligomerization or the conformational changes required for fusion (Teissier, *et al.*, 2011)[147]. Using the S-HR1 and S-HR2 sequence in the protein as a target, Liu et al. (2004), [148.149.150] Lu et al. (2014) and Xia et al. (2019) have previously designed and developed several potent fusion inhibitors against the Severe Acute Respiratory Syndrome corona virus (SARS-CoV), the Middle East Respiratory Syndrome (MERS-CoV) and the Human corona virus (H-coV) respectively. Antimicrobial compounds from garlic have been shown to react with viral envelope and inhibit the penetration and exponentiation of influenza virus in animals using hemagglutination (HA), methyl tetrazolium (MTT) cytotoxity assay and RT-PCR (Mehrbod, *et al.*, 2013)[151]. Interestingly, allicin and quercetin, which are bioactive compounds of garlic were found to exhibit inhibitory action on the COVID-19 $M^{pro}$protease, thereby demonstrating similar binding affinity when compared to other potent peptide inhibitors such as Nelfinavir and lopinavir in an *in silico* study of protein-protein docking (Khaerunnisa, *et al.,* 2020)[152]. Furthermore, it was demonstrated by Weber et al. (1992)[140] that treatment of different bioactive components of garlic against different viral strains led to the inhibition of viral adsorption or penetration. Taken together, we suggest that through this mechanism, garlic could prevent the attachment of the corona virus to the host's cellular machinery.

## 3.0 Vitamin C (Ascorbic acid)

Vitamin C or ascorbic acid (AA), a water soluble vitamin was first isolated in 1923 by Hungarian biochemist and Nobel laureate Szent-Gyorgyi and synthesized by Howarth and Hirst (1933)[153]. Humans cannot synthesize ascorbic acid as they lack an enzyme called gulonolactone oxidase. It plays an important role in bone formation, wound healing and the maintenance of healthy gums, metabolic functions including the activation of the B vitamins, folic acid, the conversion of cholesterol to bile acids and the conversion of the amino acid, tryptophan, to the neurotransmitter, serotonin. As an antioxidant that protects body from free radical damage (Chambial *et al.,* 2013)[154].

### 3.1Therapeutic Roles

It is used as therapeutic agent in many diseases and disorders. Vitamin C protects the immune system, reduces the severity of allergic reactions and helps to fight off infections. Large doses of vitamin C have been widely used in the treatment and prevention of a large number of disorders like diabetes, atherosclerosis, common cold, infertility, cataracts, glaucoma, macular degeneration, stroke, heart diseases, neurodegenerative diseases, cancer etc.

### 3.2 Dietary Sources

Vitamin C is commonly found in fruits and vegetables. Fruits containing vitamin C, includes; Guava, red pepper, orange, grape fruit, strawberries, banana, Brussels sprouts, pawpaw, tomatoes, mango etc. (Schlueter and Johnston, 2010)[155]. Milk, eggs, cheese, and nuts are also rich sources of vitamin C.

### 3.3 Deficiency

Ascorbic acid deficiency gives rise to the appearance of scurvy, which is more common in developed countries. Symptoms develop with plasma levels below 0.15 mg/dL. Scurvy is characterized by the presence of weakness, joint pain or skin lesions in form of petechias, gum bleeding, ease of developing bruises or delay in wound healing. The most characteristic skin manifestations are purpuric perifollicular hyperkeratotic papules and the presence of kinky hair (Valdes, 2006)[156] .

### 3.4 Toxicity

Vitamin C is generally safe and well tolerated, even in large doses. The IOM set the Tolerable Upper Intake Level for oral vitamin C ingestion at 2 g daily for adults based on gastrointestinal disturbances observed in some individuals at higher doses. High amounts of vitamin C intake have been associated with an increased risk of kidney stones, although the evidence is mixed and inconsistent. The current recommendation is to avoid vitamin C supplementation in those susceptible to kidney stone

formation. Vitamin C consumed with iron could increase the risk of iron overload in susceptible individuals. Patients with these conditions should not avoid eating fruit and vegetables but limit their intake of iron instead. Vitamin C has been reported to cause hemolysis in individuals with glucose-6-phosphate dehydrogenase deficiency, but these reports have not been substantiated (Lykkesfeldt, *et al.*, 2014) [157].

### 3.5 Possible Mechanisms of action of Vitamin C against Corona virus

#### 3.5.1 Improve host's immune responses to combat diseases

Vitamin C (Ascorbic acid) has been reportedly found to exhibit many of its therapeutic functions, partly due to it been able to improve the body's immune responses through a number of mechanisms. We therefore opine that through this physiological response, it would prove to be effective as a chemo-preventive alternative to antiviral drugs against COVID 19 corona virus.

Vitamin C plays important roles in immune function and the modulation of host resistance to infectious agents, reducing the risk, severity, and duration of infectious diseases as supplementation of vitamin C was found to improve components of the human immune system such as antimicrobial and natural killer cell activities, lymphocyte proliferation, chemotaxis, and delayed-type hypersensitivity (Wintergerst, *et al.*, 2006) [158]. Vitamin C contributes to immune defense by supporting various cellular functions of both the innate and adaptive immune system. It supports epithelial barrier function against pathogens and promotes the oxidant scavenging activity of the skin, thereby potentially protecting against environmental oxidative stress (Lauer, *et al.*, 2013; Valacchi, *et al.*, 2016). [159,160] Vitamin C accumulates in phagocytic cells, such as neutrophils, and can enhance chemotaxis, phagocytosis, generation of reactive oxygen species, and ultimately microbial killing (Carr and Maggini, 2017)[161]. It is also needed for apoptosis and clearance of the spent neutrophils from sites of infection by macrophages, thereby decreasing necrosis/NETosis and potential tissue damage. (Sharma, *et al.*, 2004)[162]. Based on this established premises, we suggest that Vitamin C consumption can serve as a prophylactic measure against the pandemic. It is therefore necessary that diet formulations with adequate vitamin C supplement should be given more attention by different regulatory agencies in the local and international communities, while the populace should consume more of foods that are rich in this vitamin as we have afore mentioned.

## 4.0 Conclusion

Coronavirus is a respiratory viral infection of global health concern because the virus is contagious and may cause life-threatening respiratory infection and severe pneumonia in humans. The pathophysiology of SARS-CoV-2 infection, is associated with aggressive inflammatory responses which uncontrolled inflammation inflictsmulti-organ damage leading to organ failure, especially of the cardiac, hepatic and renal systems and most patients with this infection who progressed to renal failure eventually death.

In this review, some medicinal foods were elucidated which include ginger, garlic, onion, bitter kola, alligator pepper, black seed, turmeric, bitter leaf, zinc and vitamin C which possess potent pharmacological activities which include anti-inflammatory, anti-viral, anti-pyretic properties, inhibition of viral replication properties against the symptoms displayed by SARS-COV-2 infection.

These frugal medicinal foods offer great chemoprophylaxis benefits and can play potent roles in the prevention and curtailing of the community spread of COVID-19 as it enhances boosted immunity and defence of the body system as a result of its cost effectiveness and availability.

We hereby recommend that further research should be done to evaluate the protective roles of these medicinal foods on COVID-19 infection as well as promote the development of drugs and improved plant medicines as this outcome can prepare the global populace against subsequent global outbreak of viruses.

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