Academia Journal of Medicinal Plants 9(12): 185-190, December 2021
DOI: 10.15413/ajmp.2021.0133
ISSN: 2315-7720

Academia Publishing

Review Article

Pharmacological properties and toxicity of Garlic and Ginger: A review

Serigne Ibra Mbacké Dieng[1]*, Fatoumta Bah[2], Abdou Sarr[1], Linda Hatini Konde[1], Alioune Dior Fall[1]

[1] Laboratory of Pharmacognosy and Botany, Cheikh Anta Diop University, Dakar, Senegal
[2]Laboratory of Toxicology and Hydrology, Cheikh Anta Diop University, Dakar, Senegal

*Corresponding author. E-mail : simbdieng@yahoo.fr ; Tel : +221 77 576 97 99

Accepted 29th November, 2021

ABSTRACT

These medicinal plants are used directly as drugs or indirectly as a source of raw materials for hemisynthesis of medicines from isolated molecules. Today, spices and herbs are used more and more both for culinary and medicinal purposes including garlic and ginger. Numerous studies have highlighted the pharmacological properties of extracts from garlic (*Allium sativum*) and ginger (*Zingiber officinale*). Given to the important place that these two plants occupy in the treatment of certain diseases but also in our diet, it seems important to summarize the scientific evidence that has been reported.

Key words : Garlic *(Allium sativum),* Ginger (*Zingiber officinale*), pharmacological properties.

INTRODUCTION

Naturally, plants synthesize a large number of molecules, including the active compounds responsible for therapeutic effects. Plants are now the main source of raw material for the pharmaceutical and cosmetic industries. These medicinal plants are used directly as drugs or indirectly as a source of raw materials for hemisynthesis of medicines from isolated molecules. The successful use of any therapeutic agent is compromised by the potential development of tolerance or resistance to that compound from the time it is first employed. This is true for agents used in the treatment of bacterial, fungal, parasitic, and viral infections and for treatment of chronic diseases such as cancer and diabetes (Davies and Davies, 2010). Therefore, the search for new drugs more effective and less toxic than those already used, would be appropriate (Sovova and Sova, 2003). Thus, currently reliance on natural products is gaining popularity to combat various physiological threats including oxidative stress, cardiovascular complexities, cancer insurgence and immune dysfunction (Butt et al., 2009). Today, more and more scientists are considering spices and herbs used for centuries both for culinary and medicinal purposes. Spices enhance not only the flavor, aroma, and color of food and beverages, but they can also protect from acute and chronic diseases (Jiang, 2019). Numerous studies have highlighted the pharmacological properties of extracts from garlic (*Allium sativum*) and ginger (*Zingiber officinale*).

In the past, antibiotics and pharmaceuticals were not available, so garlic was used in different epidemics, such as typhus, dysentery, cholera and flu (Petrovska and Cekovska, 2010). For its virtues of strength and vitality, garlic was consumed by the slaves of the Pharaohs as well as by the athletes of ancient Greece (during the Olympic Games) before each effort. Most often, garlic is traditionally used for heart and circulatory system diseases such as high blood pressure, cholesterol, high blood fat or hardening of the arteries (Rahman, 2001). These therapeutic effects are mainly due to the impressive activity of its bioactive compounds, such as sulfur compounds (Figure 1) like alliine, allicine, ajoènes (Setiawan et al., 2005) phenolic compounds like flavonoids (Gorinstein et al., 2008), saponins (Diretto et al., 2017) and polysaccharides (Wang et al., 2018). Ginger on the other hand, is the subject of numerous botanical, chemical and toxicological studies, in order to prove its scientific efficiency as well as its safety. For centuries, ginger rhizomes have been used as a spice and as an essential ingredient in medicinal preparations to treat various physiological disorders such as rheumatism, nervous diseases, asthma, stroke and diabetes (Tapsell et al., 2006). These properties of ginger are thought to be due

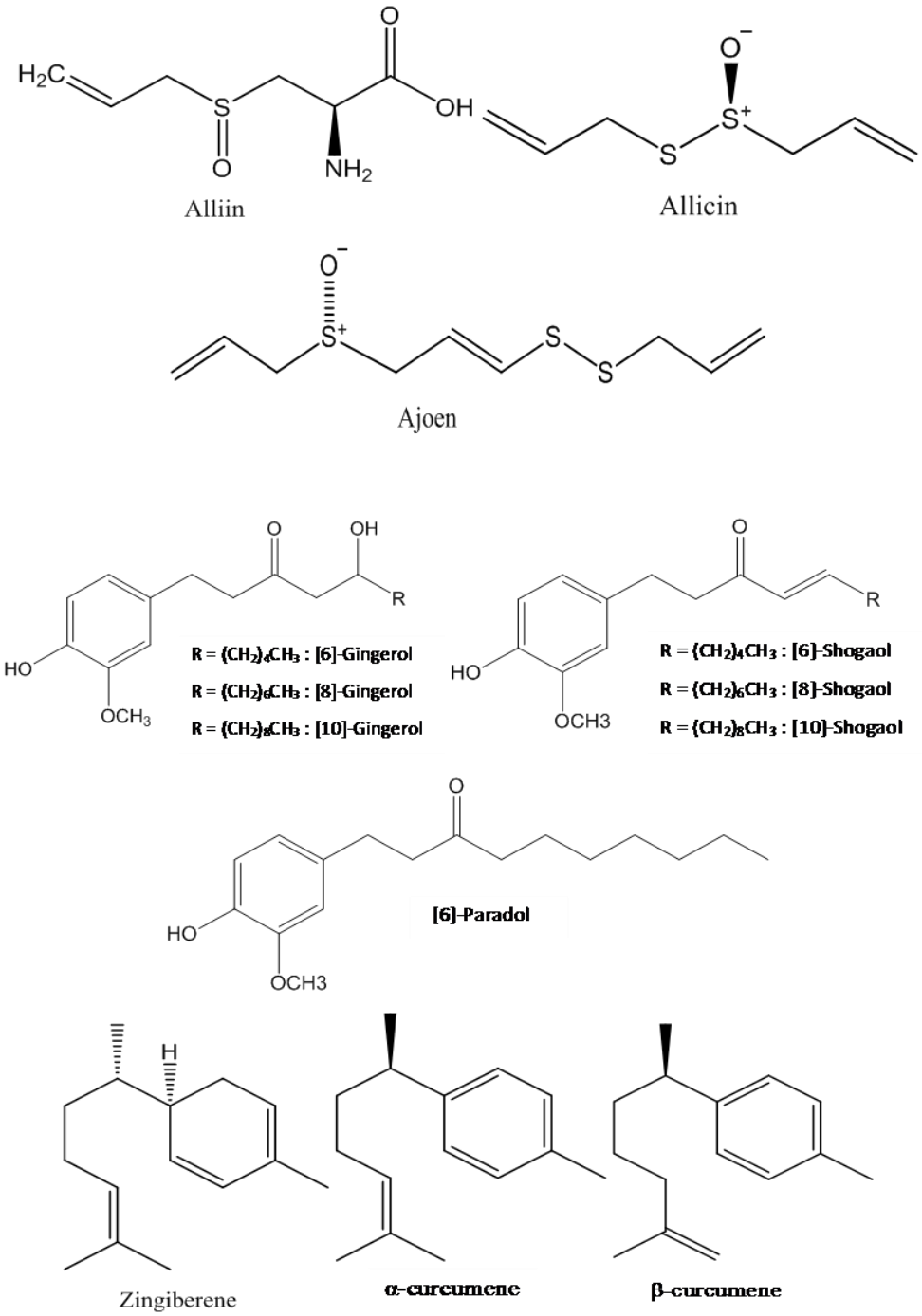

Figure 1 : Chemical structure of some compounds from garlic et ginger

to the presence of numerous bioactive active compounds isolated from rhizomes (Figure 1) such as gingerol, shogaol, [6]-paradol, zingiberene, α-curcumen, β-curcumen, camphene, pinene, limonene, citral, linalooland flavonoids (Rani, 1999); (Parthasarathy et al., 2008). Given to the important place that these two plants occupy in the treatment of certain diseases but also in our diet, it seems important to summarize the scientific evidence that has been reported.

ANTIBACTERIAL ACTIVITY

The fresh, oven- and freeze-dried garlic extracts have been shown to have a wide spectrum of antibacterial activity. Garlic has been reported to inhibit *Aeromonas, Bacillus,*

Clostridium, Cryptocaryon, Escherichia, Helicobacter, Klebsiella, Mycobacterium, Photobacterium, Proteus, Pseudomonas, Salmonella, Staphylococcus, Streptococcus, Citrella, *Citrobacter*, *Enterobacter*, *Escherichia*, *Lactobacillus*, *Leuconostoc*, *Micrococcus*, *Proteus*, *Providencia*, *Serratia*, *Staphylococcus*, *Streptococcus* and *Vibriosp.* (Guo et al., 2015). The incidence of stomach cancer is lower in individuals with a high intake of allium vegetables in developed and developing countries. The antbacterial activity of allium vegetables, particularly garlic, has lead to the investigation of its antimicrobial activity of garlic against *H. pylori* (Sivam, 2001). Garlic has even been shown to be effective on resistant bacterial strains of antibiotics (Sivam, 2001 ; Kyung, 2012). Ginger extract (10 mg/kg) intraperitoneally had a dose dependent anti-microbialactivity against *Pseudomonas aeruginosa, Salmonella typhimurium* and *Escherichia coli*. The leaf and rhizomeoils of *Zingiber officinale* have been shown to be moderately active against the Gram-positive bacteria *Bacillus licheniformis, Bacillus spizizenii* and *Staphylococcus aureus*, and the Gram-negative bacteria *Escherichia coli*, *Klebsiella pneumoniae, Salmonella typhymurium, Pseudomonas aeruginosa* and *Pseudomonas stutzeri* (Ali et al., 2008 ;Sivasothy et al., 2011). According to Mahady et al. (2005), the active constituents of methanol extract of ginger, gingirols, are effective *in vitro* against *Helicobacter pylori*. Park et al. (2008) revealed that the ethanol and *n*-hexane extracts of ginger exhibited antibacterial activities against three anaerobic Gram negative bacteria, *Porphyromonas gingivalis* ATCC 53978, *Porphyromonas endodontalis* ATCC 35406 and *Prevotella intermedia* ATCC 25611, causing periodontal diseases.

ANTIVIRAL ACTIVITY

Alliums are inhibitory against all tested micro-organisms such as, fungi, viruses, and parasites (Kyung, 2012). There is little research on the antiviral activity of garlic, but It was recently shown that garlic extract inhibits the proliferation of influenza virus A (H1N1) and Herpes Simplex viruses *in vitro* with allicin as the main active component (Mehrbod et al., 2009; Goncagul and Ayaz, 2010). However antiviral activity of ginger was proved against various viruses. Antiviral effect of fresh ginger against human respiratory syncytial virus on HEp2 and A549 cell line has been reported (Chang et al., 2013 ; Ahmed et al., 2017). Fresh ginger dose-dependently inhibited HRSV-induced plaque formation in both HEp-2 and A549 celllines . In contrast, dried ginger didn't show any dose-dependent inhibition (Chang et al., 2013). According to Camero et al. (2019) study, ginger essential oil showed a virucidal activity against caprine alpha Herpes Virus-1 (HSV-1) and this activity might rely on the fact that this substance is able to disrupt herpes virus envelope. Ginger aqueous extracts in activated Feline Calici virus, a surrogate for human Norovirus (Aboubakr et al., 2016).

ANTIPARASITIC ACTIVITY

Garlic has activity on parasites such as *Plasmodium* that cause malaria. These results of a study clearly indicate that by adding garlic pearl oil to arteether therapy as a partner drug antimalarial activity can be enhanced. Particularly this combination was successful in avoiding the recrudescence problem which is often the major limiting factor in artemisinin and its derivative based monotherapy (Palakkod et al., 2016). This activity would be due to allicin, acysteine protease inhibitor present in freshly crushed garlic cloves, which significantly inhibits sporozoite infectivity *in vivo* and decreases parasite loads in mice with blood stage infections (Coppi et al., 2006). Other studies have demonstrated the inhibitory activity of garlic against parasites such as *Leishmania donovani et Leishmania infantum*, *Schistosoma mansoni*, *Trichomonas vaginalis* (Corzo-Martínez et al., 2007; Gaafar, 2012; Kamel and El-Shinnawy, 2015).

ANTIFUNGAL ACTIVITY

According to some authors, allicin, essential oil and aqueous or ethanolic extracts from garlic showed very good potential as an antifungal compound against mycoses-causing dermatophytes as *Trichophyton* and candida spp *Candida albicans*, *Candida glabrata, Candida krusei* and *Candida tropicalis* (Khodavandi et al., 2010; Aala et al., 2010; Diba and Alizadeh, 2018). However if allicin in combination with ketoconazole or with fluconazole frequently showed synergistic or additive interactions against dermatomycosis (Aala et al., 2010), no synergy was not demonstrated in the majority of *Candida spp* (Khodavandi et al., 2010). Ginger ethanolic extract as a potential mouthwash has good antibiofilm by fungi and antifungal activity against C. *albicans* and *C. Krusei in* the oral cavity with a greater activity than those of fluconazole and nystatin(Aghazadeh et al., 2016). Activity study of essential oil from *Zingiber officinale* against fluconazole resistant vaginal isolates of *Candida albicans* showed it was effective against all isolates of *Candida albicans* (Mohammadi and Moattar, 2007).

ANTI-INFLAMMATORY ACTIVITY

Garlic extracts have been shown to exert anti-inflammatory effects. Garlic treatment significantly attenuated inflammation and injury of the liver induced by *Eimeria papillata* infections and this anti-inflammatory activity exhibited by garlic oil is mainly through inhibiting the assembly-disassembly processes of the cytoskeleton.

According to the same authors, a sulfur compound isolated from garlic, inhibits neuro inflammation and amyloido genesis through inhibition of NF-κB activity, and thus could be applied for intervention in inflammation-related neurodegenerative diseases including Alzheimer's disease (Hussein et al., 2017). Lee et al. (2012) demonstrated that the sulfur compounds attenuated the LPS-induced expression of the inducible NO synthase (iNOS) and cyclooxygenase-2 (COX-2) proteins and mRNA. Moreover, these sulfur containing compounds suppressed the nuclear factor-jB (NF-jB) transcriptional activity and the degradation of inhibitory jBa in LPS-activated macrophages. Currently ginger is one of the most popular herbal alternative treatments for chronic and painful inflammatory diseases. Aqueous extract of *Zingiber officinale* at different doses (200 mg/kg or 400 mg/kg) showed significant anti-inflammatory activity in the rats model studied, it can be investigated further as a promising anti-inflammatory agent (Zaman and Mirje, 2014). Indeed, ginger suppresses prostaglan dinsynthesis through inhibition of cyclooxygenase- 1 and cyclooxygenase-2 (Grzanna et al., 2005). Otherwise, Funk et al. (2009) demonstrate that gingerol and gingerol derivative containing fractions were most potent in inhibiting PGE2 production.

CARDIOVASCULAR ACTIVITY

Hypercholesterolemia and Oxidation of LDL are a major risk factor for atherosclerosis. Thus a experimental evidence showed that several garlic compounds can suppress LDL oxidation *in vitro* (Lau, 2006). A lot of studies were reviewed for garlic powder supplementation was significantly effective in the reduction of total cholesterol levels in both the lower and higher-dose. The LDL-Cholesterol values were more striking in studies that used a lower dose. However, HDL-Cholesterol level was demonstrated in any study a small increase at higher-dose (Kwak et al., 2014). Otherwise, a systematic review and meta-analysis study suggests that garlic is an effective and safe approach for hypertension. Thus it can be recommended to treat hypertensive patients (Xiong et al., 2015). Regarding the ginger, studies of ginger aqueous extract reported a hypotensive, endothelium dependent, independent vasodilator, hypoglycaemic, hypocholesterolaemic and hypolipidaemic effects of its aqueous extract in rats and guinea-pigs (Ghayur et al., 2005; Al-Amin et al., 2006). Thus, aqueous extract of raw ginger possesses hypoglycaemic, hypocholesterolaemic and hypolipidaemic potential in induced diabetic rats. Activity that has been confirmed to be a dietary supplementation with both of two ginger varieties. This study showed that ginger rhizomes inhibited arginase activity and prevented hypercholesterolemia in high-cholesterol-diet-fed rats (Akinyemi et al., 2016). In animals, ginger significantly lowered serum total cholesterol, LDL, VLDL, triglycerides and phospholipids, reduced atherosclerotic lesions and has a generally dose-dependent hypotensive effect (Nicoll and Henein, 2009).

ANTICANCER ACTIVITY

Epidemiological studies suggest a link between regular and significant consumption of garlic and protection against the development of some cancers. Thus specifically, dark leafy vegetables, cruciferous vegetables, yellow vegetables, beans, onions and garlic, and carrots were associated with a reduced risk of pancreatic cancer (Hsing et al., 2002; Chang et al., 2005). Individual garlic consumption is inversely associated with the risk of pancreatic cancer (Chang et al., 2005). Recently there have been several clinical trials investigating the benefits of ginger for treating colorectal cancer because it can also interfere with several cell signaling pathways that are important in the early development of cancer. Thus, ginger extract taken daily may reduce proliferation in the crypts of normal-appearing colorectal epithelium and increase apoptosis and differentiation of colonic mucosal cells (Citronberg et al., 2013). A recent study report to describe identification and detailed evaluation of *in vitro* and *in vivo* anticancer activity of whole ginger in the therapeutic management of human prostate cancer. He showed that ginger at 100 mg/kg body weight of whole ginger extract inhibited the growth and progression of xenografts of human prostate cancer cells in mice (Karna et al., 2012). The anticancer properties of ginger are attributed to the presence of certain compounds like the [6]-gingerol, paradol, shogaols, zingerone etc. Gingerol seems to be the most important compound. It has been reported to inhibit in laboratory animals, the promotion of skin carcinogenesis, the growth of human colorectal cancer cells, the tumor growth and pulmonary metastasis (Shukla and Singh, 2007). The anticancer efficacy of [6]-gingerol for the prevention of colorectal cancer progression is linked to its target, theleukotriene A4 hydrolase (LTA4H) protein (Jeong et al., 2009). A recent study showed that the [6]-gingerol has potential to bind with DNA and induce cell death by autophagy and caspase 3 mediated apoptosis (Chakraborty et al., 2012).

TOXICITY AND ADVERSE EFFECTS

A recent studies evaluated the acute toxicity of garlic. The aqoeus extract induced behavioural signs like loss of appetite, depression, partial paralysis and death at the higher doses (3200 and 4200 mg/kg but, there was no death recorded in experimental rabbits given 300 - 2200 mg/kg. LD50 was found to be 3034 mg/kg and maximum tolerated dose was 2200 mg/kg (Mikail, 2010). This has been confirmed by Lawal et al. (2016) study that animals

were apparently healthy with no sign of toxicity up to the dose of 2500 mg/kg. However, at 5000 mg/kg, animals were weak and had intense ethrematachy-cardia and disorientation but no death was recorded. Several studies have demonstrated that consumption of excessive amounts of these vegetables, especially when the stomach is empty, can cause burning sensations and diarrhea, flatulence and changes in the intestinal flora. Garlic odor on the breath and skin, allergic reactions, contact dermatitis, and bronchial asthmamayals ooccur. Garlic may increase the risk of bleeding after surgery (Amagase, 2006; Corzo-Martínez et al., 2007; Scharbert et al., 2007; Fukao et al., 2007). Toxicity assessment of ginger in volunteers showed no signs of toxicity. The main toxic effects associated with oral treatment were minor gastrointestinal upsets, including eructation, heartburn, and indigestion (Zick et al., 2008). Subacutetoxicity study in albino rats noticed that ginger administration was not associated with any mortalities and abnormalities in general conditions, behavior, growth, food and water consumption except for that the animals were calmer than their control (Amin and Hamza, 2006). A study concluded that the ginger preparation, when administered by oral gavage to pregnant rats during the period of organogenesis, caused neither maternal nor developmental toxicity at daily doses of up to 1000 mg/ kg body weight (Ali et al., 2008). Adverse effects after ingestion of ginger are uncommon, but they can include mild gastrointestinal effects such as heartburn, diarrhea, and irritation of the mouth. Ginger has been reported to have positive inotropic effects in animal models and has also led to case reports of arrhythmia (White, 2007). However, ginger can be known as a highly effective treatment in the reduction of menstrual blood loss (Kashefi et al., 2015).

CONCLUSION

Garlic and ginger have in common many pharmacological properties such as anti-infective activity, anticancer, anti-inflammatory and cardiovascular. Thus, the use of their extracts in combination form could result in a synergistic beneficial effect against certain pathologies. Moreover, they show no major adverse effects and studies show no toxicity at usual doses. Garlic and ginger are therefore potential sources of drugs for the treatment of several diseases.

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Cite this article as:

Dieng SIM, Bah F, Sarr A, Konde LH, Fall AD (2021). Pharmacological properties and toxicity of Garlic and Ginger: A review. Acad. J. Med. Plants. 9(12): 185-190.

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