



## Antiviral Activity, Phytochemistry and Toxicology of Some Medically Interesting Allium Species: A Mini Review

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### Authors' contributions

This work was carried out in collaboration of all authors. Authors PTM, DDT, DSTT and KNN wrote the first draft of the manuscript. Authors CMF, EML, CLI, EMN, BZG, JTK and DTM collected information on plants bioactivity. Authors CMM, AM, SOM and GNB collected information on plant phytochemistry. All authors read and approved the final manuscript.

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### ABSTRACT

**Aims:** COVID-19 pandemic affects hundreds of thousands of people worldwide. Since there is no effective treatment, the need of finding alternative methods, which can help to curb this pandemic is urgent. This study aims to collect the information on the virucidal and toxicity properties of the

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*Allium* species. This genus is known to be source of nutraceuticals and also used as food. In this context, species of this genus can be proposed as an alternative solution against COVID-19.

**Methodology:** The literature review was conducted on *Allium spp* during searches on different databases such as PubMed, PubMed Central, Science Direct, Scielo, DOAJ, Science alert and Google scholar. The scientific names of *Allium* species, antiviral compounds, antiviral activity and toxicology of the plants of interest were used as keywords. Mendeley was used to make bibliographic references and the chemical structures of the natural compounds from *Allium* genus were drawn using ChemBioDraw Ultra 12.0 software.

**Results:** The findings from literature review showed that the *Allium* genus has demonstrated antiviral activity on several types of virus (Herpes simplex virus type 1, Herpes simplex virus type 2, Human immunodeficiency virus, Influenza virus, Cytomegalovirus, Human papillomavirus, Vesicular stomatitis virus, vaccinia virus, and human rhinovirus type 2 human cytomegalovirus). The species of this genus have also been used as food. Some species of *Allium* genus contain minerals such as Zinc, which have shown an effect on SARS-CoV-1, and could be involved in account for the reported antiviral effect.

**Conclusion:** Edible *Allium* species could be used in the management of COVID-19. Molecular docking of main molecules of *Allium* species with SARS-CoV-2 protease is in progress.

**Keywords:** *Allium* species; antiviral activity; SARS-CoV-2; COVID-19.

## 1. INTRODUCTION

Coronaviruses (CoV) are a large family of viruses that cause illness ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV). The current novel coronavirus (nCoV) is a new strain that has not been previously identified in humans [1].

The COVID-19 pandemic is the defying global health crisis of this new decade and constitutes the greatest challenge we have faced since the Second World War. Since its emergence in Asia late last year, the virus has spread to every continent except in Antarctica.

In view of the collateral damage caused by this virus, most countries have embarked on in-depth research with a view to find a life-saving solution; in order to respond and recover from this pandemic.

Thus, several research studies have demonstrated the validity of the pharmacopoeia in the fight against this viral monster. In fact, medicinal plants have been widely used in African and other countries around the world for many years, and are still being used as an important source of antiviral therapeutic agents for the treatment of infectious diseases [2,3]. The role of traditional medicine in the treatment of COVID-19 has recently been reported [4]. In addition, it has also been shown that medicinal plants are an important source of molecules having pharmacological properties, including

antiviral properties that can be used in the search for the solution to COVID-19 [5].

Furthermore, *Allium* species have been used intensively in traditional foods and as anti-infectious agents in traditional medicine. For instance, garlic (*Allium sativum* L.) and onions (*Allium cepa* L.) have long been used as food but also as spices in most of African recipes especially in the Congolese food system and for the treatment of many diseases [6]. While other *Allium* species such as leek (*Allium porrum* L.) and shallots (*Allium ascalonicum* L.) are also rich sources of volatile and non-volatile chemicals, particularly quercetin. Some other compounds such as allicin, diallyl trisulfide and ajoene, derived from garlic extracts have been shown to have antiviral activity [7]. Previous studies have also shown that onions are characterized by the highest content of flavonoids (including quercetin and its derivatives) and several other studies reported the antiviral activity of quercetin. As Onions contain also quercetin, this may be the main active principle which confers the antiviral potential to this genus [7].

The current study aims to review the literature on the virucidal and cytotoxic properties of *Allium* species considered as nutraceuticals. The found data would make it possible to use these edible *Allium* species for the management of COVID-19.

## 2. METHODOLOGY

Different databases such as PubMed, PubMed Central, Science Direct, Scielo, DOAJ, Science

alert and Google scholar were used to constitute the bibliography. The scientific names of *Allium* species, antiviral compounds, antiviral activity and toxicology of the plant of interest were used as keywords. Mendeley was used to make bibliographic references and the chemical structures of the natural compounds from *Allium* genus were drawn using ChemBioDraw Ultra 12.0 software.

### 3. PHYTOCHEMISTRY AND PHARMACOLOGY OF ALLIUM SPECIES

#### 3.1 Overview of *Allium spp*

*Allium* species have been used for centuries for their exceptional flavour as vegetables and spice besides being valued as ornamentals while in ethnomedicine, they are used for the prevention of various diseases. Members of the *Allium* genus are known for their sulphur compounds enriched in volatile oils [8] which imparts a unique taste to different species [9]. Apart from sulphur compounds, species of *Allium* genus contain many other important chemical constituents like anthocyanins, flavonoids, phenols, tannins and carotenoids [10]. Various pharmacological activities of *Allium* species including antioxidant, anti-inflammatory, antimicrobial, anticancer, antiviral, anticoagulant, neuroprotective, immunomodulatory, antitubercular and anti-allergy were attributed to the presence of the aforementioned key compounds [11].

#### 3.2 *Allium cepa* L.

Fig. 1 gives images of *Allium cepa* L or onion

##### 3.2.1 Phytochemistry

Onion contains 89% water, 1.5% protein, 4% sugar, 2% fiber, 0.1% fat, and vitamins B1, B2, B3, B5, B9 and C, along with potassium, calcium and selenium. Onion also contains important dietary polysaccharides such as fructosans, saccharose, peptides, flavonoids (mostly quercetin), and essential oils. Quercetin glycosides are heat-stable and show chemopreventive activity. Onion contains numerous sulfur compounds, including thiosulfonates and thiosulfonates; cepaenes; S-oxides; Sulphur, S-dioxides; mono-, di-, and trisulfides; and sulfoxides, which inhibit cell growth of cancer cells through induction of DNA damage mediated G2/M arrest and apoptosis [12].

Several phytochemical studies have been carried out on *A. cepa* L, and it has been found to

harbour a myriad of compounds responsible for its particular flavour and medicinal properties. Among the different classes of phytochemical constituents, phenolic compounds have received much attention thanks to their contribution to the biological properties of medicinal plants. A study was conducted on four varieties of *A. cepa* L. (red, purple, white and green) for their respective phenolic composition by high performance liquid chromatography (HPLC) and led to the identification of Ferulic acid, gallic acid, protocatechic acid, quercetin and kaempferol. There were significant variations in the number of phenolic compounds in each variety as follows: ferulic acid (13.5-116 µg/g), gallic acid (9.3-354 µg/g), protocatechic acid (3.1-138 µg/g), quercetin (14.5-5110 µg/g), and kaempferol (3.2-481 µg/g). In addition, a number of flavonoids were also detected in different varieties of onion, namely: quercetin aglycone, quercetin-3,4'-diglucoside, quercetin-4'-monoglucoside, quercetin-3-monoglucoside, quercetin 3-glycosides, delphinidine 3,5-diglycosides [13], quercetin 3,7,4'-triglucoside, quercetin 7,4'-diglucoside, quercetin 3,4'-diglucoside, isorhametine 3,4'-diglucoside. Compared to other vegetable and fruit species, *A. cepa* L has a quercetin content (300 mg kg<sup>-1</sup>) 5 to 10 times higher than broccoli (100 mg kg<sup>-1</sup>), apple (50 mg kg<sup>-1</sup>) and blueberry (40 mg kg<sup>-1</sup>) [14]. Some other studies have identified various anthocyanins in onions: cyanidin 3-O- (3"-O-β-glucopyranosyl-6"-O-malonyl-β-glucopyranoside)-4'-O-β-glucopyranoside, cyanidine 7-O-(3"-O-β-glucopyranosyl-6"-O-malonyl-β-glucopyranoside)-4'-O-β-glucopyranoside, cyanidine 3,4'-di-O-β-glucopyranoside, cyanidin 4'-O-β-glucoside, peonidin 3-O-(6"-O-malonyl-β-glucopyranoside)-5-O-β-glucopyranoside and peonidin 3-O-(6"-O-malonyl-β-glucopyranoside), which were present in trace amounts in the pigmented parts of red onion.

Vazquez-Armenta et al. [15] identified dipropyl disulphide and dipropyl trisulphide as the main constituents of onion. A class of biologically active organo-sulphur compounds, S-allyl-L-cysteine sulphoxides (such as alliin and γ-glutamylcysteine) were dominant. During the milling of the plant material, allicin, methionine, propiin, iso-alliin and fat-soluble sulphur compounds (such as, diallyl disulphide) are released and are responsible for the smell and taste of fresh onions. It has been assumed that the irritant and lacrimation factor released by the chopped onion is produced spontaneously as a result of the action of the enzyme alliinase [16].



**Fig. 1. *Allium cepa* L**

Meanwhile, several disulfide radicals (allyl, methyl, propyl) have been found in red onion varieties by TLC using dichloromethane extraction. Quantitative analysis showed that di- and trisulphides, such as cis- and trans-methyl-1-propenyl disulphide, methyl-2-propenyl disulphide, dipropyl disulphide, cis- and trans-propenyl disulphide, methyl-propyl trisulphide and dipropyl trisulphide, were abundant and accounted for about 60% of the sulphur compounds [17].

### 3.2.2 Antiviral activity

The antiviral activity of extracts from five *Allium* plants (shallot, garlic, onion, leek and green onion) and pure compounds of quercetin, zalcitabine (ddC), and allicin against adenovirus was assessed. Regarding the antiviral activity of ddC, both MTT and PRD (plate reduction) methods showed a high correlation ( $R^2 = 0.8952$ ) without significant difference (paired t-test,  $p > 0.05$ ). Most of the *Allium* plants tested were non-toxic to human lung carcinoma cells (A549), and shallots had the highest level of antiviral activity for ADV41 and ADV3, followed by garlic and onions. Shallots had the highest level of antiviral activity against ADV3 and ADV41 infection between 0 and 2 h, during the first replication period of the virus. The MTT test with A549 cells was shown to be a rapid and sensitive test system for the detection of anti-adenoviral drugs. The potential of shallots for the treatment of adenoviral infections deserves further study [7].

Several studies suggest that flavonoids have long been known to be very effective against viruses. Many scientists have proven that flavonoids have antiviral activity and that they can serve as inhibitors to kill viruses [18]. The mechanism of viral growth inhibition consists of blocking and destroying viral protein and nucleic

acid synthesis [19]. Phytochemicals in onions, such as quercetin and kaempferol, play an important role in reducing the growth of various viruses [20]. Moreover, quercetin and kaempferol have been shown to have virucidal activity against herpes simplex virus type 1, rabies virus, poliovirus, meningitis virus, rabies pseudovirus, sindbis virus and para influenza virus type 3 [21]. Yet, cell culture data have shown that quercetin flavonol can inhibit the replication of various respiratory viruses, thereby reducing their numbers [22].

The antiviral activities of various commercial garlic products, including garlic powder tablets and capsules, oil-macerated garlic, steam-distilled garlic oils, garlic aged in aqueous alcohol and fermented garlic oil, against herpes simplex virus Types 1 and 2, influenza A and B viruses, human cytomegalovirus, vesicular stomatitis virus, rhinovirus, human immunodeficiency virus (HIV), viral pneumonia and rotavirus, have been studied. Antiviral activities of these commercial products seem to be dependent on their preparation process and those products with the highest levels of allicin and other thiosulfinates, mainly DADS, DATS and ajoene, have the best antiviral activities [23]. In addition to sulphur compounds, it has been reported that quercetin, the major onion flavonoid, also possesses antiviral activity and enhances the bioavailability of some antiviral drugs. Lectins are a very heterogeneous group of glycoproteins with the ability to recognize and bind specifically to carbohydrate ligands. Onion lectins, unlike the garlic lectins, have a pronounced anti-HIV activity [7].

### 3.3 *Allium sativum* L.

Fig. 2 displays images of *Allium sativum* or garlic.



**Fig. 2. *Allium sativum***

### 3.3.1 Phytochemistry

The nutritional value of the edible parts of *A. sativum* L. has been reported as 410.7 kcal/100 g with 33 g of carbohydrates, 0.34 g of fat, 9.26 g of proteins, 1.2 mg of vitamin B6, 5.29 mg of iron, 36.3 mg of calcium, and 600.9 mg of phosphorus. Garlic bulb contains water (65%), carbohydrates (28%), organosulfur compounds (2.3%), proteins (mostly allinase; 2%), amino acids (1.2%), and fiber (1.5%). Fresh or crushed garlic contain sulfur-containing compounds enzymes, saponins, and phenolics [24].

### 3.3.2 Antiviral activity

The antiviral activity of hydro-distilled essential oils of *Allium sativum* L. (bulbs) against (HSV1) was tested by using cytopathicity (CPE) assay. African green monkey kidney (Vero) cell line (virus infected cells) was incubated with different levels of essential oils. The antiviral activities were increased with increasing essential oils concentrations. The additions of 200, 500 and 1000 µg/mL of garlic essential oils increased antiviral activity percentages to 37.66, 72.94 and 93.81%, respectively [25]. Nagai reported that garlic extract has preventive effect against infection with influenza virus and possesses the antiviral activity against the human cytomegalovirus, influenza B, herpes simplex virus type 1, herpes simplex virus type 2, parainfluenza virus type 3, vaccinia virus, vesicular stomatitis virus, and human rhinovirus type 2 [26]. Ajoene was found to block the integrin-dependent processes in a human immunodeficiency virus-infected cell system [27]. The antiviral effect of diallyl thiosulfinate (allicin), allyl methyl thiosulfinate, methyl allyl thiosulfinate, ajoene, alliin, deoxyalliin, diallyl disulfide, and diallyl trisulfide was determined against selected viruses including, herpes simplex virus type 1, herpes simplex virus type 2, parainfluenza virus type 3, vaccinia virus, vesicular stomatitis virus, and human rhinovirus type 2. The order for virucidal activity was generally as follows: ajoene > allicin > allyl

methyl thiosulfinate > methyl allyl thiosulfinate. Ajoene was found in oil-macerates of garlic but not in fresh garlic extracts. No activity was found for the garlic polar fraction, alliin, deoxyalliin, diallyl disulfide, or diallyl trisulfide. Fresh garlic extract, in which thiosulfates appeared to be the active components, was virucidal to each virus tested. The predominant thiosulfinate in fresh garlic extract was allicin. Lack of reduction in yields of infectious virus indicated undetectable levels of intracellular antiviral activity for either allicin or fresh garlic extract [23].

The *in vitro* antiviral activity of garlic extract (GE) on human cytomegalovirus (HCMV) was evaluated by tissue culture, plaque reduction and early antigen assay. A dose dependent inhibitory effect of GE was evident when GE was applied simultaneously with HCMV. But the effect was stronger when the monolayers were pretreated with GE. In addition, the antiviral effect of GE persisted long in infected cells after its being removed from the culture medium. The strongest antiviral effect of GE was demonstrated when it was applied continuously [28]. *Allium sativum* L. extraction has been reported having anti-HCMV efficacy by a mechanism associated with suppression of the gene transcription. The effect of allitridin (diallyl trisulfide, a compound from *A. sativum* L. extraction) on the replication of HCMV and the expression of viral immediate-early genes was investigated. In HCMV plaque-reduction assay, allitridin appeared to be a dose-dependent inhibitory ability with EC<sub>50</sub> value of 4.2 microg/mL. Time-of-addition and time-of-removal studies showed that allitridin inhibited HCMV replication in earlier period of viral cycle before viral DNA synthesis. Both immediate early gene (ie1) transcription and IEA (IE(1)72 and IE(2)86) expression was suppressed by allitridin. Furthermore, allitridin displayed a stronger inhibition on IE (2)86 than on IE (1)72. Decrease of viral DNA load in infected cells was also detected under allitridin treatment, probably due to an indirect consequence of the reduction in ie gene transcription [29]. Allitridin can inhibit

HCMV, IEA expression *in vitro* was remarkable which is probably one of the major mechanisms of Allitridin anti-HCMV activity because IEAs are the very important regulatory factors for the expression of all HCMV genes.

The cytotoxicity of Allitridin was evaluated through MTT colorimetry and cell morphology. HCMV IEA levels were quantitatively detected by Flow Cytometry. Allitridin was given before (pre-treated for 24 h), during, or after viral inoculation in which serial doses (maximum tolerant concentration, MTC for human embryo lung cells, HEL) of Allitridin was used to treat HCMV infected HLE cells for different durations (24, 48, 72, 96 h) after viral infection. The MTC of Allitridin was  $9.60 \text{ mg} \times \text{L}^{-1}$ . Allitridin remarkably inhibited the expression of HCMV IEA *in vitro*. Within MTC, the inhibitory rate had a significant correlation with its dosage ( $r = 0.96$ ). At the time of IEA highest expression (72 h after infection), inhibitory effect was the highest (inhibitory rate: 89.3%). With pre-treatment of Allitridin, the inhibitory rate was 28.6%. When Allitridin was used together with HCMV inoculation, IEA inhibitory rate was only 10.3% [30, 31]. Garlic inhibited CBV3 and ECHO11 at the concentration ranging from 2.5 micrograms/mL to 7.5 micrograms/mL and 5 micrograms/mL was the most effective [32].

The antiviral activity of garlic extracts has been evaluated against influenza B, human rhinovirus type 2, human cytomegalovirus (HCMV), Parainfluenza virus type 3, herpes simplex type 1 and 2, vaccinia virus, and vesicular stomatitis virus [33]. Interestingly, *in vivo* experiment exhibited the antiviral activity of garlic extract and it was reported that garlic showed protective activity against influenza viruses by improving the production of neutralizing antibodies when given to mice and this activity was based on the presence of several phytochemicals namely, ajoene, allicin, allyl methyl thiosulfinate, and methyl allyl thiosulfinate [34]. Allicin acts by preventing several thiol enzymes, while ajoene's antiviral activity was due to the prevention of adhesive interaction and fusion of leukocytes. Moreover, DATS was active against the HCMV replication and viral immediate-early gene expression and it acts by enhancing natural killer-cell (NK-cell) activity that destroys virus-infected cells [35-36].

### 3.3.3 Toxicity

Garlic generally poses little in terms of safety issues though some side effects have been

reported. Garlic may interact with warfarin, antiplatelets, saquinavir, antihypertensives, calcium channel blockers, and quinolone family of antibiotics, such as ciprofloxacin and hypoglycemic drugs. Isolated cases of tropical garlic burns and anaphylaxis were reported. In fact, one of garlic's adverse local effects is contact dermatitis [37]. Garlic application usually results in local inflammation, but, if applied under a pressure bandage, or if there is poor wound care or a secondary infection, it can cause a severe dermal reaction and a deep chemical burn [38]. Three patients were reported in the Department of Plastic Surgery, Assaf Harofeh Medical Center, Zerifin in Israel for suspected self-inflicted lower extremity burns caused by garlic. In a two case report in China, an anaphylactic reaction and a food dependent exercise-induced anaphylaxis caused by eating fresh younger garlic was reported in two patients sensitized to Artemisia pollen [39]. Even though not common, garlic allergy has been attributed to the protein alliin lyase, which was reported to induce immunoglobulin E (IgE)-mediated hypersensitivity responses from skin prick testing [40]. Garlic intake has been reported to be associated with decreased platelet aggregation and bleeding events [41], explaining why it is generally cautioned against using garlic while using anticoagulant therapy [42] as well as other medications.

### 3.4 *Allium schoenoprasum* L.

Fig. 3 gives an image leaves and flowers of *Allium schoenoprasum* L



Fig. 3. *Allium schoenoprasum* L.

*Allium schoenoprasum* L also called Arsenic or Chive is used as a condiment which provides a more delicate flavour than the other *Allium*

species. The young leaves and bulbs are eaten as salad and used in cookery [43]. In China, chives is often served with fish and are used to garnish several food items such as cookies, buns, pancakes, dumplings and also in many dairy and meat products. In Indonesia, As is used as a traditional drug for antihypertensive actions. In East Asia, this species is used to relieve cold, flu and lung congestion. As is used to alleviate the pain from sunburn and sore throat. Chives stimulate appetite and aids digestion [43].

### 3.4.1 Phytochemistry

Chives contain a variety phytochemical components especially phenolic compounds, flavonoids, anthocyanins, steroids, sulphur compounds, and miscellaneous essential oils. It also has minerals like calcium, iron, magnesium, phosphorus, potassium, sodium, zinc, copper, manganese and selenium. Besides, it contains a variety of vitamins such as vitamin A/C/E/K, B6, (B2), Thiamin, Niacin (B3), Pantothenic acid (B5), Total Folate(B9) and  $\beta$ -carotene ; Lipids : Total saturated fatty acids, total monounsaturated fatty acids, total polyunsaturated fatty acids and phytosterols. The following arsenal of amino acids : tryptophan, threonine, Isoleucine, Leucine, Lysine, Methionine, Phenylalanine, Tyrosine, Valine, Aspartic acid, Arginine, Histidine, Glycine, Proline and Serine are found in this species [43].

### 3.4.2 Pharmacological activities

*Allium schoenoprasum* L. (chive) is an herbaceous perennial plant grown for its leaves which are used for both culinary and medicinal purposes. Chives have a beneficial effect on the circulatory system by lowering the blood pressure, and they have antimicrobial activity, especially antifungal, and antioxidant, and antiviral properties. The pharmacological effects are due to diallyl sulfides (diallyl monosulfide, diallyl disulfide, diallyl trisulfide, diallyl tetrasulfide), flavonoids, vitamin C, and carotenoids [44]. Scientific evaluation of chives validates its traditional claims and demonstrates diverse pharmacological potentials including an anti-inflammatory, anticancer, antioxidant, antihelminthic and antihypertensive [43]. In Malaysia this plant species is failing to show either antiviral or cytotoxic activity against herpes simplex virus-type 1 and vesicular stomatitis virus [45].

### 3.5 *Allium fistulosum* L.

Fig. 4 displays images of *Allium fistulosum* L or Welsh onion.

*Allium fistulosum* L. is a very popular vegetable in East Asian countries, and it has been recorded as a crude drug in oriental medical dictionaries for abdominal pain and phlegmon. In addition, Welsh onion has been used as a folk remedy for the common cold in Japan. These traditional usages of *A. fistulosum* L. suggest that it might contain active substances that contribute to the prevention and/or cure of respiratory infectious diseases, including flu [46].

#### 3.5.1 Phytochemistry

The structure of the fructan was characterised and elucidated by chemical and spectroscopic analyses. The fructan was composed of terminal (21.0%) and 2,1- linked  $\beta$ -D-Fruf residues (65.3%) with 1,6-linked  $\beta$ -D-Glcp residues (13.7%). The molecular weight of the polysaccharide and polydispersity was estimated to be 1.5-103 and 1.18, respectively [46].

#### 3.5.2 Pharmacological activity

The antiviral activity of fructan was evaluated *in vitro*. The results revealed that fructan did not show the antiviral activity against influenza A virus *in vitro*, on the contrary it demonstrated an inhibitory effect on virus replication *in vivo* when it was orally administered to mice. In addition, the polysaccharide enhanced the production of neutralising antibodies against influenza A virus. Therefore, the antiviral mechanism of the polysaccharide seemed to be dependent on the host immune system, i.e., enhancement of the host immune function was achieved by the administration of the polysaccharide [46].

### 3.6 *Allium vineale* L.

Fig. 5 gives images of *Allium vineale* L.

*Allium vineale* L. has been used as a substitute for *A. sativum* L. in cooking; the bulb is used as a flavouring agent and the leaves as an addition to salad [47,48]. Cherokee Native Americans used both *A. vineale* L. and *A. sativum* L. as carminatives, diuretics, and expectorants [49].

#### 3.6.1 Phytochemistry

Gas chromatographic analysis of *A. vineale* L. essential oils showed that the major components were sulfur-containing compounds allyl methyl trisulfide (7.9–13.2%), allyl (*E*)-1-propenyl



**Fig. 4. *Allium fistulosum* L**



**Fig. 5. *Allium vineale* L.**

disulfide (7.9–12.5%), dimethyl trisulfide (4.3–17.4%), diallyl disulfide (4.4–12.2%), diallyl trisulfide (2.8–10.5%), and methyl (*E*)-1-propenyl disulfide (2.6–12.5%). The high proportion of sulfur containing components (ranged between 74.9 and 91.6%) [50,51].

Antiviral activity of some species of *Allium* genus is summarized in (Table 1).

#### **4. DISCUSSION**

Natural products provide a rich resource for novel antiviral drug development. In this brief report, we summarize the antiviral activities from *Allium* genus, which has been used as

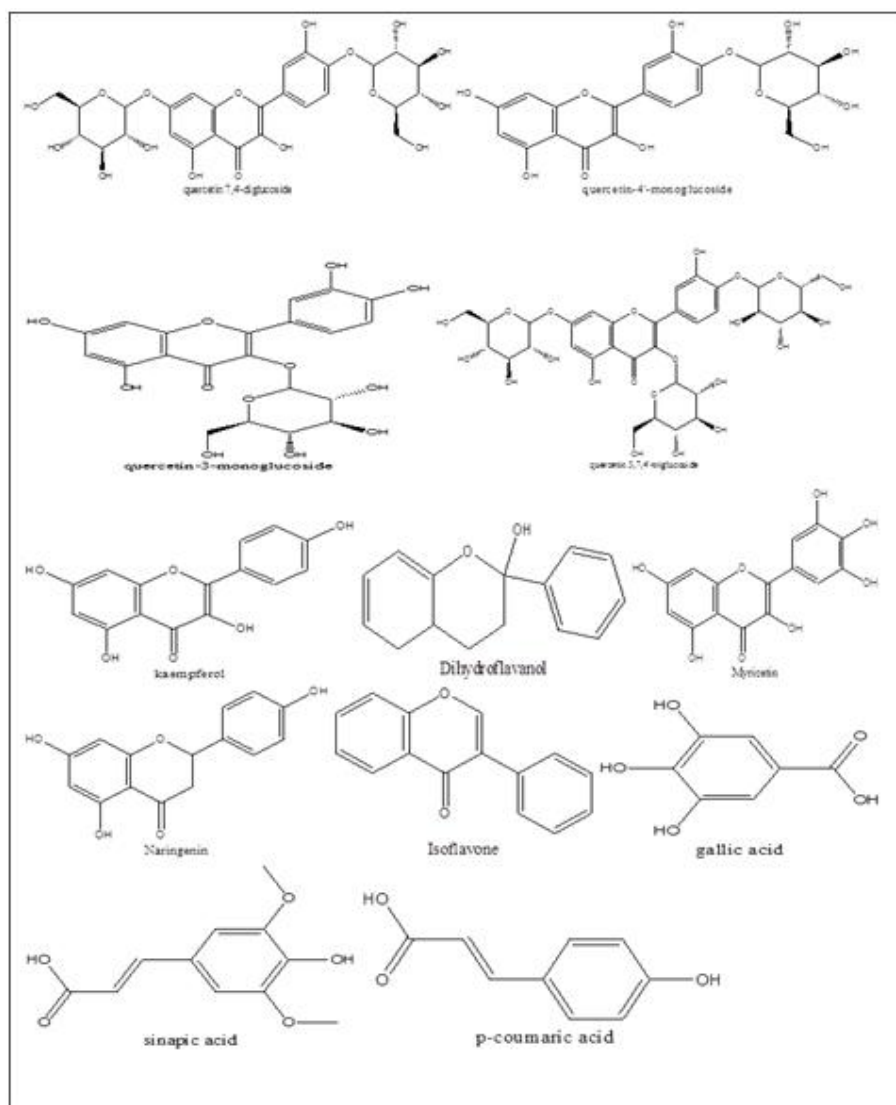
nutraceuticals and against some notable viral pathogens [4, 6]. To this end, *Allium* genus is a high-potential anti-COVID-19 plant nutraceutical candidate for the management of this disease in DRC. Species of the *Allium* genus have many uses in traditional foods and medical applications as anti-infectious agents. These data pave the way for research on anti-COVID-19 herbal medicines. Indeed, in addition to its secondary metabolites endowed with virucidal properties, some species of the *Allium* genus contains zinc [40]. This chemical element, although indispensable as an enzymatic co-factor, a slight increase of the intracellular concentration inhibits the replication of retroviruses including SARS-CoV-1 [4].



**Table 1. Antiviral activity of some species of Allium genus**

Species	Vernacular name	Type of virus	Target viruses	Compounds	Mecanism of action	Reference
<i>Allium fistulosum</i> L.	Ndembi (lingala), bola, niasibola (kikongo), ciboule (french), welsh onion (english)	Enveloped RNA virus	Influenza virus	The fructan was composed of terminal and 2,1-linked b-D-Fruf residues with 1,6-linked b-D-Glcp residues.	inhibitory effect on virus replication in vivo	[42]
<i>Allium thunbergii</i> L.	Thunberg garlic (english), oignon ornamental (french)	Non-enveloped DNA virus	Adenovirus types 3 and 41	Quercetin, diallyl thiosulfinate (allicin)	Inhibitory effet on virus replication	[7]
<i>Allium sativum</i> L.	Ail (french), garlic (english)	Enveloped RNA virus Non-enveloped RNA virus Enveloped DNA virus	Herpes simplex virus type 1 and 2, parainfluenza virus type 3, vesicular stomatitis virus, vaccinia virus, and human rhinovirus type 2 human cytomegalovirus.	Allitridin, diallyl thiosulfinate (allicin), allyl methyl thiosulfinate, methyl allyl thiosulfinate, ajoene, alliin, deoxyalliin, diallyl disulfide, and diallyl trisulfide, limonene	Inhibitory effet on virus replication as earlier period of viral cycle before viral DNA synthesis; mecanism suppression of gene transcription.	[22,28]
<i>Allium cepa</i> L.	Matungulu (lingala), oignon (french), onion (english)	Enveloped DNA virus	Human immunodeficiency virus	Quercetin, Lectins (heterogeneous)	Suppression of gene transcription, inhibitory effet on virus replication	[7]
		Non-enveloped DNA virus	Adenovirus types 3 and 41	Quercetin, diallyl thiosulfinate (allicin)	Inhibitory effet on virus replication	[7]
<i>Allium ascalonicum</i> L.	Echalote (french), shallot (english)	Non-enveloped DNA virus	Adenovirus types 3 and 41	Quercetin, diallyl thiosulfinate (allicin),	Inhibitory effet on virus	[7,47,48]

Species	Vernacular name	Type of virus	Target viruses	Compounds	Mecanism of action	Reference
				flavone, ascalin, and furostanol saponins	replication	
<i>Allium porrum</i> L.	Poireau, ail poireau (french), leek (english)	Non-enveloped DNA virus	Adenovirus types 3 and 41	Quercetin, diallyl thiosulfinate (allicin)	Inhibitory effet on virus replication	[7]
<i>Alliumschoenoprasum</i> L.	Ciboulette, civette, ciboule ou ail civette (french), chives (english)	Enveloped DNA virus	Herpes simplex virus type 1 and Vesicular Stomatitis Virus	Anthocyanins, namely 3-(3,6 dimalonylglucoside), 3-(6-malonylglucoside), 3-(3-malonyl-glucoside) and 3-glucoside of cyanidin ; quercetin, kaempferol, gallic acid, p-coumaric acid, sinapic acid, isorhamnatin and rutin	Inhibitory effet on virus replication	[40]



**Fig. 6. Structures of antiviral chemical compounds of genus *Allium***

It is now evident that species of the *Allium* genus contains the sulfur compounds and quercetin [49] that prevent chronic diseases such as cancer, cardiovascular disease, inflammation, diabetes, etc. From a biomolecular point of view, these compounds would cause apoptosis of cancer cells (quercetin); sulfur compounds would increase the bioavailability of  $H_2S$  while inhibiting adipogenesis (anti-obesity activity), etc. [50]. Thus, during this period of health crisis, these food plants, especially because of their anti-inflammatory effects, may play an important role in the management of patients with coronavirus related co-morbidities (COVID-19) [51]. Indeed, an infection with COV-SARS2 may

increase the risk of complications. Hence the need for education about these drugs.

Fig. 6 displays some structures of antiviral chemical compounds of *Allium* genus.

## 5. CONCLUSION

The world is going through a major crisis due to COVID-19. This pandemic still has no acceptable remedy. It is therefore important to search for alternative solutions, especially for African countries. *Allium* genus is widely used for its various properties including antiviral activity. The purpose of this work was to do the survey on the

antiviral properties of the *Allium* species. The results obtained show that some *Allium* species possess antiviral properties and which can be used in the management of COVID-19.

The aforementioned results are sufficient proof that the exploitation of the traditional pharmacopoeia has a bright future in store for us, which would be of great benefit in the fight against COVID-19. Edible *Allium* species could be used in the management of COVID-19. Molecular docking of the main molecules of *Allium* species with SARS-CoV-2 protease is in progress

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### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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