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Review

The Phytochemistry and Pharmacology of *Tulbaghia*, *Allium*, *Crinum* and *Cyrtanthus*: 'Talented' Taxa from the Amaryllidaceae

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Abstract: Amaryllidaceae is a significant source of bioactive phytochemicals with a strong propensity to develop new drugs. The genera *Allium*, *Tulbaghia*, *Cyrtanthus* and *Crinum* biosynthesize novel alkaloids and other phytochemicals with traditional and pharmacological uses. Amaryllidaceae biomolecules exhibit multiple pharmacological activities such as antioxidant, antimicrobial, and immunomodulatory effects. Traditionally, natural products from Amaryllidaceae are utilized to treat non-communicable and infectious human diseases. Galanthamine, a drug from this family, is clinically relevant in treating the neurocognitive disorder, Alzheimer's disease, which underscores the importance of the Amaryllidaceae alkaloids. Although Amaryllidaceae provide a plethora of biologically active compounds, there is tardiness in their development into clinically pliable medicines. Other genera, including *Cyrtanthus* and *Tulbaghia*, have received little attention as potential sources of promising drug candidates. Given the reciprocal relationship of the increasing burden of human diseases and limited availability of medicinal therapies, more rapid drug discovery and development are desirable. To expedite clinically relevant drug development, we present here evidence on bioactive compounds from the genera *Allium*, *Tulgbaghia*, *Cyrtanthus* and *Crinum* and describe their traditional and pharmacological applications.

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1. Introduction

Amaryllidaceae belongs to the order Asparagales and consists of bulbous flowering plants separated into three infrageneric ranks: Agapanthoideae, Allioideae and Amaryllidoideae, as delineated by the Angiosperm Phylogeny Group [1]. The term "Amaryllidaceae" is frequently used in either phytochemical or pharmacological literature to refer to plants or alkaloids originating from the subfamily Amaryllidoideae [2,3]. Monocotyledonous plants constitute seventy-nine genera (including *Allium*, *Crinum*, *Cyrtanthus*, and *Tulbaghia*) with over 1000 species [4]. Aside from their broad pantropical distribution, Amaryllidaceae are located in Africa, the Mediterranean Coast and South America, and have high adaptation and speciation [5]. The genus *Allium* is distributed in temperate, arid, semi-arid and subtropical areas such as the Mediterranean region, central Asia, Africa and parts of Europe. As herbaceous geophyte perennials, *Allium* comprises a plethora of species with pungent linear leaves that may or may not arise from a bulb or rhizome [6,7]. The *Tulbaghia* genus, popularly called "sweet garlic", "wild garlic", or "pink agapanthus", is crown shaped with outgrowth or appendages of the perianth and predominantly colonizes the Eastern cape belt of South Africa, and is adapted for growth in areas such as Europe and America [8,9]. The genus *Crinum* encompasses 104 species and appear as showy flowers on leafless stems, which thrive in the tropics and warm temperate parts, specifically Asia, Africa, America, and Australia [10]. *Cyrtanthus* is popularly known as "fire lily" due to its unique rapidly flowering response to natural bush fires. Most species are found in South Africa and play an important role in South African traditional medicine [11].

Amaryllidaceous plants are known for their ornamental, nutritional, and medicinal value. Given their attractive flowering plant-like features, *Crinum* species are prized for their umbel lily-like blossoms in China and Japan [3]. Concurrently, Amaryllidaceae are known for their longstanding exploitation in medicinal therapy owing to their inherent biosynthesis of chemically diverse bioactive compounds with peculiar biological properties. The use of proximate and mineral composition analysis enabled the identification of phytoconstituents [10,12], while in vitro, in vivo, and in silico model systems have permitted the unravelling of intrinsic pharmacological activities of the natural products and other alkaloids isolated from this source [13–15]. Of note, bioactive compounds from Amaryllidaceae possesses a wide range of bioactivities ranging from antioxidant [16,17], anti-inflammatory [16,18], antimicrobial [17], antifungal [19], antiviral [20,21], antiplasmodial [22–24], anticarcinogenic [18,25,26], antispasmodic [1,27], antiplatelet [28], antiasthmatic [29], antithrombotic [30,31], antitumor [25], antihyperlipidemic [25], antihyperglycemic [25,32,33], antiarthritic [25], antimutagenic [16], immunomodulatory [16] and several others [34].

Given the aforementioned biological activities, *Allium*, *Tulbaghia*, *Cyrtanthus* and *Crinum* are utilized in traditional medicinal therapy for varying diseases and conditions [35–41]. For example, *Allium* is used as concoctions, decoctions, extracts, and herbal preparations to treat angina, amoebic dysentery, arthritis, cardiovascular diseases, cholera, catarrh, dysmenorrhea, fever, headaches, hepatitis, stomach disorders, throat infections, and prostatic hypertrophy [30,31,35–38]. The genus *Tulbaghia* has unique pharmacotherapeutic properties and is utilized to manage ailments such as earache, pyrexia, tuberculosis, and rheumatism [9,42]. *Crinum* species are used to treat haemorrhoids, malaria, osteoarthritis, varicosities, wounds, urinary tract infections, and gynaecological remedies [40,41]. *Cyrtanthus* are also employed in the management of ailments associated with pregnancy, as well as cystitis, age-related dementia, leprosy, scrofula, headaches, chronic coughs, among others [43,44]. In modern clinical practice, galanthamine from Amaryllidaceae is a primary choice of drug in managing symptomatic neurological disorders such as Alzheimer's

disease due to its selective inhibitory action on the acetylcholine biosynthetic enzyme, acetylcholinesterase [45]. The pancratistatin phenanthridone class of alkaloids are also promising chemotherapeutic drug candidates with unique cell line-specific antiproliferative properties, conferring a selective advantage for clinical development [46].

Although Amaryllidaceae represents a source of valuable bioactive compounds, developing promising drug candidates into clinically relevant therapeutics has been slow. Similarly, other genera in this family, including *Cyrtanthus*, *Crinum* and *Tulbaghia*, are untapped reservoirs and could serve as an alternative window for novel drug targets and warrant further investigation. This review consolidates evidence on the bioactive compounds from *Allium*, *Tulbaghia*, *Crinum* and *Cyrtanthus* and ascertains their traditional and pharmacological applications. Specifically, bibliographic searches were conducted on multiple standard databases (such as, Scopus, Web of Science, MEDLINE, Sci verse, Embase, Google scholar among others) using MESH and non-MESH terms to retrieve and synthesize relevant publications over the 3-month search period. This review highlights panoply of promising biomolecules from the taxa Amaryllidaceae and their prominent medicinal values. The evidence from this study could hasten drug discovery among the pharmaceutical industries. An update on the natural products from these lesser explored genera could also augment the lean pipeline of novel therapeutics.

2. The Genus *Tulbaghia*

2.1. Botanical Description

Tulbaghia is made up of monocotyledonous species with herbaceous perennial bulbs covered by brown scales and are mostly found in Africa [8]. South African species possess bulb-like corms or rhizomes which are swollen, irregularly shaped and wrapped in dry, fibrous leaves [8]. Members of this genus usually possess a raised crown-like structure or ring at the center of their flower tube [8]. Their seeds are black, flat and elongated with the mature ones having embryos [8]. Examples of species of this genus are *Tulbaghia violacea* (*T. violacea*), *Tulbaghia acutiloba* Harv. (*T. acutiloba*), *Tulbaghia capensis* L. (*T. capensis*) and *Tulbaghia cepacea* L.f (*T. cepacea*) [8].

2.2. Geographical Distribution and Traditional Uses of Tulbaghia Species

With approximately 66 species (https://www.kew.org/science accessed on 22 February 2022) [47], *Tulbaghia* is the second-most species-rich genus within Amaryllidaceae. *Tulbaghia* is a monocotyledonous genus comprised morphologically of herbaceous perennial bulbous species, which produce a variety of volatile sulfur compounds, hence resulting in a distinct pungent garlic odor released by bruised plants [8,48]. The genus was named by Carl Linnaeus after Ryk Tulbagh (1699–1771), a former governor of the Cape of Good Hope in South Africa, where most of the native species are to be found, particularly in the Eastern Cape Province [49]. In addition to South Africa, the genus is widely distributed across southern African countries including Botswana, Lesotho, Swaziland, and Zimbabwe, where the plant is revered in folk medicine being used for the treatment of a plethora of infectious and non-infectious diseases [9] as highlighted in Table 1.

Table 1. Geographical distribution and traditional uses of *Tulbaghia* species.

Plant Species	Geographical Distribution	Traditional Uses	References
T. violacea	Indigenous to the Eastern Cape, KwaZulu-Natal, Gauteng, Free State and Mpumalanga Provinces of South Africa.	The leaves and bulbs are used in the management of fever and colds, tuberculosis, asthma, and stomach problems. The leaves are eaten as vegetables and for the management of oesophageal cancer. It is also used as a snake repellent.	[8,50]
T. alliacea	Native to South Africa and grows mostly in the Eastern Cape and southern KwaZulu-Natal Provinces of South Africa.	Its bruised rhizome is used locally in bathwater to relieve fever, rheumatism, and paralysis, and in small doses as a laxative. *T. alliacea* is used for the management of stomach problems, asthma, and pulmonary tuberculosis. Its rhizome infusion is administered as an enema.	[8,51]

Table 1. *Cont.*

Plant Species	Geographical Distribution	Traditional Uses	References
T. simmleri	Native to the South African Drakensberg mountains growing as isolated plants on rocky ledges.	Bulbs and leaves are used as a remedy for gastrointestinal ailments, enemas, high blood pressure, heart problems, chest complaints, high cholesterol, constipation, rheumatism, asthma, fever, pulmonary tuberculosis, earache, human immunodeficiency virus (HIV), paralysis, and cardiovascular diseases.	[50,52]
T. acutiloba	Found in the rainfall regions of southern Africa, occurring in the Eastern Cape, KwaZulu-Natal, Limpopo, Free State, Gauteng, North West, and Mpumalanga Provinces of South Africa, as well as in Lesotho, Swaziland and Botswana.	*T. acutiloba* leaves are used as a culinary herb and snake repellent. It is used to treat barrenness, flu, bad breath, and as an aphrodisiac. It is also cultivated to keep snakes away from the homestead.	[8]
T. natalensis	Although native to South Africa, but is now grown worldwide.	It is used as a culinary herb and snake repellent.	[53]
T. cernua	Commonly found in the Eastern Cape, Free State, Gauteng, KwaZulu-Natal, Limpopo, Mpumalanga, North West and Western Cape Provinces of South Africa.	It is used for ornamental purposes.	[8]
T. leucantha	Widely distributed in southern Africa including Botswana, Lesotho, South Africa, Swaziland, Zambia, and Zimbabwe.	Its rhizome is scraped clean and boiled in stews or roasted as a vegetable. Its leaves and stems are used as a culinary herb and protective charm.	[53]
T. ludwigiana	Commonly found in the Eastern Cape, KwaZulu-Natal, Northern Provinces of South Africa and in Swaziland.	It is traditionally used as a love charm.	[53]

2.3. Phytochemistry of Tulbaghia

Tulbaghia produces many different classes of compounds with diverse chemical structures dominated by sulfur-containing natural products (Figure 1; Table S1).

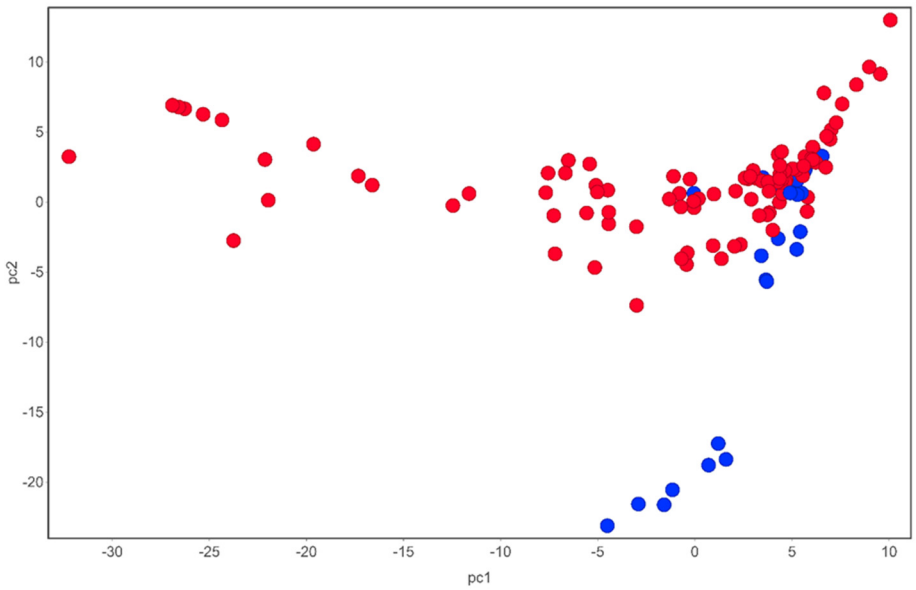

Figure 1. Chemical space of compounds identified from *T. violacea*. Blue circles are sulfur-containing compounds while red circles are compounds devoid of sulfur in their chemical structures. PCA analysis carried out using DataWarrior [54].

Most compounds reported have a small molecular weight (<500) and are of a broad lipophilicity (Figure 2).

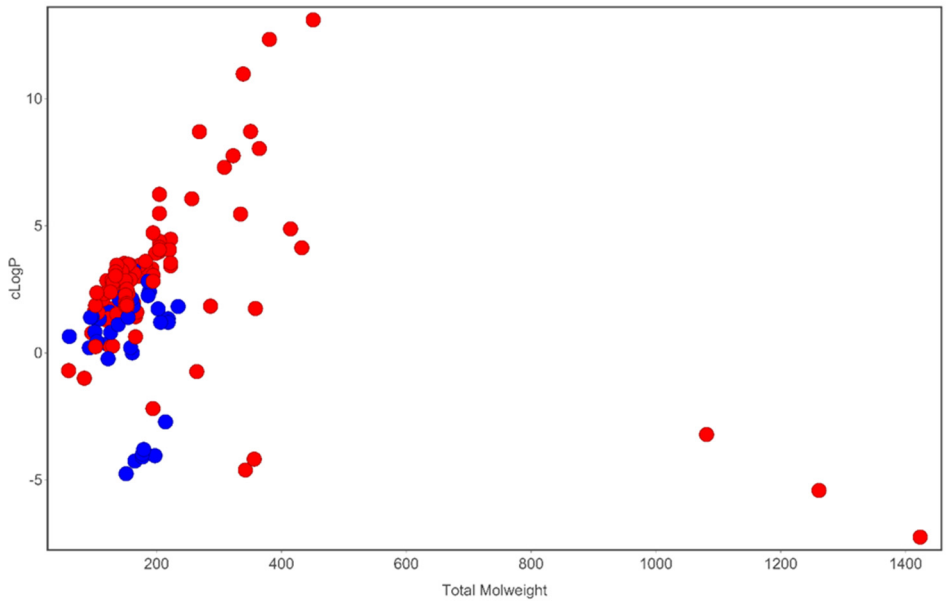

Figure 2. Analysis of cLogP and molecular weight space occupied by compounds identified in *T. violacea*. Blue circles are sulfur-containing compounds while red circles are compounds devoid of sulfur in their chemical structures. Plot generated using DataWarrior [54].

Tulbaghia violacea has been the most widely investigated for its phytochemistry and pharmacological properties. To date, close to 100 compounds have been tentatively identified, largely using gas chromatography techniques, from different parts of this species (Supplementary File S1) [55]. Most prominent are the sulfur compounds with reported broad-spectrum pharmacological activity. The thiosulfinate marasmicin (**1**) is the most prolific antimicrobial compound reported thus far from this genus [56]. This compound is formed from its precursor compound marasmin (**2**), by the enzyme c-lyase. Marasmicin is responsible for the characteristic garlic odor generated by damaged plants [48]. Other notable compounds produced by this species include phenols, tannins and flavonoids [55], which are also responsible for several observed biological activities. Phytochemical characterization has been carried out, albeit minimally for other *Tulbaghia* species particularly *T. alliacea* and *T. acutiloba*. Unlike other genera in Amaryllidaceae, *Tulbaghia* is so far devoid of any alkaloids [57,58]. Despite the extensive in vitro pharmacological screening of extracts of *Tulbaghia*, it is possible that less effort has been made to isolate and identify their active principles. Hence, the phytochemistry of the genus *Tulbaghia* largely remains understudied. The chemicals structurers of noteworthy compounds isolated from *T. violacea* have been represented in Figure 3.

2.4. Pharmacological Studies of Tulbaghia Species

Because of its perceived medicinal value, *Tulbaghia* has received marked interest within the scientific community which has meticulously subjected it to various in vitro and in vivo studies experimentally evaluating its pharmacological activities. The volume of published studies generated from these investigations mirror the distribution of the genus with most articles on *Tulbaghia* having emerged from South Africa (Table 2), a country highly rich in this genus both in terms of species diversity and abundance.

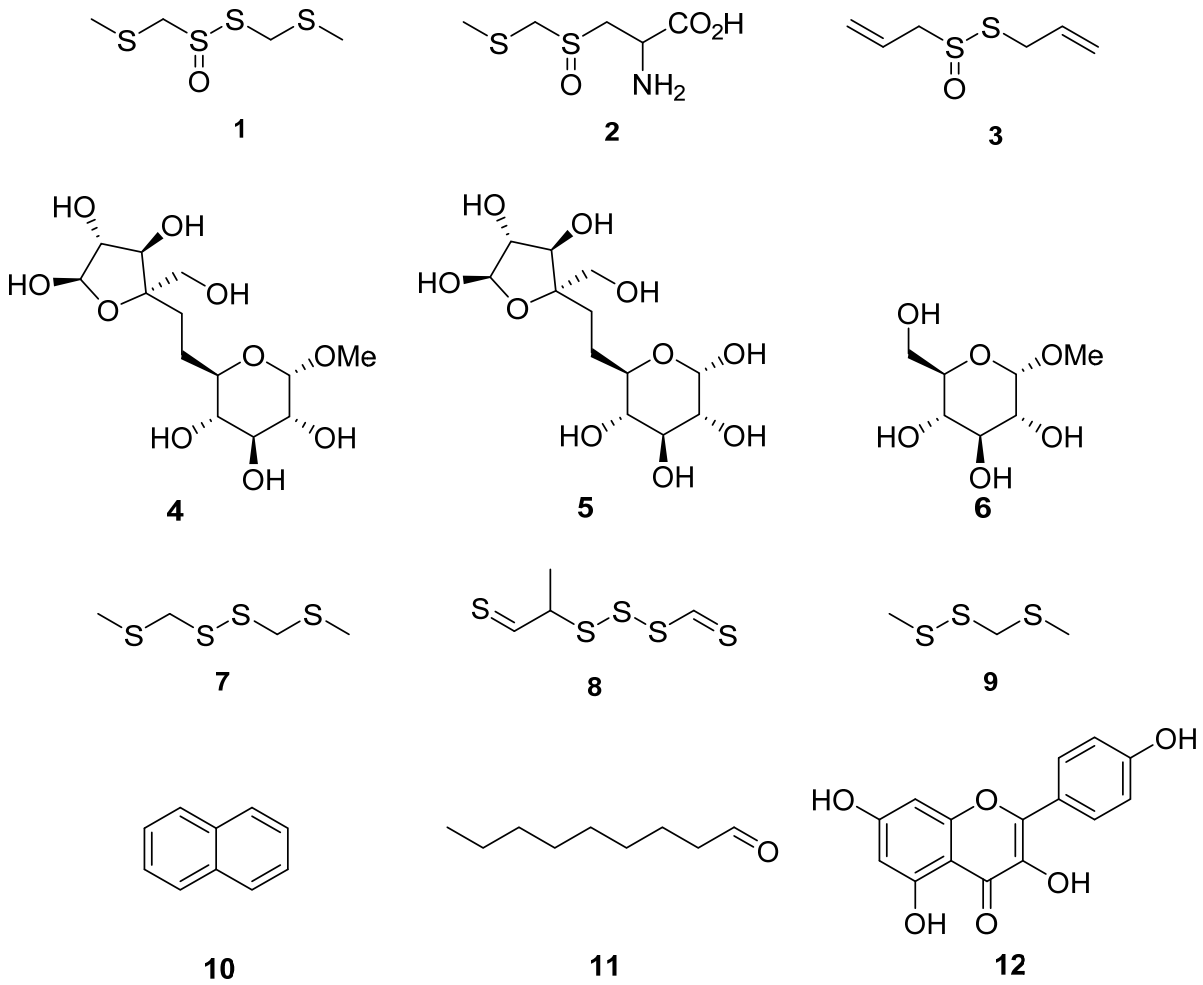

Figure 3. Chemical structures of compounds identified in *T. violacea*. (1) Marasmicin (**1**), (2) marasmin (**2**), allicin (**3**)—possesses antibacterial and antifungal activity, D-fructofuranosyl-β(2→6)-methyl-α-D-glucopyranoside (**4**), β-D-fructofuranosyl-(2→6)-α-D-glucopyranoside (**5**), methyl-α-D-glucopyranoside (**6**), bis(methylthiomethyl) disulfide (**7**)—found to constitute 48% of volatiles in aerial parts of *T. violacea* [55], methyl-2-thioethyl thiomethyl trisulfide (**8**)—found to constitute 16% of volatile compounds in aerial parts of *T. violacea* [55], methyl (methylthio)methyl disulfide (**9**)—found to constitute 10 % of volatile compounds in aerial parts of *T. violacea* [55], naphthalene (**10**)—interestingly observed to significantly increase in concentration in plants infected by the fungus *Beauveria bassiana* in comparison to untreated controls [59], nonanal (**11**)—also observed to significantly decrease in concentration in plants infected by the fungi *Beauveria bassiana* in comparison to untreated controls [59] and finally kaempferol (**12**)—which possesses multiple biological activities including antioxidant, anticancer and anti-inflammatory properties [60–62].

Table 2. Published documents on the genus *Tulbaghia* per country.

Country	No. of Documents *
South Africa	99
United Kingdom	15
United States	12
Czech Republic	8
Italy	7
India	6

Table 2. *Cont.*

Country	No. of Documents *
Germany	5
Australia	3
China	3
Belgium	2

* Data retrieved following query of the Scopus database (https://www.scopus.com/, accessed on 22 February 2022) using the keyword "*Tulbaghia*". The search was carried out on 22 February 2022.

The greatest numbers of pharmacological screens have been on interrogating the antimicrobial properties of this genus. This is closely followed by cardiovascular, antioxidants and cancer investigations as shown in Table 3. *T. violacea* prominently features, being the most studied species, with *T. alliacea* and *T. aticulata* having received minimal attention.

Table 3. Number of published studies per specific disease or pharmacological area.

Disease	No. of Published Studies #
Antimicrobial	26
Cancer	11
Antioxidant	13
Diabetes	2
Cardiovascular	12
Antithrombogenic	2
Miscellaneous	17

Studies considered are those published from 1997 to 2022. A number of these, published before 2013, have been succinctly discussed by Aremu and Van Staden [8].

2.4.1. Antimicrobial and Antiparasitic Activity

As antimicrobial resistance continues to be a global health threat, the need to find therapeutic alternatives has never been more urgent [63]. This has encouraged scientists to search for novel alternatives with natural products having drawn marked interest as a potential oasis of new antimicrobial agents [64–66]. *Tulbaghia* has received significant relevance in this regard, with multiple studies providing ample evidence substantiating its use as an antimicrobial agent. Extracts of *T. violacea* have potency against many microbial species including those designated as priority by the World Health Organization. These include *Pseudomonas aeruginosa* (*P. aeruginosa*), *Staphylococcus aureus* (*S. aureus*) and *Klebsiella pneumoniae* (*K. pneumoniae*) with MIC values ranging between 20 and 300 µg/mL [67]. This activity was confirmed in another study where the disc diffusion method was used [68]. In addition to bacteriostatic activity, extracts of *T. violacea* have shown noteworthy potency against yeasts including *Candida albicans* (*C. albicans*) and *Candida parapsilosis* (*C. parapsilosis*) with MIC and MMC values ranging between 20 and 40 µg/mL [68]. Beyond human pathogens, extracts of *T. violacea* have activity against microorganisms of agricultural significance, for example against the fungus *Aspergillus flavus* (*A. flavus)*, which is responsible for significant agricultural produce loss at a global scale due to production of aflatoxins [69]. Extracts of *T. violacea* compromised cell wall synthesis by significantly reducing β-glucan and chitin synthesis in *A. flavus* corresponding to a dose-dependent inhibition of the enzymes β-glucan and chitin synthase, respectively [70]. Further studies suggested an alternative mode of action (MoA) via reduction of ergosterol production in fungi [71]. Interestingly, related to value in agriculture, a patent has been filed on the use of extracts of *T. violacea* as a plant protecting remedy as a substitute for chemical agents [72]. Some thought-provoking studies have shown that growth conditions including light intensities, watering frequency and pH, substantially impact both growth and biological potency of *T. violacea* extracts against *Fusarium oxysporum* (*F. oxysporum*) [73,74]. Likewise, storage conditions of dried plant material also affect the antimicrobial potency of extracts [56]. In addition to antimicrobial activity, *T. violacea* has shown good antiparasitic activity against the parasitic worm *Meloidogyne incognita* (*M. incognita*) on tomato roots and in soil [75]. Antiparasitic activity has also

been observed against *Trypanosoma brucei* (*T. brucei*) (IC_{50} = 2.83 µg/mL) and *Leishmania tarentolae* (*L. tarentolae*) (IC_{50} = 6.29 µg/mL) [67]. Table 4 highlights the antimicrobial activity of *Tulbaghia* species.

Table 4. Antimicrobial activity of *Tulbaghia* species.

Plant Species	Extraction Solvent	Plant Part Used	Biological Activity	References
T. violacea	Dichloromethane	Bulbs	MIC ranging from 20 to 300 µg/mL against *Bacillus subtilis*, methicillin-resistant *S. aureus*, *S. epidermidis*, *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *C. albicans* and *C. parapsilosis*.	[67]
T. violacea	Hexane and ethanol	Flowers and callus cultures	Moderate to strong broad-antimicrobial (*E. coli*, *P. aeruginosa*, *S. aureus*, *Aspergillus niger* and *C. albicans*) activity observed by zone of inhibition in the agar well disc diffusion method.	[68]
T. violacea	Water	Bulbs	Significant reduction in *A. flavus* β-glucan and chitin synthesis corresponding to a dose-dependent inhibition of the enzymes β-glucan and chitin synthase, respectively.This results in inhibition of ergosterol production in the fungus.	[70,71]
T. violacea	Acetone	Bulbs	Varied light intensities, pH and watering frequencies substantially impacted both growth and potency of plant extracts against the fungi *F. oxysporum*.	[73,74]
T. violacea	Water	Roots, bulbs, leaves and flowers	Significantly compromised population densities of the nematode *M. incognita* race 2 on tomato roots and in the soil.	[75]
T. violacea	Dichloromethane	Bulbs	Antiparasitic activity against *T. brucei* (IC_{50} = 2.83 µg/mL) and *L. tarentolae* (IC_{50} = 6.29 µg/mL).	[67]

2.4.2. Anticancer Activity

Owing to the need for novel anticancer agents [76] and motivated by the success of cancer drug discovery projects from natural products [77], Mthembu and Motadi in (2014), evaluated the in vitro anticancer properties of crude methanol extracts of *T. violacea* using an MTT assay [78]. Extracts displayed time- and concentration-dependent antiproliferative properties against cervical cancer cell lines with an IC_{50} of 150 µg/mL. The MoA was deciphered to be induction of apoptosis by a p53-independent pathway [78]. However, in contrast to this finding, continued work showed a proportional increase in the activity of caspase 3/7, and the expression of p53 genes strongly suggests apoptosis was triggered by a p53-dependent pathway [79]. This latter finding has been partly substantiated by data emerging from a study examining the antineoplastic properties of *T. violacea* against ovarian tumor cells. These extracts were shown to partially induce both apoptosis and necrosis with the most pronounced activity due to induction of autophagy [80].

Triple-negative breast cancer remains one of the most challenging cancers, being highly aggressive [81]. *T. violacea* extracts have demonstrated good cytotoxic activity against MDA-MB-231, with an IC_{50} of 300 µg/mL [82]. Additionally, extracts inhibited migration of the cancer cell lines (metastasis), an important physiological process in the progression of this cancer [83]. In addition to the gynecological cancers, antineoplastic properties of *T. violacea* were further observed against pancreatic cancer with 63% inhibition of cell proliferation at a concentration of 250 µg/mL [68]. Against a non-sex-specific cancer, *T. violacea* showed noticeable activity against oral cancer with an IC_{50} of 0.2 and 1 mg/mL for acetone and water-soluble extracts, respectively. Extracts activated caspase activity in a dose-dependent manner leading to induction of apoptosis in the human oral cancer cell line [84]. Using a bioassay guided approach, the active anticancer compounds in *T. violacea* have been identified to be glucopyranosides D-fructofuranosyl-β (2→6)-methyl-α-D-glucopyranoside and β-D-fructofuranosyl-(2→6)-α-D-glucopyranoside. Both compounds act by mediating induction of apoptosis in Chinese hamster cells by targeting the mitochondrial (intrinsic) pathway [85,86]. A summary of the anticancer activity of *Tulbaghia* species is shown in Table 5.

Table 5. Anticancer activity of *Tulbaghia*.

Plant Species	Extraction Solvent	Plant Part Used	Biological Activity	References
T. violacea	Methanol	Leaves and roots	Marked time- and dose-dependent cytotoxic effect on cancer cell lines. Induced apoptosis using p53-independent pathway.	[78]
T. violacea	Methanol, butanol, and hexane	Leaves	Methanol extract was prolific against multiple cell lines. Hela and ME-180 cell lines treated with methanol and hexane extracts showed an increase in caspase 3/7 activity. Both methanol and hexane extracts induced a 10-fold increase in expression of p53 gene in Hela cells.	[79]
T. violacea	Methanol:water:formic acid (80:20:0.1, *v/v/v*)	Flowers	Demonstrated activity against ovarian tumor cells.	[80]
T. violacea	Water and methanol	Leaves	Water-soluble extract emerged as the most cytotoxic (IC_{50} = 314 µg/mL), compared to the methanol extract (IC_{50} = 780 µg/mL), against the MDA-MB-231 triple-negative breast cancer cell line. Water-soluble extract prevented cell migration completely for 13 h at 300 µg/mL.	[82]
T. violacea	Hexane and ethanol	Flowers and callus cultures	Extracts showed marked cytotoxicity (60–74% growth inhibition at 250 µg/mL) against three different cell lines (Hep G2, PC-3 and MCF-7).	[68]
T. violacea	Acetone and water	Leaves	Anticancer activity against oral cancer with an IC_{50} (acetone extract) of 0.2 mg/mL; IC_{50} (water extract) of 1 mg/mL.	[84]
T. violacea	Methanol:water (1:1)	Whole plants	Two pro-apoptotic glucopyranosides D-fructofuranosyl-β (2→6)-methyl-α-D-glucopyranoside and β-D-fructofuranosyl-(2→6)-α-D-glucopyranoside isolated and identified as active anticancer agents in the plant.	[85]
T. violacea	Water	Whole plants	MoA of the three compounds, namely methyl-α-D-glucopyranoside, D-fructofuranosyl-β (2→6)-methyl-α-D-glucopyranoside and β-D-fructofuranosyl-(2→6)-α-D-glucopyranoside isolated from the water extract, deciphered to be through induction of apoptosis by targeting the mitochondrial (intrinsic) pathway	[86]

2.4.3. Antioxidant Activity

The imbalance of reactive oxygen species (ROS) and antioxidants in the body can lead to oxidative stress [87]. This physiological condition can result in cellular and tissue damage [88]. Oxidative stress is associated with pathologies including cancer, cardiovascular disease, diabetes, and neurodegenerative diseases amongst others [88,89]. To avert the development of oxidative stress, attenuation of ROS has been identified as a viable target, with natural products seen as a potential source capable of neutralizing it [88]. *Tulbaghia* has generated some interest on this front particularly as it is rich in compounds with proven antioxidant activity including phenols, tannins and flavonoids. Multiple studies have demonstrated that extracts of *Tulbaghia* have marked antioxidant activity as assessed using different assays in vitro including Trolox equivalent antioxidant capacity (TEAC; also commonly referred to as the ABTS assay), ferric-reducing antioxidant power (FRAP) and 2,2-diphenyl-1-picryl-hydrazyl-hydrate (DPPH) (Table 6) [58,80,90,91]. Furthermore, using an in vivo model of *Caenorhabditis elegans*, *T. violacea* extracts attenuated oxidative stress produced by a free radical generator, (2,2′-azobis-2-amidinopropane dihydrochloride; AAPH), in the roundworm [80]. Data from these studies strongly suggested continued investigation of other species in the search for more potent antioxidant agents from *Tulbaghia*. The antioxidant activity of *Tulbaghia* species is highlighted in Table 6.

Table 6. Antioxidant activity of *Tulbaghia* species.

Plant Species	Extraction Solvent	Plant Part Used	Biological Activity	References
T. violacea	Water	Leaves	Dose-dependent antioxidant activity measured using the DPPH (Log IC_{50} = 0.49 mg/mL) and ABTS (Log IC_{50} = 0.24 mg/mL) assays	[92]
T. violacea	Methanol/water/formic acid (80:20:0.1, *v/v/v*)	Flowers	Marked antioxidant activity was observed using 3 different types of assays, namely DPPH, FRAP and TREC	[80]
T. acutiloba	Hydro-methanolic extracts	Roots, rhizomes, leaves and flowers	Dose-dependent antioxidant activity observed with the rhizome extract emerging as the most active plant part (IC_{50} DPPH = 0.202 mg/mL and peak scavenging activity of 95)	[91]
T. violacea	Hexane and ethanol	Flowers and callus cultures	Dose-dependent antioxidant activity with IC_{50} ranging from 1.933 to 7.350 mg/mL in the DPPH assay	[68]
T. violacea	Acetone	Leaves	IC_{50} DPPH = 0.08 mg/mL; IC_{50} ABTS = 0.03 mg/mL	[84]
T. acutiloba	Acetone	Leaves	IC_{50} DPPH = 0.16 mg/mL; IC_{50} ABTS = 0.07 mg/mL	[84]
T. alliacea	Acetone	Leaves	IC_{50} DPPH = 0.06 mg/mL; IC_{50} ABTS = 0.06 mg/mL	[84]
T. cernua	Acetone	Leaves	IC_{50} DPPH = 0.21 mg/mL; IC_{50} ABTS = 2.34 mg/mL	[84]
T. leucantha	Acetone	Leaves	IC_{50} DPPH = 0.39 mg/mL; IC_{50} ABTS = 0.03 mg/mL	[84]
T. ludwigiana	Acetone	Leaves	IC_{50} DPPH = 0.26 mg/mL; IC_{50} ABTS = 0.09 mg/mL	[84]
T. natalensis	Acetone	Leaves	IC_{50} DPPH = 2.70 mg/mL; IC_{50} ABTS = 0.04 mg/mL	[84]

2.4.4. Antidiabetic, Anticardiovascular and Antithrombogenic Activity

The incidence of diabetes and cardiovascular diseases continues to grow substantially across the globe, with both conditions combined accounting for the highest global morbidity and mortality [93,94]. Both of these chronic conditions are closely linked with cardiovascular disease being responsible for high morbidity and mortality in diabetic patients [95]. *Tulbaghia* has been documented in ethnopharmacological studies for the treatment of these ailments with emerging scientific data strongly validating its use. In streptozotocin diabetes-induced rat models, *T. violacea* attenuated diabetes-associated physiological conditions resulting in improved body weights, reduced fasting blood glucose levels, enhanced glucose tolerance and significantly elevated plasma insulin and liver glycogen content [96]. These data were corroborated in another study in which *T. violacea* noticeably reduced blood glucose and serum lipid (triglyceride (TG), total cholesterol (TC), and very low-density lipoprotein (VLDL)) levels while raising plasma insulin in a streptozotocin-induced diabetic rat model [97]. In an assessment for negating cardiovascular associated conditions, *T. violacea* in in vivo models markedly reduced systolic blood pressure (BP), diastolic BP, mean arterial pressure (MAP) and the heart rate in both age-induced and spontaneous hypertensive rats [98]. Furthermore, dosing rats with extracts of *T. violacea* led to improved kidney function [99]. This is an essential pharmacological property as kidney function is impaired in hypertension leading to high morbidity and mortality in people suffering from cardiovascular diseases [100].

One of the multiple factors strongly associated with cardiovascular disease is atherothrombotic vascular disease (AVD). Platelet aggregation plays a role in development of AVD and subsequent cardiovascular events [90,101]. Against this background, platelet aggregation has been identified as a key process to target to prevent AVD. Encouragingly, *T. violacea* demonstrated marked potency being able to significantly inhibit platelet adhesion 15 min post-exposure (Table 7) [90,92].

Table 7. Antidiabetic, anticardiovascular and antithrombogenic activity of *Tulbaghia* species.

Plant Species	Extraction Solvent	Plant Part Used	Biological Activity	References
Diabetes				
T. violacea	Methanol	Rhizome	Attenuated diabetes associated physiological complications in streptozotocin-induced diabetic rats.	[96]
T. violacea	Methanol	Rhizome	Noticeably reduced blood glucose and serum lipid (TG, TC, and VLDL) levels while raising plasma insulin in a streptozotocin-induced diabetic rat model.	[97]

Table 7. *Cont.*

Plant Species	Extraction Solvent	Plant Part Used	Biological Activity	References
Cardiovascular				
T. violacea	Methanol	Leaves	Markedly reduced systolic BP, diastolic BP, mean arterial pressure and the heart rate in both age-induced and spontaneous hypertensive rats.	[98]
T. violacea	Methanol	Rhizome	50 mg/kg significantly improved kidney function in vivo.	[99]
T. acutiloba	Hydro-methanolic extracts	Roots, rhizomes, leaves and flowers	All extracts inhibited the Angiotensin-1-Converting Enzyme in vitro (> 50 % inhibition at a concentration range of 125–1000 µg/mL). Extracts of leaves demonstrated activity comparable to that of the control drug ramipril.	[91]
Antithrombogenic				
T. violacea	Water	Leaves	Noticeable inhibition of platelet adhesion by a novel scaffold consisting of polycaprolactone incorporated with 10 % (*w*/*w*) plant extracts.	[90]
T. violacea	Water	Leaves	Marked inhibition of platelet adhesion (70% inhibition at 0.1 mg/mL within 15 min post-exposure).	[92]

2.4.5. Miscellaneous Pharmacological Activity

In addition to diabetes and cardiovascular diseases, *T. violacea* has shown activity against another chronic condition, Alzheimer's disease. In an in vivo Alzheimer's disease transgenic *C. elegans* strain model, *T. violacea* significantly reduced 1-42 β-amyloid peptide formation (Table 8) [80]. *T. violacea* exhibited in vivo anticonvulsant activity by attenuating tonic convulsions induced by either pentylenetetrazole, bicuculline, picrotoxin, strychnine or NMDLA [102] and validating its traditional use for the treatment of epilepsy. *T. violacea* displayed marked tick repellence properties of fungus-exposed plants at low treatment concentrations (5% *w*/*v* and 10% *w*/*v*) [59], further enhancing its credentials as a potential agricultural product. Somewhat concerning is that, extracts of *T. violacea* also induced genotoxic effects albeit at high test concentrations (250, 500 and 1000 µg/mL) in the *Allium cepa* assay [103]. Furthermore, broad murine macrophage antiproliferative and cytotoxicity activity, influenced by extract test concentrations, type of solvent and plant part used, have been observed (Table 8) [104]. There is consequently a need for rigorous assessment of safety of extracts of this and other species of the genus *Tulbaghia*.

Table 8. Miscellaneous biological properties of extracts of *Tulbaghia* species.

Plant Species	Extraction Solvent	Plant Part Used	Biological Activity	References
T. violacea	Methanol/water/formic acid (80:20:0.1, *v*/*v*/*v*)	Flowers	Reduced 1-42 β-amyloid peptide formation and arrested oxidative stress in vivo.	[80]
T. violacea	Methanol	Leaves	Demonstrated in vivo anticonvulsant activity by attenuating tonic convulsions induced by either pentylenetetrazole, bicuculline, picrotoxin, strychnine or NMDLA.	[102]
T. violacea	Acetone	Mixture of leaves and bulbs	Marked tick repellence properties of fungus-exposed plants at low treatment concentrations (5 % *w*/*v* and 10 % *w*/*v*).	[59]
T. violacea	Water	Leaves, stems, and roots	Induced conspicuous genotoxicity effects at high test concentrations (250, 500 and 1000 µg/mL) in the *A. cepa* assay.	[103]
T. violacea	Water and ethanol	Leaves, stems, and roots	Broad murine macrophage antiproliferative and cytotoxicity activity influenced by both extract test concentrations, type of solvent and plant part used.	[104]

3. The Genus *Allium*

3.1. Botanical Description

Species of the genus *Allium* are mostly found in warm–temperate and temperate zones of northern hemisphere as well as the boreal zone [105]. They are petaloid perennial herbs with parallel narrow leaves [33] and possess true bulbs, which are sometimes found on rhizomes [106]. *Allium* species are also characterized by onion or garlic odor and flavor similar to *Tulbaghia* [106]. Well known species include *Allium cepa* (*A. cepa*), *Allium sativum*

(*A. sativum*), *Allium ascalonicum* (*A. ascalonicum*,), *Allium porrum* (*A. porrum*), and *Allium schoenoprasum* (*A. schoenoprasum*) (chive) [33]

Allium has over 500 species making it the largest genus of Amaryllidaceae [6,7]. There are plethora of species, notably *A. cepa* and *A. sativum* [107–109]. Other examples grown for their medicinal and nutraceutical value are *Allium ducissae* (*A. ducissae*), *Allium strictum* (*A. strictum*), *Allium umbilicatum* (*A. umbilicatum*), *Allium victorialis* (*A. victorialis*), *A. ascalonicum*, *Allium chinense* (*A. chinense*), *Allium tuberosum* (*A. tuberosum*), *Allium griffithianum* (*A. griffithianum*), *Allium oreoprasum* (*A. oreoprasum*), and *Allium oschaninii* (*A. oschaninii*). Species tolerate varying climatic conditions, hence are geographically distributed across several continents, including Asia, Africa, the Americas, and Europe [107,110]. Fernandes et al. identified *A. cepa* that colonizes four different geographical regions of the Madeira island, an archipelago near the North Atlantic ocean with a hot and/or warm-summer Mediterranean climate conditions [107]. As the world's second-most relevant and cultivated horticulture vegetable crop, the onion (*A. cepa*), is distributed in over 175 countries and covers approximately six million hectares of the total land size of the world. Approximately two-thirds (66%) of global onion production emanates from the Asia, with China and India being the world's largest producers [111]. The maximal diversification of *A. cepa* is found in Iran and Afghanistan's Mediterranean basin. *A. cepa* thrives in areas with boreal, temperate, and tropical climates [108]. Similarly, *A. sativum* (garlic) bears close resemblance to onions and originates from Central Asia but has spread to include regions in Europe, America, and Africa [112]. The global garlic production estimates show that out of the 28.5 million tonnes (MT) of *A. sativum* cultivated, the majority (91.6%; 26.1 MT) were from Asia, followed by Europe (3.0%; 0.86 MT), America (2.9%; 0.83 MT), and with the least from Africa (2.7%; 0.73 MT) [112]. Bartolucci et al. identified *A. ducissae*, a new breed of *Allium* that grows in the mountainous regions of the Central Apennines in the Abruzzo and Lazio counties of Italy [113]. Furthermore, *A. strictum*, a Eurasian species, is distributed across China, Europe, Russia, Kazakhstan, Kyrgyzstan, and Mongolia [114,115]. *A. umbilicatum*, also called gladiolus or leek is usually localized in semi-arid regions and can tolerate sub-zero freezing winters [116]. It occurs as a weed in oases and span across Afghanistan, Iran, Pakistan, Turkmenistan, Tajikistan, and central and Eastern Asian regions [116]. As a representative circumboreal plant, *A. victorialis* has a wide altitudinal climatic tolerance [117]. It is predominantly located in lowland deciduous forest and subalpine birch forest, but seldom found in the subalpine meadows [117]. This species is scattered distribution on the island stretches of Japan, Russia, and Northern China [117,118]. Although practically grown throughout the world, *A. ascalonicum*, also called shallot, is native to the Middle East, and the name is derived from the Syrian city Ascalon. These shallots are distributed on the main islands of Indonesia, in Bangladesh, Japan, Korea, Malaysia, Taiwan, and Thailand [119]. *A. chinense* (locally referred to as Chinese/Japan onion or scallion, Kiangski scallion, oriental onion, Rakkyo) is an uncommon *Allium* species found mainly in the tropical and sub-tropical regions of China, Japan, Vietnam, and eastern areas of India [111,120]. *A. tuberosum* is an indigenous species native to southeastern Asia and regarded as a late-seasonal bloomer. During the initial growth phases, *A. tuberosum* is evergreen in hot climates but succumbs to cold climatic conditions. However, the Chinese chive becomes tolerant to all seasonal variations [121,122]. *A. griffithianum* and *A. oreoprasum* are geographically skewed towards the mountainous regions of Pakistan, Afghanistan, Kyrgyzstan, Uzbekistan, and Tajikistan [123], whereas *A. oschaninii* are located in the Darvaz mountains of Central Tajikistan [124].

3.2. Traditional Uses of Genus Allium

Increasing scientific evidence asserts the traditional uses of plants in folklore medicine [124–126]. Researchers over the years have investigated various parts of local medicinal plants to identify phytoconstituents with potential bioactivity, and further develop them into new drug therapies [127,128]. *Allium* species contain the common phytocompounds (anthocyanins, flavonoids, organosulfur, sterols, saponins, phe-

nolic acids, amino acids, vitamins and minerals) [129–132] with innumerable biological properties [130–133]. Owing to these biological advantages, *Allium* species are locally used in managing various diseases affecting human organs and organ systems such as inflammation, microbial pathologies and oxidative stress injuries [130–133]. In particular, *A. cepa* is used to treat alopecia, hearing impairment, menstrual disorders, erectile dysfunction and ocular and metabolic diseases [133–135]. Similarly, *A. sativum* is employed in the management of hematological disorders, carcinomas, muscle weakness and compromised airways [135–139]. Other varieties of *Allium* species also serve as appetizers, nerve soothers, and relieving agents against digestive, respiratory, and urinary system discomfort as seen in Table 9.

Table 9. Traditional medicinal uses of *Allium* species.

Plant Species	Mode of Preparation	Traditional Medicinal Uses	Reference
A. cepa	Raw, juice of bulb or rhizome, paste, decoctions, cataplasm, maceration, infusion	Alopecia, antilithic (stone disease), anti-obesity, blood purifying, bronchitis, constipation, cardiovascular disease, cough, diabetes, eye diseases, erectile dysfunction, fever, hearing loss, headaches, hemorrhoids, epilepsy, oligomenorrhea, jaundice, lower gastrointestinal bleeding, prostate cancer, rheumatism, rubefacient, sinusitis, stomach pains, snake bites, skin diseases, teeth disorders, reduce flatulence, wound healing	[133–135]
A. sativum	Extracts of leaves or bulb	Antiseptic, anthelmintic, antithrombotic, antilipidemic, aphrodisiac, anti-greying of hair, bronchitis, carminative, cough, colic, cancers (gastric, prostate, colorectal adenomatous polyps, squamous cell carcinoma), diabetes, diaphoretic, dysentery, eczema, facial paralysis, fever, flatulence, galactagogue, high blood pressure, intestinal worms, liver disorders, rheumatism, scabies, tetanus, stomach pains, tuberculosis	[135–139]
A. umbilicatum	Raw or cooked bulb, leaves, flowers	Non-specific reduction in blood cholesterol levels, tonify digestive and circulatory systems	[116]
A. victoralis	Fresh, pickled, boiled and salted flowers, leaves and roots	Appetizer, amenorrhea, pediatric otitis, bronchitis, diarrhea, dropsy, expectorant, hypofunction of stomach, inflammatory eye diseases, meteorism, gastroenteritis, heart diseases (atherosclerosis), rheumatism	[140]
A. ascalonicum/*A. cepa var aggregatum*	Bulb and leaves	Allergies, appetizer, cold, cancers, fever, obesity, rheumatoid arthritis, soothes nerves, diabetes, post-menopausal syndrome	[141–145]
A. chinense	Flower, leaves, roots, seedpods	Angina pectoris, astringent, bronchitis, carminative, chest pains, diarrhea, expectorant, pleurisy, tenesmus in cases of dysentery, reducing cholesterol, tonic to the digestive and circulatory systems	[146]
A. tuberosum	Raw or cooked leaves, roots, oils from seed	Asthma, abdominal pain, carminative, cuts and wounds, diabetes, diarrhea, kidney and bladder weakness, nocturnal emission, urinary incontinence, spermatorrhea, stomachic	[147]
A. griffithianum	Leaves and bulb	Carminative, colic indigestion, dyspepsia, diabetes control	
A. oreoprasum	Leaves and bulb	Cough and cold, diabetes control, diarrhea, dysentery, fever, gastritis, oedema, headache, jaundice, stomachache, rheumatism, numbness of limbs	[124]

3.3. Phytochemistry of Allium

Owing to the numerous traditional uses of these species, it is not surprising that the genus contains several phytoconstituents which may be responsible for their observed activity. Table 10 outlines various phytochemicals isolated, their geographic location and their biological activity.

Table 10. Bioactive compounds isolated from *Allium* species.

Plant Species	Plant Part	Country	Isolated Compounds	Bioactivity	References
A. ursinum L.	Leaves, underground parts, fresh flowers	Poland Bulgaria	1,2-di-*O*-α-linolenoyl-3-*O*-β-D-galactopyranosyl-sn-glycerol; β-sitosterol3-*O*-β-D-glucopyranoside; kaempferol 3-*O*-β-glucopyranoside and kaempferol 3-*O*-β-neohesperidoside. (-S-)-spirost-5-en-3β-ol tetrasaccharide, (25*R*)-spirost-5,25(27)-dien-3 β-ol tetrasaccharide, 3-hydroxypregna-5,16-dien-20-one glycoside. Thymidine, adenosine, astragalin (kaempferol-3-*O*-β-D-glucopyranoside, kaempferol-3-*O*-β-D-glucopyranosyl-7-*O*-β-D-glucopyranoside, kaempferol-3-*O*-β-D-neohesperoside, and kaempferol-3-*O*-β-D-neohesperoside-7-*O*-β-D glucopyranoside.	Anti-ADP-aggregation activity in human blood platelets. Inhibition of human platelet aggregation. Cytotoxic activity against murine melanoma B16 and sarcoma XC.	[148–151]
A. mongolicum	Aerial parts	China	Mongoflavonoids A_1, A_2, A_3, A_4, B_1, B_2 and monogophenosides A_1, A_2, A_3, B. Quercetin.	Increase in the height of mouse small intestine.	[152]
A. cepa. *A. cepa L.*	Pigmented scales of red onion, bulbs, red onion skin waste	Naples	3-*O*-(3″-*O*-β-glucopyranosyl-6″-*O*-malonyl-β-glucopyranoside)-4-*O*-β-glucopyranoside, cyanidin 3,4′-di-*O*-β-glucopyranoside, cyanidin-4′-*O*-β-glucoside, peonidin 3-*O*-(6″-*O*-malonyl-β-glucopyranoside). 5-hydroxy-3-methyl-4-propylsulfanyl-5H-furan-2-one, (hydroxymethyl) furfural, acetovanillone, methyl 4-hydroxyl cinnamate and ferulic acid methyl ester. 3-*O*-β-glucopyranoside and 3-*O*-(6″-*O*-malonyl-β-glucopyranoside) of 5-carboxypyranocyanidin. Ceposide A, ceposide B and ceposide C. Spiraeoside (4′-*O*-glucoside of quercetin). Onionin A_1, onionin A_2, onionin A_3, onionin B_1 and B_2. Onionin A_1 (3,4-dimethyl-5-(1E-propenyl)-tetrahydrothiophen-2-sulfoxide-*S*-oxide). Cyanidin 3-glucoside (Cy 3-Glc), 3-malonylglucoside (Cy3-MaGlc), cyanidin 3-laminaribioside (Cy 3-Lam) and 3-malonyllaminaribioside (Cy 3-MaLam).	Anti-inflammatory and immunomodulatory effect. Induction of quinone reductase. Antifungal activity. Radical scavenging, anti-inflammatory, inhibition of the expression of B-cell lymphoma 2. Suppression of tumor progression in mouse ovarian cancer (Onionin A_1). Suppression of tumor-cell proliferation through the inhibition of polarization of M_2 activated macrophages.	[153–161]

Table 10. *Cont.*

Plant Species	Plant Part	Country	Isolated Compounds	Bioactivity	References
A. sativum. *A. sativum L. var. voghiera.* *A. sativum L.*	Root, protobulb, leaf sheath and blade, bulbs, tuber	Italy	Nerolidol, α-pinene, terpinolene. Voghieroside A1/A2, voghieroside B1/B2, voghieroside C1/C2, voghieroside D1/D2 and voghieroside E1/E2. Adenosine and guanosine.	Antifungal activity against *Sclerotium cepivorum*. Antimicrobial activity. Strong inhibitory effect on human platelet aggregation generated by 2 μM ADP in both primary and secondary waves (adenosine).	[162–164]
A. schoenoprasum	Whole plant, pale-purple flowers		(20S, 25S)-spirost-5-en-3β, 12β,21-triol 3-*O*-α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranoside, (20*S*, 25*S*)-spirost-5-en-3β, 11α,21-triol 3-*O*-α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranoside, laxogenin 3-*O*-α-L-rhamnopyranosyl–(1→2)-[β-D-glucopyranosyl-(1→4)]-[β-D-glucopyranoside, (25*R*)-5α-spirostan-3β, 11α-diol 3-*O*-β-D-glucopyranosyl-(1→4)]-β-D-galactopyranoside. (cyanidin 3-*O*-β-glucosideAII) (kaempferol 3-*O*-(2-*O*-β-glucosylFIII-β-glucosideFII)-7-*O*-β-glucosiduronic acid FIV) malonate AIII (AII-6→AIII-1, FIV-2→AIII-3), 1, (cyanidin 3-*O*-(3-*O*-acetyl-β-glucosideAII) (kaempferol 3-*O*-(2-*O*-β-glucosylFIII-β-glucosideFII)-7-*O*-β-glucosiduronic acid FIV) malonate AIII (AII-6→AIII-1, FIV-2→AIII-3), 2, and 7-*O*-(methyl-*O*-β-glucosiduronateFIV).	Cytotoxicity against HCT 116 and HT-29 human colon cancer lines.	[165,166]
A. minutiflorum Regel	Bulbs		Minutoside A, minutoside B, Minutoside C, alliogenin, neoagigenin 3-*O*-{[2-*O*-α-1-rhamnopyrnosyl-4-*O*-β-D-glucopyranosyl]-β-D-glucopyranoside}, isorhamnetin; 3-*O*-{[2-*O*-α-1-rhamnopyrnosyl-6-*O*-β-D-glucopyranosyl]-β-D-glucopyranoside}, isorhamnetin; 3-*O*-{[2-*O*-α-1-rhamnopyranosyl-4-*O*-β-D-glucopyranosyl]-β-D-glucopyranoside}-7-*O*-β-D-glucopyranoside and isorhamnetin; 3-*O*-{[2-*O*-α-1-rhamnopyranosyl-6-*O*-β-D-gentiobiosyl]-β-D-glucopyranoside}.	Antifungal activity.	[167]
A. neapolitanum	Extracts			Antiplatelet aggregation activity.	[168]

Table 10. *Cont.*

Plant Species	Plant Part	Country	Isolated Compounds	Bioactivity	References
A. tripedale	Bulbs, leaves	Iran	6,7-dimethoxy-*N*-trans-caffeoyltyramine; *N*-trans-feruloyltyramine. (+)-*S*-(1-butenyl)-*L*-cysteine sulfoxide (homoisoalliin), *S*-(1-butenyl)-*L*-cysteine (desoxyhomoisoalliin).	NR.	[167,168]
A. porrum L.	Bulbs		Kaempferol 3-*O*-[2-*O*-(trans-3-methoxy-4-hydroxycinnamoyl)-β-D-galactopyranosyl]-(1→4)-*O*-β-D-glucopyranoside; Kaempferol 3-*O*-[2-*O*-(trans-3-methoxy-4-hydroxycinnamoyl)-β-D-glucopyranosyl]-(1→6)-*O*-β-D-glucopyranoside. (25*R*)-5 α-spirostan-3 β, 6 β-diol 3-*O*-[*O*-β-D-glucopyranosyl-(1→2)-*O*-[β-D-xylopyranosyl-(1→3)]-*O*-β-D-glucopyranosyl-(1→4)-β-D-galactopyranoside}; (25*R*)-5 α-spirostan-3 β, 6 β-diol 3-*O*-{*O*-β-D-glucopyranosyl-(1→3)-*O*-β-D-glucopyranosyl-(1→2)-*O*-[β-D-xylopyranosyl-(1→3)]-*O*-β-D-galactopyranosyl-(1→4)-β-D-galactopyranoside}	Antiplatelet aggregation activity. Antifungal activity.	[169–171]
A. chinense. *A. chinense* G. Don	Bulbs		Chinenoside II and chinenoside III. (25 *R*,*S*)-5 α-Spirostan-3β-ol tetrasaccharide, (25*R*)-3 β-hydroxy-5 α-spirostan-6-one di- and tri-saccharides. Xiebai-saponin I (laxogenin 3-*O*-β-xylopyranosyl (1→4)-[α-arabinopyranosyl (1→6)-β-glucopyranoside), laxogenin 3-*O*-α-arabinopyranosyl (1→6)-β-glucopyranoside, laxogenin, isoliquiritigenin, isoliquiritigenin-4-*O*-glucoside, and β-sitosterol glucoside.	Inhibition of cAMP phosphodiesterase. Antitumor-promoting activity (laxogenin).	[172–175]

Table 10. *Cont.*

Plant Species	Plant Part	Country	Isolated Compounds	Bioactivity	References
A. macrostemon. *A. macrostemon* Bunge	Bulbs, leaves	Japan	Macrostemonoside G (26-*O*-β-D-glucopyranosyl-22-hydroxy-5-β-furost-25(27)-ene-3 β,12 β,26 triol 3-*O*-β-D-glucopyranosyl(1–>2)-β-D-galactopyranoside) and I (26-*O*-β-D-glucopyranosyl-22-hydroxy-5 β-furost-25(27)-ene-12-one-3 β,26-diol 3-*O*-β-D-glucopyranosyl(1→2)-β-D-galactopyranoside). tigogenin-3-*O*-β-D-glucopyranosyl(1–>2) [β-D-glucopyranosyl(1→3)1]-β-D-glucopyranosyl(1→4)-β-D-galactopyranoside (1) and tigogenin-3-*O*-β-D-glucopyranosyl(1→2)[β-D-glucopyranosyl (1→3)(6-*O*-acetyl-β-D-glucopyranosyl)] (1→4)-β-D-galactopyranoside (2). Macrostemonoside E-(25*R*)-26-*O*-β-D-glucopyranosyl-5 α-furost-20(22)-ene-3 β,26-diol-3-*O*-β-D-glucopyranosyl (1→2) [β-D-glucopyranosyl (1→3)]-β-D-glucopyranosyl (1→4)-β-D-galactopyranoside; Macrostemonoside F(II)-(25*R*)-26-*O*-β-D-glucopyranosyl-5 β-furost-20(22)-ene-3 β,26-diol-3-*O*-β-D-glucopyranosyl (1→2)-β-D-galactoside. Allimacronoid A (1-*O*-(*E*)-feruloyl-β-D-glucopyranosyl (1-2)-[β-D-glucopyranosyl (1-6)]-β-D-glucopyranose), Allimacronoid B (1-*O*-(*E*)-feruloyl-{β-D-glucopyranosyl (1-4)-[β-D-glucopyranosyl (1-2)]}-[β-D-glucopyranosyl (1-6)]-β-D-glucopyranose) and Allimacronoid Cn1-*O*-(*E*)-feruloyl-{β-D-glucopyranosyl (1-6)-[β-D-glucopyranosyl (1-2)]}-[β-D-glucopyranosyl (1-6)]-β-D-glucopyranose.	In vitro inhibition of ADP-induced human platelet aggregation (macrostemonoside G). Inhibitory activity against rabbit platelet aggregation induced by ADP (1).	[176–179]

Table 10. *Cont.*

Plant Species	Plant Part	Country	Isolated Compounds	Bioactivity	References
A. schubertii	Bulbs		(25*R* and *S*)-5 α-spirostan-2 α,3 β,6 β-triol 3-*O*-β-D-glucopyranosyl-(1→2)-*O*-[4-*O*-benzoyl-β-D-xylopyranosyl-(1→3)]-*O*-β-D-glucopyranosyl-(1→4)-β-D-galactopyranoside, (25*R* and *S*)-5 α-spirostan-2α,3β,6 β-triol 3-*O*-β-D-glucopyranosyl-(1→2)-*O*-[3-*O*-benzoyl-β-D-xylopyranosyl-(1→3)]-*O*-β-D-glucopyranosyl-(1→4)-β-D-galactopyranoside, (25*R* and *S*)-5 α-spirostan-2α,3β,6 β-triol 3-*O*-β-D-glucopyranosyl-(1→2)-*O*-[4-*O*-(3*S*)-3-hydroxy-3-methylglutaroyl-β-D-xylopyranosyl-(1→3)]-*O*-β-D-glucopyranosyl-(1→4)-β-D-galactopyranoside and 26-*O*-β-D-glucopyranosyl-(25*R* and *S*)-5 α-furostan-2α,3β,6β,22 zeta,26-pentol 3-*O*-β-D-glucopyranosyl-(1→2)-*O*-[β-D-xylopyranosyl-(1→3)]-*O*-β-D-glucopyranosyl-(1→4)-β-D-galactopyranoside.	NR.	[180]
A. tuberosum	Seeds	Shanghai	(2α, 3β, 5α, 25*S*)-2,3,27-trihydroxyspirostane 3-*O*-α-*L*-rhamnopyranoyl-(1→2)-*O*-[α-*L*-rhamnopyranosyl-(1→4)]-β-D-glucopyranoside. Tuberoside J-(25*R*)-5 α-spirostan-2α,3 β,27-triol 3-*O*-α-*L*-rhamnopyranosyl-(1–>2)-β-D-glucopyranoside; Tuberoside K-(25*R*)-5α-spirostan-2α,3β 27-triol 3-*O*-α-*L*-rhamnopyranosyl-(1→2)-[α-*L*-rhamnopyranosyl-(1→4)]-β-D-glucopyranoside; and Tuberoside L-27-*O*-β-D-glucopyranosyl-(25*R*)-5α-spirostan-2α,3 β,27-triol 3-*O*-α-D-rhamnopyranosyl-(1–>2)-[α-*L*-rhamnopyranosyl-(1→4)]-β-D-glucopyranoside. Tuberoside M-(25*S*)-5β-spirostane-β,3 β-diol 3-*O*-α-L-rhamnopyranosyl-(1→4)-β-D-glucopyranoside. Tuber-ceramide (*N*-(2′,3′-dihydroxy-tetracosenoyl)-2-amino-1,3,4-trihydroxy octadecane), and Cerebroside (*N*-(2′,3′-dihydrox-tetra-cosenoyl)-2-amino-1,3,4-trihydroxy octadecane).	Tuberoside M inhibits the proliferation of the human promyelocytic leukemia cell line (HL-60)	[181–183]

Table 10. *Cont.*

Plant Species	Plant Part	Country	Isolated Compounds	Bioactivity	References
A. albopilosum and *A. ostrowskianum*	Bulbs		(25 *R* and *S*)-5 α-spirostane-2α, 3 β,6 β-triol 3-*O*-(*O*-β-D-glucopyranosyl-(1→2)-*O*-[3-*O*-acetyl-β-D-xylopyranosyl-(1→3)]-*O*-β-D-glucopyranosyl-(1→4)-β-D-galactopyranoside), (25*R*)-2-*O*-[(*S*)-3-hydroxy-3-methylglutaroyl]-5 α-spirostane-2α, 3β, 6β-triol 3-*O*-(*O*-β-D-glucopyranosyl-(1→2)-*O*-[β-D-xylopyranosyl-(1—>3)]-*O*-β-D-glucopyranosyl-(1→4)-β-D-galactopyranoside), (22*S*)-cholest-5-ene-1β, β,16 β,22-tetraol 1-*O*-α-*L*-rhamnopyranoside 16-*O*-(*O*-α-*L*-rhamnopyranosyl-(1→3)-β-D-glucopyranoside), 1β, 3β, 16β-trihydroxycholest-5-en-22-one 1-*O*-aα-L-rhamnopyranoside 16-*O*-(*O*-α-*L*-rhamnopyranosyl-(1→3)-β-D-glucopyranoside), 1β,3β,16 bβ-trihydroxy-5 α-cholestan-22-one 1-*O*-α-*L*-rhamnopyranoside 16-*O*-(*O*-α-*L*-rhamnopyranosyl-(1→3)-β-D-glucopyranoside) and (22*S*)-cholest-5-ene-1β,3β, 16β,22-tetraol 16-*O*-(*O*-β-D-glucopyranosyl-(1→3)-β-D-glucopyranoside).	NR.	[184]
A. fistulosum. *A. fistulosum* L.	Whole plant, leaves, seeds	Iran	Fistulomidate A ((1*Z*,2*E*)-Methyl3-(3,4-dimethoxyphenyl)-*N*-(4-hydroxyphenethyl) acrilimidate) and Fistulomidate B ((1Z,2E)-Methyl3-(3,4-dihydroxyphenyl)-*N*-(4-hydroxyphenethyl)acrilimidat). Onionin A_1, onionin A_2, and onionin A_3. Glycerol mono-(E)-8,11,12-trihydroxy-9-octadecenoate, tianshic acid, 4-(2-formyl-5-hydroxymethylpyrrol-1-yl) butyric acid, p-hydroxybenzoic acid, vanillic acid, and daucosterol.	Antibacterial and cytotoxic activity. Suppression of tumor progression in mouse ovarian cancer (onionin A_1). Inhibition of the growth of *Phytophtohora capsici* on V8 media (glycerol mono-(E)-8,11,12-trihydroxy-9-octadecenoate and V).	[159,185,186]
A. carolinianum DC	Bulb	Mongolia	Cinnamoylphenethylamine derivative	Weak cytotoxic activity	[187]

Table 10. *Cont.*

Plant Species	Plant Part	Country	Isolated Compounds	Bioactivity	References
A. ampeloprasum var. porrum (*Leek*)	Plant parts		A-β- D -glucopyranoside	Anticancer activity against MCF-7 human breast cancer cell.	[187]
A. ascalonicum L.		China	Ascalonicoside C-(25*R*)-26-*O*-β-D-glucopyranosyl-22-hydroxy-5α-furost-2-one-3β,5,6β, 26-tetraol-3-*O*-α-*L*-rhamnopyranosyl-(1→2)-β-D-glucopyranoside. Ascalonicoside D-(25*R*)-26-*O*-β-D-glucopyranosyl-22-methoxy-5α-furost-2-one-3β,5,6β, 26-tetraol-3-*O*-α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranoside. (25*R*)-26-*O*-β-D-glucopyranosyl-22-hydroxy-5-ene-furostan-3β,26-diol-3-*O*-α-L-rhamnopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→4)-[α-L-rhamnopyranosyl-(1→2)]-β-D-glucopyranoside. 25*R*)-26-*O*-β-D-glucopyranosyl-22-hydroxy-5-ene-furostan-3β, 26-diol-3-*O*-α-L-rhamnopyranosyl-(1→2)-[α-L-arabinofuranosyl-(1→4)]-β-D-glucopyranoside.	NR.	[188,189]
A.siculum	Bulbs	Zwanenburg, The Netherlands	(*Z*)-Butanethial *S*-oxide, (*R*(S),*R*(C),E)-*S*-(1-butenyl)cysteine *S*-oxide (homoisoalliin).	NR.	[190]
A.chrysanthum	Barks	Guangzhou, China	Chrysanthumones A (6″,6″-dimethyl-4″,5″-dihydropyrano [2″,3″: 8,7]-6‴,6‴-dimethyl-prenyl-4‴,5‴-dihydropyrano [2‴,3‴:2′,3′]apigenin) and B ((*E*)-5,7-dihydroxy-2-(4-hydroxyphenyl)-8-(3-methylbut-1-enyl)-4H-chromen-4-one).	NR.	[191]
A. L. *melanocrommyum* section *Megaloprason.*	Bulbs	Central Asia	*L*-(+)-*S*-(2-pyridyl)-cysteine sulfoxide.	NR.	[192]

Table 10. *Cont.*

Plant Species	Plant Part	Country	Isolated Compounds	Bioactivity	References
A. ampeloprasum L.	Bulbs	United States of America	Ampeloside Bs_1 (apigenin 3-*O*-β-glucopyranosyl (1 → 3)-β-glucopyranosyl (1 → 4)-β-galactopyranoside), ampelosides Bf_1 ((25*R*)-26-*O*-β-glucopyranosyl-22-hydroxy-5α-furostane-2α,3β,6β,26-tetraol-3-*O*-β-glucopyranosyl(1 → 3)-β-glucopyranosyl-(1 → 4)-β-galactopyranoside) and Bf_2 ((25*R*)-26-*O*-β-glucopyranosyl-22-hydroxy-5α-furostane-2α,3β,6β,26-tetraol-3-*O*-β-glucopyranosyl(1 → 4)-β-galactopyranoside).	Weak antifungal activity by ampeloside Bs_1.	[193]
A. bakeri Reg.	Tuber		Adenosine, guanosine, and tryptophan, β-sitosterol β-D-glucoside.	Strong inhibitory effect on human platelet aggregation generated by 2 μM ADP in both primary and secondary waves (adenosine).	[162]
A.victorialis var. platyphyllum	Aerial parts, bulbs	Korea	Gitogenin 3-*O*-lycotetroside, astragalin and kaempferol 3, 4′-di-*O*-β-D-glucoside.	Cytotoxic activity.	[194]
A. nutans L.	Underground plant parts		Deltoside, nolinofuroside D, 25*R* Δ(5)-spirostan 3β-ol-3-*O*-α-L-rhamnopyranosyl(1–>2)-[β-D-glucopyranosyl(1→4)]-*O*-β-D-galactopyranoside and 25*R* Δ(5)-spirostan 1 β, 3β-diol 1-*O*-β-D-galactopyranoside.	NR.	[195]
A.giganteum	Bulbs	Japan	3-*O*-acetyl-(24*S*,25*S*)-5α-spirostane-2α,3β,5α,6β,24-pentol 2-*O*-β-D-glucopyranoside.	Inhibition of cAMP phosphodiesterase activity.	[196]
A. hookeri Thwaites	Rhizomes	China	Di-2-propenyl trisulfide, diallyl disulfide, and dipropyl trisulfide.	Antimicrobial activity against *Aspergillus fumigatus* and *C. albicans*.	[197]

NR: not reported.

The chemical structures of compounds from the genus *Allium* are shown in Figure 4.

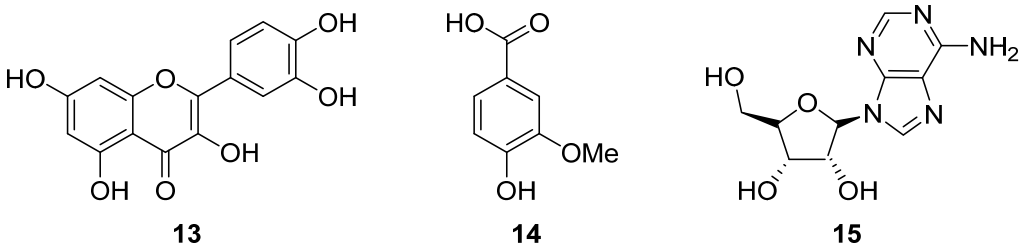

Figure 4. Chemical structures of compounds isolated from the genus *Allium*. Quercetin (**13**), vanillic acid (**14**) and adenosine (**15**).

3.4. Pharmacological Effects of Allium

There are several species within *Allium* whose biological activities have been well established [198]. This section focuses on the pharmacological activities associated with these species.

3.4.1. Antimicrobial Activities

Garlic has shown antimicrobial effects against Gram-positive, Gram-negative and acid fast stain organisms [199–201]. Allicin from garlic showed effectiveness toward methicillin-resistant *S. aureus* (MRSA) [200]. Extracts from garlic also showed broad-spectrum fungicidal effect against several fungi including *Candida*, *Trichophyton*, *Cryptococcus*, *Aspergillus*, *Trichosporon* and *Rhodotorula* species. Garlic extract was recently found to inhibit *Meyerozyma guilliermondii* and *Rhodotorula mucilaginosa* germination and growth [202]. A study by Fufa reported the antifungal activity of various *A. sativum* extracts, namely aqueous, ethanol, methanol, and petroleum ether against human pathogenic fungi such are *Trichophyton verrucosum*, *T. mentagrophytes*, *T. rubrum*, *Botrytis cinereal* (*B. cinerea*), *Candida species*, *Epidermophyton floccosum*, *A. niger*, *A. flavus*, *Rhizopus stolonifera*, *Microsporum gypseum*, *M. audouinii*, *Alternaria alternate*, *Neofabraea alba*, and *Penicillium expansum* [203]. Essential oil from garlic showed antifungal activity against a number of fungi such as (*C. albicans*, *C. tropicalis* and *Blastoschizomyces capitatus*). Saponins extracted from *A. sativum* had antifungal activity against *B. cinerea* and *Trichoderma harzianum* [204]. *Allium* species from Ghana were reported by Danquah et al. to possess anti-infective and resistance modulatory effects on selected microbial strains [205]. *Allium hirtifolium* was found to exhibit antimicrobial activities against *E. faecalis* [206].

Previous studies have shown that garlic extract inhibit the growth of *Blastocystis* species in vivo and this effect was attributed to the several phytochemicals contained in garlic extracts. Examples of these phytochemicals are thiosulfinates and allicin which have been investigated to possess antibacterial and antiprotozoal effects [204,207]. Garlic extracts have been evaluated for antiviral effects 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 [208]. Danquah et al. again reported the antitubercular effects of analogues of disulfides from *A. stipitatum* as well as their anti-biofilm and anti-efflux effects [209].

3.4.2. Antioxidant Properties

It has been reported that frequent garlic intake promotes internal antioxidant activities and reduces oxidative adverse effects either by increasing the endogenous antioxidant synthesis or reducing the production of oxidizing agents such as oxygen-free radical species (ORS) [210]. It has also been demonstrated that garlic possesses protective properties against gentamycin as well as acetaminophen-induced hepatotoxicity by improving antioxidant status, and regulating oxidative stress [200]. Garlic extract was found to elevate the activities of selected antioxidant enzymes (e.g., superoxide dismutase (SOD)) and decrease

glutathione peroxidase (GSH-Px) in rats' hepatic tissues [13,118,211]. Saponins extracted from garlic were reported to scavenge intracellular ROS and protect mouse-derived C_2C_{12} myoblasts towards growth inhibition and H_2O_2-induced DNA damage [13,212]. *A. ursinum* aqueous extract also demonstrated antioxidant effect which lasted approximately 16 h [213]. *A. hirtifolium* was reported to possess antioxidant capacity by neutralizing the free radical species in a system [214].

3.4.3. Anti-Inflammatory Properties

It has been reported widely that garlic extracts and its related phytochemicals possess anti-inflammatory activity. A study by Ahmad et al. revealed that garlic extracts significantly impaired liver inflammation and damage caused by *Eimeria papillata* infections [215]. The mechanism underlying the anti-inflammatory effects of garlic was attributed to the inhibition of emigration of neutrophilic granulocytes into epithelia as described by Hobauer et al. [216] and Gu et al. [217]. The chloroform extract of aged black garlic acts by reducing NF-κB activation in human umbilical vein endothelial cells caused by tumor necrosis factor-α (TNF-α) and the methanolic extract also reported to prevent the cyclooxygenase-2 (COX-2) and prostaglandin E_2 (PGE_2) production by NF-κB inactivation [218]. A report by Jin et al. confirmed that thiacremonone (a sulfur compound isolated from garlic) prevents neuroinflammation and amyloidogenesis by blocking the NF-κB activity, and therefore makes it an ideal remedy to manage neurodegenerative disorders (e.g., Alzheimer's disease) related to inflammation [219].

Krejčová et al. reported that pyrithione and related sulfur-containing pyridine *N*-oxides from Persian shallot possessed anti-inflammatory and neurological activity [220]. The extracts of *A. stipitatum* were reported to exhibit antibacterial effect in vivo against methicillin-resistant *S. aureus* [221]. Anti-inflammatory effect of *A. hookeri* on carrageenan-induced air pouch mouse model was also established by Kim et al. [222].

3.4.4. Anticancer Activity

Comparison of the anticancer effect of raw garlic extracts against other extracts from different plants found garlic to be the most effective and highly specific anticancer agent [223]. The anticancer mechanisms of garlic extracts were reported to be mediated via inhibition of cell growth and proliferation, regulation of carcinogen metabolism, stimulation of apoptosis, prevention of angiogenesis, invasion, and migration; and thus affording the anticancer agent with minimal negative effects [13]. Chabria et al. reported that allicin isolated from garlic suppresses colorectal cancer metastasis through enhancing immune function and preventing the formation of tumor vessels as well as surviving gene expression to enhance the cancer cell's apoptosis [224]. Fleischauer and Arab [225] reported that continuous garlic intake could decrease different kinds of cancer propagation such as cancer of the lung, colon, stomach, breast, and prostate. Piscitelli et al. reported that garlic reduced the plasma concentrations of saquinavir by approximately 50% in healthy participants after a 3-week garlic supplement intake. In addition to this, many researchers evaluated the antitumor and cytotoxic actions of garlic and its related constituents in vitro and in vivo [226].

3.4.5. Other Pharmacological Effects of Allium Species

Investigations on extracts of *A. sativum* (garlic) revealed anticholinesterase effects, which could be further developed and utilized in the management of Alzheimer's disease [227–229]. Garlic is known to possess hypolipidemic effects by reducing the total glycosaminoglycans concentration in heart and aorta [230]. Garlic is also known to reduce the level of cholesterol either by acid stimulation and excretion of neutral steroids or by reducing the cholesterogenic and lipogenic effects of fatty acid synthase, 3-hydroxy-3-methyl-glutaryl-CoA reductase, malic acid, and glucose-6 phosphate dehydrogenase in hepatocytes [231]. Garlic tablets formulated by Ashraf et al. and administered at a dose of

600 mg/day for 12 weeks in diabetic patients with dyslipidemia resulted in high HDL, low LDL and TC levels [232].

Allicin, a constituent in garlic, was found to reduce diabetes mellitus in rats, which was similar to that demonstrated by glibenclamide and insulin [233]. Garlic extracts reduce body weight, adipose tissue mass and improved plasma lipid profiles in mice with high-fat diet-induced obesity [234]. The mechanism of these activities is downregulation of multiple gene expression such as adipogenesis along with upregulation of the mitochondrial inner membrane proteins expression [234]. Garlic extract is widely known to significantly control blood pressure by reducing both systolic and diastolic pressures [235]. Moreover, several reports have confirmed the antihypertensive effects of garlic [236]. Extracts of *A. stipitatum* were also assessed and established to possess significant wound healing properties [237].

4. The Genus *Crinum*

4.1. Geographical Distribution of Crinum

Crinum, which also belongs to the Amaryllidaceae family, comprises approximately 160 beautiful lilies that grow naturally in coastal areas of the tropics and subtropics. They are widely distributed in Africa, Asia, Australia and America [238–241]

4.2. Traditional Uses of Crinum

Plants of the genus *Crinum* have been used to treat various diseases across the world [242]. In China and Vietnam, *Crinum* plants in traditional medicine are believed to possess antiviral and immune-stimulatory properties. A hot aqueous extract of *Crinum latifolium* (*C. latifolium*) is used as an antitumor agent. *Crinum asiaticum* (*C. asiaticum)* is used in Malaysia to treat rheumatism and to relieve local pain [239]. *Crinum amabile* Donn. (*C. amabile*) is used in Vietnam to induce emesis, as well as for rheumatism and earache [241].

The bulbs of *C. asiaticum* L. are used as a tonic, laxative and expectorant in Indian traditional medicine, as well as for treating urinary tract diseases [241]. The seeds are used as purgatives, diuretics, and tonics, while the raw roots are used as an emetic. The leaves are also very useful in the management of skin problems, inflammation and cough [241]. *C. latifolium* L. is also used to treat rheumatism, abscesses, earaches, and as a tonic. *Crinum pratense* (*C. pratense)* and *Crinum longifolium* (*C. longifolium)* are also used as bitter tonics, laxatives and in the management of chest illnesses [243].

Crinum zeylanicum (*C. zeylanicum)* L. is used in Sri Lanka to treat abscesses and fevers; the bulbs are also used as rubefacient in rheumatism and against snake bites; and the juice from the leaves used to treat earaches [244].

The roots of *Crinum* species have been used in African traditional medicine to cure urinary infections, coughs and colds, renal and hepatic disorders, ulcers, sexually transmitted infections, and backache, as well as enhance breastfeeding in both animal and human mothers [241]. *Crinum kirkii* Bak. (*C. kirkii)*, a widespread East African grassland plant, is used to heal wounds in Kenya. In Tanzania, the fruit and inner part of the bulbs are used as purgatives, and the outer scales employed as rat poison [245,246]. Extracts of *Crinum delagoense* (*C. delagoense)* Verdoorn is utilized in Zulu and Xhosa traditional medicine in South Africa to treat urinary tract infections and body oedema [247–249]. Rheumatism, aching joints, septic sores, varicose veins, and kidney and bladder infections have all been treated using the South African *Crinum bulbispermum* (*C. bulbispermum)* [250]. In Cameroon, *Crinum pupurascens* (*C. pupurascens)* Herb is used to treat sexual asthenia and spleen disorders. *Crinum* species (*C. defixum* Keraudren et Gawl., *C. firmifolium* Baker, *C. modestum* Baker) are as well used in Madagascar to treat abscesses, anthrax, and otitis. It is also employed as an emetic, diaphoretic, and emollient. Externally, *Crinum firmifolium* (*C. firmifolium*) is used to treat a variety of parasite skin afflictions [40,243].

4.3. Phytochemistry of Crinum

Several phytochemical and pharmacological studies have been conducted on the genus *Crinum*. The compounds isolated from various species of *Crinum* as well as their biological activities have been outlined in Table 11.

Table 11. Bioactive compounds isolated from *Crinum* species.

Plant Species	Plant Part	Country	Isolated Compounds	Bioactivity	References
C. x *amabile* *C.* x *amabile* Donn ex Ker Gawl	Bulbs Stems, roots	Ecuador Brazil Thailand	Haemanthamine/crimine-type alkaloid. Lycorine-type alkaloid Galanthamine-type alkaloid. Augustine *N*-oxide, buphanisine *N*-oxide.	Anticholinesterase (anti-AChE) and antibutyrylcholinesterase (anti-BuChE) activity.	[249–251]
C. defixum Ker-Gawl	Bulbs	India	Amabiloid A. Hydrazide derivative. (*E*)-*N*-[(*E*)-2-butenoyl]-2-butenoylhydrazide.	Anti-genotoxic activity.	[252]
C. moorei	Bulblets		Cherylline, crinamidine, crinine, epibuphanisine, lycorine, powelline, undulatine, 1-epideacetylbowdensine, 3-*O*-acetylhamayne.	NR.	[253]
C. biflorum	Bulbs	Senegal	3-[4′-(8′-aminoethyl) phenoxy] bulbispermine, mooreine. 5,6,7-trimethoxy-3-(4 hydroxybenzyl) chroman-4-one, 3-hydroxy-5,6,7-trimethoxy-3-(4-hydroxybenzyl) chroman-4-one, 3-hydroxy-5,6,7-trimethoxy-3-(4-methoxybenzyl) chroman-4-one, 5,6,7-trimethoxy-3-(4-methoxybenzyl) chroman-4-one, (*E*)-*N*-(4-hydroxyphenethyl)-3-(4-hydroxyphenyl) acrylamide.	Anticancer, anti-AChE, anti-glucosidase activity.	[254,255]
C. asiaticum *C. asiaticum* var. *sinicum* *C. asiaticum* L. *C. asiaticum* var. japonicum. *C. asiaticum* L. var. *sinicum*.	Seeds, rhizome, fruits Bulbs, stems, leaves	Beijing, China, Hainan Province, Japan, Island of Jeju in Korea	Flavonoids Isopowellaminone. (2*R*,3*S*)-7-methoxyflavan-3-ol (1:), (2*R*,3*S*)-7-hydroxy-flavan-3-ol (2:), (2*R*,3*S*)-2′-hydroxy-7-methoxy-flavan-3-ol (3:). Norgalanthamine. Crinamine CAL-n. Crijaponine A, crijaponine B, ungeremine, lycorine, 2-*O*-acetyllycorine, 1,2-*O*-diacetyllycorine, (-)-crinine, 11-hydroxyvittatine, hamayne,(+)-epibuphanisine, crinamine, yemenine A, epinorgalanthamine. Criasiaticidine A, pratorimine, Lycorine, 4′-hyd'oxy-7-methoxyflavan. Crinamine, lycorine, norgalanthamine, epinorgalanthamine. Asiaticumines A, asiaticumines B.	Inhibitory activity against LPS-induced nitric oxide production. Anticancer activity (against cervical cancer SiHa cells). Inhibition of platelet aggregation. Promotion of hair growth through dermal papilla proliferation. Inhibition of the growth of HepG2 tumor cells. Anti-AChE activity, cytotoxic activity. Cytotoxic against Meth-A (mouse sarcoma) and Lewis lung carcinoma (mouse lung carcinoma). Inhibition of the activity of hypoxia inducible factor-1 (crinamine). Cytotoxicity.	[256–266]

Table 11. *Cont.*

Plant Species	Plant Part	Country	Isolated Compounds	Bioactivity	References
C. kirkii Baker	Bulbs		Noraugustamine, 4a*N*-dedihydronoraugustamine, 3-*O*-acetylsanguinine, 1,2-diacetyllycorine.	Antiparasitic activity against *Trypanosoma brucei* (*T. brucei)* rhodesiense, *Trypanosoma cruzi* (*T. cruzi).*	[267,268]
C. macowanii	Bulbs		Macowine, lycorine, cherylline, crinine, krepowine, powelline, buphanidrine, crinamidine, undulatine, 1-epideacetylbowdensine, 4a-dehydroxycrinamabine.	NR.	[249]
C. firmifolium	Leaves	Madagascar	2-alkylquinolin-4(1H), 2-alkylquinolin-4(1H).	Antiplasmodial activity.	[269]
C. latifolium	Bulbs Leaves	China. Hanoi, Vietnam	4,8-dimethoxy-cripowellin C. 4,8-dimethoxy-cripowellin D, 9-methoxy-cripowellin B, 4-methoxy-8-hydroxy-cripowellin B, cripowellin C. *C.* latines A, *C.* latines B and *C.* latines C. 4-senecioyloxymethyl-3,4-dimethoxycoumarin, 5,6,3′-trihydroxy-7,8,4′-trimethoxyflavone. 4-methyloxysenecioyl-6,7-dimethoxycoumarin, 5,6,3′-trihydroxy-7,8,4′trimethoxyflavone.	Cytotoxic against tumor cell lines, antimicrobial activity, antioxidant activity. Inhibitory activity against human umbilical venous endothelial cells.	[270–272]
C. scillifolium	Bulbs		Scillitazettine, scilli-*N*-desmethylpretazettine.	Mild antiplasmodial activity	[273]
C. zeylanicum (L)	Bulbs, leaves, flowers, fruits	Cuba Sri Lanka	Crinine, Lycorine, 11-*O*-acetoxyambelline, ambelline, 6-hydroxybuphanidrine, 6-ethoxybuphanidrine, 3-acetylhamayne, 6-hydroxycrinamine, hamayne, 6-methoxycrinamine.	Antiproliferative effect.	[246,274]
C. jagus (J. Thomps) Dandy	Bulbs, leaves	Senegal Ghana	Gigantelline, gigantellinine, gigancrinine, sanguinine, cherylline, lycorine, crinine, flexinine, hippadine. Galanthamine, galanthamine *N*-oxide, powelline.	Anti-AChE activity, inhibitors of TcAchE, hAChE and hBChE	[275,276]
C. abyscinicum Hochst. ExA. Rich	Bulbs	Ethiopia	6-hydroxycrinamine, lycorine.	Antiproliferative activity against A2780 epithelial ovarian cancer and MV4-11 acute myeloid leukemia cell lines.	[277]
C. erubescens	Above ground plant parts	Puntarenas, Costa Rica	Cripowellin A, cripowellin B, cripowellin C, cripowellin D, hippadine.	Antiplasmodial activity.	[278]
C. yemense	Bulbs	Yemen	6-hydroxy-2H-pyran-3-carbaldehyde. Yemenines A, B and C, 1, (+)-bulbispermine, (+)-crinamine, (+)-6-hydroxycrinamine, (-)-lycorine.	Tyrosinase inhibitor. Inhibit nitric oxide production, induce nitric oxide synthase.	[277–280]

Table 11. *Cont.*

Plant Species	Plant Part	Country	Isolated Compounds	Bioactivity	References
C. bulbispermum *C. bulbispermum* III	Bulbs	Egypt	8-hydroxylycorin-7-one, 2-deoxylycorine, vittatine, 11-hydroxyvittatine, hippamine. 4-hydroxy-2′,4′-dimethoxydihydrochalcone, 4,5-methylenedioxy-4′-hydroxy-2-aldehyde [1,1′-biphenyl], hippacine, 4′-hydroxy-7-methoxyflavan-3-ol, 2(S),3′,4′-dihydroxy-7-methoxy flavan, isolarrien, isoliquiritigenin, liquiritigenin. Bulbispermine.	NR.	[281–283]
C. powellii	Bulbs	Switzerland Colombia	Linoleic acid ethyl ester, alkaloid hippadine, calleryanin, 4′-hydroxy-7-methoxyflavan. Lycorine, 1-*O*-acetyllycorine, ismine.	AChE inhibitor (linoleic acid ethyl ester). Inhibition of topoisomerase 1 activity.	[284,285]
C. glaucum	Bulbs	Nigeria	Hamayne, lycorine, haemanthamane, crinamine.	Choline esterase inhibitory activity.	[286]
C. purpurascens	Leaves	Cameroon	4,5-ethano-9,10-methlenedioxy-7-phenanthridone, 4,5-ethano-9-hydroxy-10-methoxy-7-phenanthridone, α-D-glucopyranoside.	Antibacterial activity	[287]

NR: not reported.

Chemical structures of common compounds from *Crinum* are shown in Figure 5.

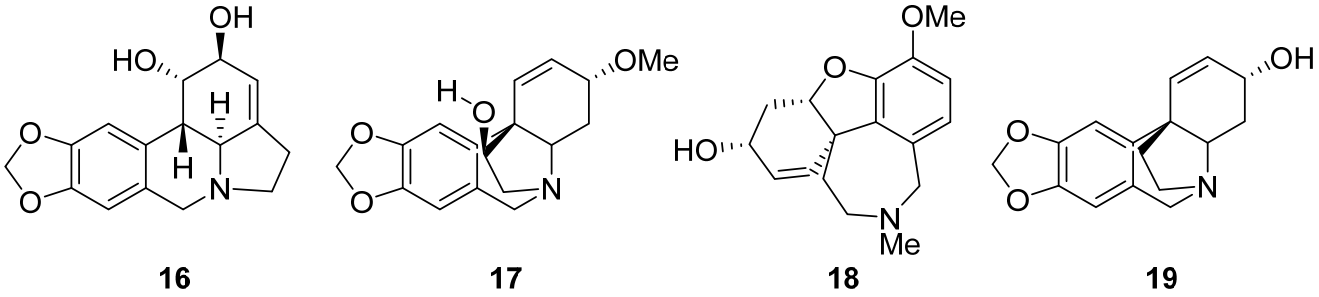

Figure 5. Chemical structures of compounds isolated from the genus *Crinum*. Lycorine (**16**), crinamine (**17**), galantamine (**18**) and crinine (**19**).

4.4. Pharmacological Activities of Crinum

4.4.1. Anti-Inflammatory and Analgesic Effects

The anti-inflammatory and the analgesic properties of various *Crinum* species have been investigated by several authors. The anti-inflammatory effect of *C. asiaticum* as well as its effect on bradykinin-induced contractions on isolated uterus has been reported [288–291]. The ethanolic extract of *C. asiaticum* demonstrated significant analgesic effect in an acetic-acid-induced writhing test [292]. Antipyretic and anti-inflammatory properties of *C. jagus* were recently reported by Minkah and Danquah [291]. Leaf extract of *C. bulbispermum* has also been established to possess antinociceptive effects [293,294].

4.4.2. Anticancer and Cytotoxicity Effects

The cytotoxic effects of *C. asiaticum* extract was investigated and was shown to exert toxic effect on brine shrimps and murine P388 D1 cells [294–298]. Yui et al. demonstrated that hot water extracts of *C. asiaticum* exhibited potent inhibition of calprotectin-induced cytotoxicity in MM46 mouse mammary carcinoma cells. This activity whi1ch was later attributed to lycorine, an active compound in *C. asiaticum* [297]. Some alkaloids isolated from the bulbs of *C. asiaticum* have been reported to show remarkable inhibition against tumor cell lines A549, LOVO, HL-60, and 6T-CEM [261].

The extract of *C. asiaticum* exhibited antiproliferative and chemosensitizing effects against multi-drug-resistant cancer cells [298,299]. The antiangiogenic activity of the methanolic leaf extract of *C. asiaticum* was evaluated and established by Yusoff [300]. The cytotoxic effect of the essential oil extracted from *C. asiaticum* was as well established in MCF-7 cells [301]. A recent work done by Yu et al. reported the inhibition of the growth of HepG 2 cells in a dose-dependent manner by polysaccharide CAL-n, an isolate from *C. asiaticum* [262]. Also, the neuroprotection and anti-neuroinflammatory effects in Neuronal Cell Lines were reported by Lim et al. [279,302]. Alkaloids from *C. bulbispermum* have also been reported to possess cytotoxic activities [284]. Evaluation of the cytoprotective potential of *C. bulbispermum*, after induction of toxicity using rotenone, in SH-SY5Y neuroblastoma cells proved that, the plant has such effect as reported [303]. Aboul-Ela et al. [279] tested the cytotoxic effect of *C. bulbispermum* bulbs using the brine shrimp bioassay.

4.4.3. Antimicrobial Properties

The in vitro antitubercular effects of *C. asiaticum* on *Mycobacterium tuberculosis* (*M. tuberculosis*) surrogate, *Mycobacterium smegmatis* (*M. smegmatis*), were reported [291,304]. *C. asiaticum* was shown to possess a broad-spectrum antimicrobial activity against Gram-positive, Gram-negative bacteria and fungal pathogens [291,299]. Antifungal activities of the essential oil and extracts of *C. asiaticum* against pathogenic fungi have also been established [305,306]. It is reported that the methanolic root extract of *C. asiaticum* exerts significant anti-HIV-1 activity [307]. The ethanolic extract of *C. asiaticum* significantly inhibited

selected bacteria as evaluated by Naira et al. [308]. Dichloromethane extract of *C. asiaticum* was found to be the most effective against selected oral and vaginal *Candida* species [309]. Minkah and Danquah again demonstrated the antimicrobial activity of extracts of *C. jagus* against clinically significant microorganisms in the High-throughput spot culture growth inhibition (HT-SPOTi) assay [291]. Water/Ethanol extract of *C. jagus* was observed to be active on *Shigella flexneri*-induced diarrhea in rats [310]. The antimicrobial and antioxidant properties of *C. jagus* make it suitable as a wound healing agent [311]. The crude methanolic extract of *C. jagus* was investigated to have effect on *Mycobacterium tuberculosis* [312,313]. The crude alkaloid of *C. jagus* inhibited Dengue virus infection [314]. *C. macowanii* has also been shown to possess biological effects such as antifungal, antiviral and antiplasmodial activities [315].

4.4.4. Antioxidant Properties

There antioxidant effects of *C. asiaticum* have been studied extensively. The ethanolic extract exhibited protective effects on human erythrocyte [316]. *C. asiaticum* bulbs also exerted remarkable free radical scavenging ability [317]. The antioxidant activity of the ethanolic extract of *C. asiaticum* leaves in alloxan-induced diabetic rats was well demonstrated [318]. More recent work on the methanolic extract of *C. asiaticum* showed antioxidant effects [319]. Potent DPPH radical scavenging activity was also observed for the aqueous *C. asiaticum* leaf extract [304]. Both the leaves and bulbs of *C. jagus* are important sources of antioxidant compounds [320]. A methanolic bulb extract of *C. bulbispermum* showed mild radical scavenging activity [321]. The leaf extracts of *C. bulbispermum* also showed modest antioxidant activity in a thiobarbituric acid reactive substances assay [297].

4.4.5. Other Pharmacological Properties

Kumar reported the wound healing activities of the ethanolic *C. asiaticum* extract. The extract was found to possess pro-healing effects when topically applied on animal models by influencing various stages of healing process [322]. *C asiaticum* extract and norgalanthamine potentially influenced hair growth via inhibition of 5α-reductase activity and TGF-β1-induced canonical pathway [39,314]. There is a report on the inhibitory effects of three *C. asiaticum* genotypes against key enzymes implicated in the pathogenesis of Alzheimer's disease and diabetes [319].

The anti-obesity effect of the *C. asiaticum* extract on a high-fat diet-induced obesity in monogenic mice has been reported [323,324]. An active fraction of *C. jagus* was shown to possess anticonvulsant activities in experimental rats [325].

Ethyl acetate and methanol extracts of *C. bulbispermum* have also been shown to exhibit acetylcholinesterase inhibitory properties [321]. The alkaloid galanthamine isolated from *C. bulbispermum* and other genera of Amaryllidaceae, has been approved for the treatment of Alzheimer's disease [326]. Cognitive enhancing effect of a hydroethanolic extract of *C. macowanii* against memory impairment induced by aluminum chloride in balb/c mice has as well been reported [327].

5. The Genus *Cyrtanthus*

5.1. Botanical Description

Another large genus of the family Amaryllidaceae is *Cyrtanthus*. *Cyrtanthus* is derived from a Greek word for curved flower [6]. Species of this genus have numerous, black, winged seeds and give off a strong onion smell [6]. They possess a rhizome or bulb, flowers and a loculicidal capsule fruit [6]. They have leaves that are linear to lorate [6]. Flowers are funnel shaped with their stamens fixed in the corolla tube [6]. Species that belong to this genus include *Cyrtanthus elatus* (*C. elatus*) (Jacq.) Traub, *Cyrtanthus obliquus* (*C. obliquus*) (L.f.) Aiton, and *Cyrtanthus mackenii* (*C. mackenii*) Hook [44].

5.2. Geographical Distribution

Cyrtanthus is diverse and is a large sub-Saharan Africa genus consisting of approximately 55 species found mostly in South Africa. *Cyrtanthus* extends from the summer-dry southwest to the summer rainfall northeast [328]. The genus displays diverse floral morphology. The three major lineages show varying biogeographic affinities.

Clade A comprises taxa located in Southern African Grassland Biome with a few outliers in the Savanna Biome to the east and north, the Indian Ocean Coastal Belt Biome to the extreme east and the Fynbos Biome to the south [328]. Hence, it falls in the Afrotemperate Phytogeographical Region [329] that encompasses Afromontane phytochorion in the north and the Cape Floristic Region in the south [328]. Most existing species in the Afrotemperate lineage (*Cyrtanthus attenuatus* (*C. attenuatus)*, *Cyrtanthus macowanii* (*C. macowanii)*, *Cyrtanthus epiphyticus* (*C. epiphyticus)*, *C. mackenii* subsp. *cooperi*, *Cyrtanthus huttonii* (*C. huttonii)*, *Cyrtanthus macmasteri* (*C. macmasteri)*, *Cyrtanthus suaveolens* (*C. suaveolens)*, *Cyrtanthus stenanthus* (*C. stenanthus* var. *stenanthus*) and *Cyrtanthus flanaganii* (*C. flanaganii)* occur currently in the south-eastern African temperate grasslands. *Cyrtanthus tuckii* var. *transvaalensis* (*C. tuckii)* is the only species found in the grassland of the Highveld in the northern parts of South Africa. Few species are found outside this grassland area and includes *Cyrtanthus angustifolius* (*C. angustifolius)*, *Cyrtanthus fergusoniae* (*C. fergusoniae)* and *Cyrtanthus aureolinus* (*C. aureolinus)* in the Cape Region together with *C. mackenii* subsp. *Mackenii* and *Cyrtanthus brachyscyphus* (*C. brachyscyphus)* that occupies drainage lines on the subtropical Indian Ocean Coastal Belt [330]. Southern Africa is the area where *Cyrtanthus breviflorus* (*C. breviflorus)* is found extending northwards in a series of disjunct populations along mountain corridors to East Africa and Angola.

Clade B is limited to the Fynbos and Succulent Karoo Biomes which constitute the Greater Cape Region, referred to hereafter as 'the Cape' [331]. *Cyrtanthus labiatus* (*C. labiatus)* and *Cyrtanthus montanus* (*C. montanus)* from the Baviaansklo of Mountains and Eastern Cape are found at the interface of the Fynbos and Albany Thicket Biomes. The Richtersveld species, *Cyrtanthus herrei* (*C. herrei)* is found in the semi-arid Succulent Karoo [328]. Most species found in 'the Cape' lineage are located on the summer-dry, southeast coast forelands with half the number in the Fynbos of the nonseasonal rainfall Eastern Cape. *Cyrtanthus carneus* (*C. carneus*, *C. elatus*, *Cyrtanthus guthrieae* (*C. guthrieae*, *C. labiatus*, *Cyrtanthus leptosiphon* (*C. leptosiphon*), *Cyrtanthus leucanthus* (*C. leucanthus*, *Cyrtanthus montanus* (*C. montanus)*, *and Cyrtanthus odorus* (*C. odorus)* are found in specific vegetation types and soils.

Only two species of this taxon, namely *Cyrtanthus collinus* (*C. collinus)* and *Cyrtanthus ventricosus* (*C. ventricosus)* are well known, inhabiting the same soils and aspect in habitats on the continuous Cape Fold mountain ranges [328]. *Cyrtanthus collinus* is found on the coastal and inland mountains of the southern Cape and *C. ventricosus* extends from the Cape Peninsula into the Eastern Cape [328].

Most species of Clade C are found in the eastern lowlands and midlands of southern Africa, where they are concentrated in the subtropical biomes, Albany Thicket and Savanna [330,332]. This lineage constitutes *Cyrtanthus flammosus* (*C. flammosus)* and *Cyrtanthus spiralis* (*C. spiralis)*, which are narrowly widespread to the Albany Thicket Biome. Confined to the Savanna Biome are *Cyrtanthus eucallus* (*C. eucallus)* and *Cyrtanthus galpinii* (*C. galpinii)* in the Lowveld. Other species span the Albany Thicket and Savanna Biomes: the Eastern Cape *Cyrtanthus helictus* (*C. helictus)* and, extending northwards from the Albany region through South Africa, Zimbabwe, western Mozambique and East Africa into Sudan, is *Cyrtanthus sanguineus* (*C. sanguineus)* [328]. *Cyrtanthus obliquus*, adapted to nutrient-poor soils, occupies rocky habitats in east–west tending valleys. A summary of their geographic distribution is presented in Table 12.

Table 12. Geographical distribution of the Genus *Cyrtanthus*.

Lineage	Location	Species	References
Clade A	Southern Africa Grassland Southeastern African temperate grasslands Grassland of the Highveld in the northern parts Subtropical Indian Ocean Coastal Belt East Africa and Angola	*C. attenuatus*, *C. macowanii*, *C. epiphyticus*, *C. mackenii* subsp. *cooperi*, *C. huttonii*, *C. macmasteri*, *C. suaveolens*, *C. stenanthus* var. *stenanthus*, *C. flanaganii* *C. tuckii* var. *transvaalensis* *C. angustifolius*, *C. fergusoniae* *C. aureolinus*, *C. mackenii* subsp. *Mackenii*, *C. brachyscyphus* *C. breviflorus*	[328]
Clade B	Baviaanskloof Mountains and Eastern Cape (Fynbos and Albany Thicket Biomes) Semi-arid Succulent Karoo Greater Cape Region ("the Cape") Coastal and inland mountains of the southern Cape Cape Peninsula into the Eastern Cape	*C. labiatus*, *C. montanus* *C. herrei* *C. carneus*, *C. elatus*, *C. guthrieae*, *C. labiatus*, *C. leptosiphon*, *C. leucanthus*, *C. montanus*, *C. odorus* *C. collinus* *C. ventricosus*	[328]
Clade C	Albany Thicket Biome Savanna Biome Northwards from the Albany region through South Africa, Zimbabwe, Western Mozambique and East Africa into Sudan Albany Thicket and Savanna Biomes Extends beyond the Savanna Biome into the Sub-Escarpment and Highveld grasslands Fynbos Biome Southern parts of the Nama Karoo	*C. flammosus*, *C. spiralis* *C. eucallus*, *C. galpinii* *C. sanguineus* *C. helictus* *C. contractus* *C. wellandii* *C. smithiae*	[328]

5.3. Traditional Uses

Cyrtanthus obliquus, locally known as umathunga in South Africa, is used traditionally in the management of chronic coughs, headaches and scrofula [43,44]. *C. obliquus* root infusions are also employed in the management of stomach aches [333] while the crushed roots have been reported to find use in the management of leprosy [334]. *Cyrtanthus* species are also employed in the management of ailments associated with pregnancy, as well as cystitis, age-related dementia and leprosy [43,44]. Bulbs of *C. contractus* extracted in May and September is widely used locally in the management of mental illness, infections, inflammation, and cancer [335]. Infusions from species such as *C. breviflorus*, *C. contractus*, *C. mackenii*, *C. sanguineus*, *C. stenanthus* and *C. tuckii* are used by the Zulu in South Africa as protective sprinkling charms against storms and evil spirits [336]. Extracts of *C. breviflorus Harv.* are used as an anti-emetic agent and in the management of worm infestations such as tapeworm and roundworm. Extracts of *C. elatus* also finds use in the management of cough, headache and in labour induction [337].

5.4. Phytochemistry of Cyrtanthus

Species of *Cyrtanthus* have been identified as reservoirs for a host of chemical compounds. In a study performed by Mahlangeni et al., four homoisoflavanones, namely 5,7-dihydroxy-6-methoxy-3-(4′-methoxybenzyl)chroman-4-one, 5,7-dihydroxy-6-methoxy-3-(4′hydroxybenzyl)chroman-4-one and two 5,7-dihydroxy-6-methoxy-3-(4′-methoxybenzylidene)chroman-4-one, 5,7-dihydroxy-3-(4′hydroxybenzylidene)-chroman-4-one were isolated from the hexane, methanol and dichloromethane extracts of *Cyrtanthus obliquus* [338]. The bulbs of *C. obliquus* extracted with ethanol also revealed the presence of novel alkaloid obliquine, as well as 1α-hydroxygalanthamine, 3-epimacronine, narcissidine, tazettine and trisphaeridine [339].

The presence of lycorine, tazettine and 11-hydroxyvittatine in dried bulb ethanol extract of *Cyrtanthus mackenii* (Hook f.) has been demonstrated by Masi et al. [340]. Fresh bulb methanol extracts of *C. contractus* also contains a phenanthridone alkaloid called narciclasine [335]. Furthermore, two crinine alkaloids; haemanthamine and haemanthidine

have been isolated from fresh bulb ethanol extracts of *C. elatus*. Further studies on the alcoholic extracts of the fresh bulbs also yielded the alkaloids zephyranthine, galanthamine and 1,2-O-diacetylzephyranthine [43,44]. Tazettine, maritidine, *O*-methylmaritidine, and papyramine are all phytochemicals that have been identified in fresh bulb methanol extracts of *C. falcatus* [337].

Chemical structure of compounds isolated from *Cyrtanthus* have been shown in Figure 6.

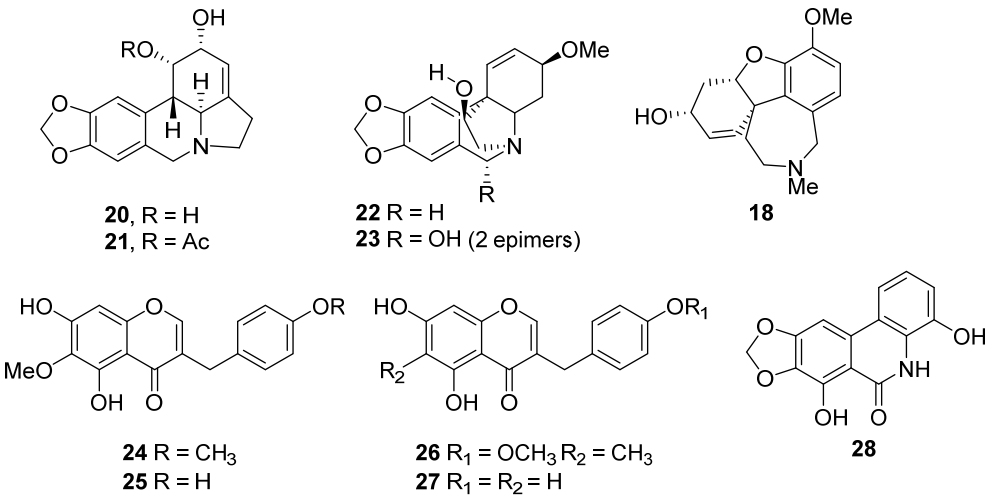

Figure 6. Chemical structures of selected compounds from *Crytanthus*. Zephyranthine (**20**), 1,2-*O*-diacetylzephyranthine (**21**), haemanthamine (**22**), haemanthadine (**23**), galanthamine (**18**), 5,7-dihydroxy-6-methoxy-3-(4′-methoxybenzyl)chroman-4-one (**24**), 5,7-dihydroxy-6-methoxy-3-(4′-methoxybenzylidene)chroman-4-one (**25**), 5,7-dihydroxy-6-methoxy-3-(4′hydroxybenzyl)chroman-4-one (**26**), 5,7-dihydroxy-3-(4′hydroxybenzylidene)-chroman-4-one (**27**) and naciprimine (**28**).

5.5. Pharmacological Activities

5.5.1. Antioxidant Activity

5,7-dihydroxy-6-methoxy-3-(4′-methoxybenzyl)chroman-4-one and 5,7-dihydroxy-6-methoxy-3-(4′-hydroxybenzyl)chroman-4-one isolated from the fresh bulbs of *C. obliquus* have been shown to possess significant antioxidant activity with an IC_{50} of 371.54 and 288.40 µg/mL, respectively [338].

5.5.2. Anti-Inflammatory Activity

The methanol extract of the bulbs of *C. contractus* has been investigated and shown to possess significant anti-inflammatory activity. The extract exhibited dose-dependent inhibition of E-selectin, a proinflammatory agent, when tested on endothelial cells. Further studies of the methanol extract on human umbilical vein endothelial cells revealed a concentration-dependent reduction in THP-1 adhesion via blockade of the expression of endothelial adhesion molecule ICAM-1. Narciclasine was identified as the main anti-inflammatory compound in the methanol extract of the bulbs of *C. contractus* [335].

The dichloromethane (DCM) extracts of *C. falcatus* (roots) and *C. mackenii* (leaves) were shown to interfere with the activity of cyclooxygenase 2 (COX-2) by at least 90%. DCM extract of *C. suaveolens* also blocked prostaglandin synthesis via antagonizing COX-2 activity by 81.6 %. Moderate inhibition (approximately 70%) of COX-2 activity was also observed with the methanol extracts of the roots and leaves of *C. falcatus* [341,342]. Selective inhibition of COX-2 by these extracts makes them suitable candidates for development for clinical use.

5.5.3. Inhibition of Acetylcholinesterase

The phenanthridone alkaloid nacriprimine, isolated from the ethanolic bulb extract of *C. contractus* has been shown to possess mild acetylcholinesterase inhibition property with

an IC_{50} of 78.9 µg/mL compared to the 40-fold more potent standard galanthamine with an IC_{50} of 1.9 µg/mL [11].

5.5.4. Antimicrobial Activity

Cyrtanthus species and their isolated compounds have demonstrated noteworthy antimicrobial activity against a panel of microorganisms. *C. suaveolens* bulbs/roots and leaves isolated with DCM demonstrated broad-spectrum antimicrobial activity against *B. subtilis*, *E. coli*, *K. pneumoniae*, *M. luteus* and *S. aureus* with zones of inhibition ranging between 0.13–0.91 mm. DCM extracts of *C. falcatus* also inhibited the growth of *B. subtilis S. aureus* and *E. coli. C. mackenii* bulb/root extracts also inhibited the growth *M. luteus and S. aureus* [337].

Haemanthamine and haemanthidine isolated from the bulbs of *C. elatus* have been investigated for their activity against parasitic protozoans [43]. Haemanthamine showed activity against trophozoite stage of *Entamoeba histolytica* (*E. histolytica)* HK9 with an IC_{50} of 0.75 µg/mL and mild activity against *Plasmodium falciparum* (*P. falciparum)* NF54 with an IC_{50} of 0.67 µg/mL. The activity against *E. histolytica* was compared to ornidazole with an IC_{50} 0.28 µg/mL whiles the activity against *P. falciparum* was compared to chloroquine with an IC_{50} of 0.004 µg/mL and artemisinin with an IC_{50} of 0.002 µg/mL [43].

Haemanthidine also showed weak activity against *P. falciparum*, *T. brucei rhodesiense* STIB 900, and *T. cruzi* Tulahuen C4 with an IC_{50} of 0.70, 1.1 and 1.38 µg/mL, respectively. Melarsoprol with an IC_{50} of 0.002 µg/mL and benznidazole with an IC_{50} of 0.56 µg/mL were used as standards for *Trypanosoma brucei rhodesiense* STIB 900, and *Trypanosoma cruzi* Tulahuen C4, respectively [43].

5.5.5. Cytotoxic Activity

Haemanthamine isolated from *C. elatus* was shown to possess cytotoxic activity which was mediated via the apoptotic pathway as depicted in rat hepatoma cell (5123tc). The ED_{50} was determined at 15 µM and this result was of particular interest due to its selectivity; haemanthamine demonstrated insignificant activity in normal human embryo kidney (293t) cells [337].

Alkaloids isolated from *C. obliquus* tested for cytotoxic activity against Chinese Hamster ovarian and human hepatoma (hepG2) cells showed no cytotoxic activity up to a concentration of 100 µg/mL [339].

Tazettine isolated from *C. falcatus* and other members of Amaryllidaceae has been reported to possess cytotoxic activity on colon cell line murine alveolar non-tumoral fibroblast [343,344]. Papyramine, also extracted from *C. falcatus* showed cytotoxic activity against murine alveolar non-tumoral fibroblast and human lymphoid neoplasm as well [343,344].

5.5.6. Miscellaneous Pharmacological Activities

Roots of *C. falcatus* and *C. surveolens* extracted with DCM exhibited mutagenicity in *Salmonella* strain TA98 which was higher than that observed in the leaves of these plants. Mutagenicity was, however, not observed in the methanol extracts of these plants [337]. The mutagenicity of *C. suaveolens* has been attributed to the compound captan isolated from the bulbs/roots using DCM [344].

A summary of the traditional uses, phytochemicals and pharmacological activities of *Cyrtanthus* species have been highlighted in Table 13.

Table 13. A summary of the traditional uses, phytochemicals and pharmacological activities of *Cyrtanthus* species.

Plant Species	Traditional Uses	Compounds	Pharmacological Activities	References
C. obliquus	Chronic cough, headache and scrofula	5,7-dihydroxy-6-methoxy-3-(4′-methoxybenzyl)chroman-4-one, 5,7-dihydroxy-6-methoxy-3-(4′-hydroxybenzyl)chroman-4-one	Antioxidant activity	[338]
C. contractus	Mental illness, protective charm against evil spirits	NarciclasineNarciprimine	Anti-inflammatory activity (via inhibition of E-selectin, blockade of the expression of endothelial adhesion molecule ICAM-1)Acetylcholinesterase inhibitor	[337]
C. breviflorus	Emesis, worm infestations, protective charm against evil spirits	haemanthamine, lycorine, crinamine hydrochloride and tazettine	Antihelminthic	[337,342]
C. elatus	Cough, headache, labor induction	Haemanthamine, zephyranthine, galanthamine and 1,2-*O*-diacetylzephyranthine	Antiprotozoan activity, selective cytotoxic activity	[43,44,337]
C. falcatus	Not known to be used by the traditional South African people	Papyramine, epipapyramine, maritidine, *O*-methylmaritidine and tazettine	Antibacterial activity against *B. subtilis S. aureus* and *E. coli*, mutagenicity, cytotoxic activity	[342–344]
C. suaveolens	No traditional use has been reported	Captan	Mutagenicity, anti-inflammatory activity via inhibition of COX-2, fungicide	[342,344]

6. Conclusions

The discovery of new drugs in response to the growing burden of infectious and non-communicable diseases is of utmost necessity in this era. The genera *Tulbaghia*, *Allium*, *Crinum*, and *Cyrtanthus* of the Amaryllidaceae family have been well presented and shown to be a source of promising medicinal compounds with varying biological properties. Further research is therefore necessary to propel these compounds through clinical trials for possible usage in therapeutics. Although natural products have been attributed with high safety profiles, the presence of mutagenic compounds in crude extracts of these plants underscores the importance of pharmacological studies prior to their use in traditional medicine. These findings are relevant in light of augmenting the lean pipeline of drug discovery.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/molecules27144475/s1, Table S1: Compounds from *Tulbaghia*. Reference [345] is cited in the Supplementary Materials.

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Abbreviations

MIC, minimum inhibitory concentration; MBC, minimum bactericidal concentration; MTT, 3-[4,5-dimethylthiazol-2-yl]-2,5 diphenyl tetrazolium bromide; MoA, mode of action; ROS, reactive oxygen species; TEAC, Trolox equivalent antioxidant capacity; FRAP, ferric-reducing antioxidant power; DPPH, 2,2-diphenyl-1-picryl-hydrazyl-hydrate; AAPH, 2,2′-azobis-2-amidinopropane dihydrochloride; TG, triglyceride; TC, total cholesterol; VLDL, very low-density lipoprotein; HDL, high-density lipoprotein; BP, blood pressure; AVD, atherothrombotic vascular disease; DCM, dichloromethane.

References

1. Barile, E.; Capasso, R.; Izzo, A.A.; Lanzotti, V.; Sajjadi, S.E.; Zolfaghari, B. Structure-activity relationships for saponins from Allium hirtifolium and Allium elburzense and their antispasmodic activity. *Planta Med.* **2005**, *71*, 1010–1018. [CrossRef] [PubMed]
2. Chase, M.W.; Reveal, J.L.; Fay, M.F. A subfamilial classification for the expanded asparagalean families Amaryllidaceae, Asparagaceae and Xanthorrhoeaceae. *Bot. J. Linn. Soc.* **2009**, *161*, 132–136. [CrossRef]
3. Takos, A.M.; Rook, F. Towards a Molecular Understanding of the Biosynthesis of Amaryllidaceae Alkaloids in Support of Their Expanding Medical Use. *Int. J. Mol. Sci.* **2013**, *14*, 11713–11741. [CrossRef] [PubMed]
4. Vosa, C.G.; Siebert, S.J.; Van Wyk, A.E.B. Micromorphology and cytology of Prototulbaghia siebertii, with notes on its taxonomic significance. *Upsp. Inst. Repos.* **2011**, *41*, 311–314.
5. Elgorashi, E.E.; van Staden, J. *Bioactivity and Bioactive Compounds of African Amaryllidaceae*; ACS Publications: Washington, DC, USA, 2009; ISBN 1947-5918.
6. Fenwick, G.R.; Hanley, A.B.; Whitaker, J.R. The genus allium—Part 1. *Crit. Rev. Food Sci. Nutr.* **1985**, *22*, 199–271. [CrossRef]
7. Fenwick, G.R.; Hanley, A.B. The genus allium—Part 2. *Crit. Rev. Food Sci. Nutr.* **1985**, *22*, 273–377. [CrossRef]
8. Aremu, A.O.; Van Staden, J. The genus Tulbaghia (Alliaceae)—A review of its ethnobotany, pharmacology, phytochemistry and conservation needs. *J. Ethnopharmacol.* **2013**, *149*, 387–400. [CrossRef]
9. Styger, G.; Aboyade, O.M.; Gibson, D.; Hughes, G. Tulbaghia—A Southern African Phytomedicine. *J. Altern. Complement. Med.* **2016**, *22*, 255–261. [CrossRef]
10. Jagtap, U.B.; Lekhak, M.M.; Fulzele, D.P.; Yadav, S.R.; Bapat, V.A. Analysis of selected Crinum species for galanthamine alkaloid: An anti-Alzheimer drug. *Curr. Sci.* **2014**, *107*, 2008–2010.
11. Nair, J.J.; Aremu, A.O.; Van Staden, J. Isolation of narciprimine from Cyrtanthus contractus (Amaryllidaceae) and evaluation of its acetylcholinesterase inhibitory activity. *J. Ethnopharmacol.* **2011**, *137*, 1102–1106. [CrossRef]
12. Torras-Claveria, L.; Berkov, S.; Codina, C.; Viladomat, F.; Bastida, J. Daffodils as potential crops of galanthamine. Assessment of more than 100 ornamental varieties for their alkaloid content and acetylcholinesterase inhibitory activity. *Ind. Crops Prod.* **2013**, *43*, 237–244. [CrossRef]
13. Shang, A.; Cao, S.-Y.; Xu, X.-Y.; Gan, R.-Y.; Tang, G.-Y.; Corke, H.; Mavumengwana, V.; Li, H.-B. Bioactive Compounds and Biological Functions of Garlic (*Allium sativum* L.). *Foods* **2019**, *8*, 246. [CrossRef] [PubMed]
14. Sharma, D.; Rani, R.; Chaturvedi, M.; Rohilla, P.; Yadav, J.P. In silico and in vitro approach of Allium cepa and isolated quercetin against MDR bacterial strains and Mycobacterium smegmatis. *S. Afr. J. Bot.* **2019**, *124*, 29–35. [CrossRef]
15. Stoica, F.; Aprodu, I.; Enachi, E.; Stănciuc, N.; Condurache, N.N.; Duță, D.E.; Bahrim, G.E.; Râpeanu, G. Bioactive's Characterization, Biological Activities, and In Silico Studies of Red Onion (*Allium cepa* L.) Skin Extracts. *Plants* **2021**, *10*, 2330. [CrossRef] [PubMed]
16. Albishi, T.; John, J.A.; Al-Khalifa, A.S.; Shahidi, F. Antioxidant, anti-inflammatory and DNA scission inhibitory activities of phenolic compounds in selected onion and potato varieties. *J. Funct. Foods* **2013**, *5*, 930–939. [CrossRef]
17. Benmalek, Y.; Yahia, O.A.; Belkebir, A.; Fardeau, M.-L. Anti-microbial and anti-oxidant activities of Illicium verum, Crataegus oxyacantha ssp monogyna and Allium cepa red and white varieties. *Bioengeineered* **2013**, *4*, 244–248. [CrossRef] [PubMed]
18. Elberry, A.A.; Mufti, S.; Al-Maghrabi, J.; Abdel Sattar, E.; Ghareib, S.A.; Mosli, H.A.; Gabr, S.A. Immunomodulatory effect of red onion (*Allium cepa* Linn) scale extract on experimentally induced atypical prostatic hyperplasia in Wistar rats. *Mediat. Inflamm.* **2014**, *2014*, 640746. [CrossRef]
19. Lanzotti, V. The analysis of onion and garlic. *J. Chromatogr.* **2006**, *1112*, 3–22. [CrossRef]
20. Rouf, R.; Uddin, S.J.; Sarker, D.K.; Islam, M.T.; Ali, E.S.; Shilpi, J.A.; Nahar, L.; Tiralongo, E.; Sarker, S.D. Antiviral potential of garlic (Allium sativum) and its organosulfur compounds: A systematic update of pre-clinical and clinical data. *Trends Food Sci. Technol.* **2020**, *104*, 219–234. [CrossRef]
21. Harazem, R.; El Rahman, S.A.; El-Kenawy, A. Evaluation of Antiviral Activity of Allium cepa and Allium sativum Extracts Against Newcastle Disease Virus. *Alex. J. Vet. Sci.* **2019**, *61*, 108–118. [CrossRef]
22. Elmi, T.; Hajialiani, F.; Asadi, M.R.; Sadeghi, S.; Namazi, M.J.; Tabatabaie, F.; Zamani, Z. Antimalarial effects of the hydroalcoholic extract of Allium paradoxum in vitro and in vivo. *J. Parasit. Dis.* **2021**, *45*, 1055–1064. [CrossRef]

23. Ruslan, M.S.; Baba, M.S. In vivo antimalarial assessment and toxicity evaluation of garlic (*Allium sativum*) in plasmodium berghei NK65-induced mice. *Malays. Appl. Biol.* **2018**, *47*, 17–24.
24. Syaban, M.F.R.; Rachman, H.A.; Arrahman, A.D.; Hudayana, N.; Khamid, J.P.; Pratama, F.A. Allium sativum as antimalaria agent via falciapin protease-2 inhibitor mechanism: Molecular docking perspective. *Clin. Res. J. Intern. Med.* **2021**, *2*, 130–135. [CrossRef]
25. Upadhyay, R.K. Nutritional and therapeutic potential of Allium vegetables. *J. Nutr. Ther.* **2017**, *6*, 18–37. [CrossRef]
26. Thomson, M.; Ali, M. Garlic [*Allium sativum*]: A review of its potential use as an anti-cancer agent. *Curr. Cancer Drug Targets* **2003**, *3*, 67–81. [CrossRef] [PubMed]
27. Corea, G.; Fattorusso, E.; Lanzotti, V.; Capasso, R.; Izzo, A.A. Antispasmodic saponins from bulbs of red onion, *Allium cepa* L. var. Tropea. *J. Agric. Food Chem.* **2005**, *53*, 935–940. [CrossRef]
28. Galmarini, C.R.; Goldman, I.L.; Havey, M.J. Genomics Genetic analyses of correlated solids, flavor, and health-enhancing traits in onion (*Allium cepa* L.). *Mol. Genet. Genom.* **2001**, *265*, 543–551. [CrossRef]
29. Takahashi, M.; Shibamoto, T. Chemical compositions and antioxidant/anti-inflammatory activities of steam distillate from freeze-dried onion (*Allium cepa* L.) sprout. *J. Agric. Food Chem.* **2008**, *56*, 10462–10467. [CrossRef]
30. Nishimura, H.; Wijaya, C.H.; Mizutani, J. Volatile flavor components and antithrombotic agents: Vinyldithiins from *Allium victorialis* L. *J. Agric. Food Chem.* **1988**, *36*, 563–566. [CrossRef]
31. Brace, L.D. Cardiovascular benefits of garlic (*Allium sativum* L.). *J. Cardiovasc. Nurs.* **2002**, *16*, 33–49. [CrossRef]
32. Ali, M.; Thomson, M.; Afzal, M. Garlic and onions: Their effect on eicosanoid metabolism and its clinical relevance. *Prostaglandins Leukot. Essent. Fat. Acids* **2000**, *62*, 55–73. [CrossRef] [PubMed]
33. Sabiu, S.; Madende, M.; Ajao, A.A.; Aladodo, R.A.; Nurain, I.O.; Ahmad, J.B. *The Genus Allium (Amaryllidaceae: Alloideae): Features, Phytoconstituents, and Mechanisms of Antidiabetic Potential of Allium cepa and Allium sativum*, 2nd ed.; Elsevier Inc.: Amsterdam, The Netherlands, 2019; ISBN 9780128138229.
34. Muñoz-Torrero López-Ibarra, D. *Recent Advances in Pharmaceutical Sciences I*; Transworld Research Network: Trivandrum, India, 2011; ISBN 8178955288.
35. Akash, M.S.H.; Rehman, K.; Chen, S. Spice plant Allium cepa: Dietary supplement for treatment of type 2 diabetes mellitus. *Nutrition* **2014**, *30*, 1128–1137. [CrossRef] [PubMed]
36. Corzo-Martínez, M.; Corzo, N.; Villamiel, M. Biological properties of onions and garlic. *Trends Food Sci. Technol.* **2007**, *18*, 609–625. [CrossRef]
37. Kumar, K.P.S.; Debjit, B.; Pankaj, T. Allium cepa: A traditional medicinal herb and its health benefits. *J. Chem. Pharm. Res.* **2010**, *2*, 283–291.
38. Shri, R.; Bora, K.S. Neuroprotective effect of methanolic extracts of Allium cepa on ischemia and reperfusion-induced cerebral injury. *Fitoterapia* **2008**, *79*, 86–96. [CrossRef]
39. Kongkwamcharoen, C.; Itharat, A.; Pipatrattanaseree, W.; Ooraikul, B. Effects of Various Preextraction Treatments of Crinum asiaticum Leaf on Its Anti-Inflammatory Activity and Chemical Properties. *Evid. Based. Complement. Alternat. Med.* **2021**, *2021*, 8850744. [CrossRef] [PubMed]
40. Fennell, C.W.; Van Staden, J. Crinum species in traditional and modern medicine. *J. Ethnopharmacol.* **2001**, *78*, 15–26. [CrossRef]
41. Maroyi, A. Ethnobotanical, phytochemical and pharmacological properties of Crinum bulbispermum (Burm f) Milne-Redh and Schweick (Amaryllidaceae). *Trop. J. Pharm. Res.* **2016**, *15*, 2497–2506. [CrossRef]
42. Takaidza, S.; Pillay, M.; Mtunzi, F.M. Biological activities of species in the genus Tulbaghia: A review. *Afr. J. Biotechnol.* **2015**, *14*, 3037–3043.
43. Herrera, M.R.; Machocho, A.K.; Nair, J.J.; Campbell, W.E.; Brun, R.; Viladomat, F.; Codina, C.; Bastida, J. Alkaloids from Cyrtanthus elatus. *Fitoterapia* **2001**, *72*, 444–448. [CrossRef]
44. Nair, J.J.; van Staden, J. Chemical and biological studies of the South African Amaryllidaceae genera Crinum, Ammocharis, Amaryllis, Cyrtanthus and Brunsvigia. *S. Afr. J. Bot.* **2021**, *142*, 467–476. [CrossRef]
45. Heinrich, M.; Teoh, H.L. Galanthamine from snowdrop—the development of a modern drug against Alzheimer's disease from local Caucasian knowledge. *J. Ethnopharmacol.* **2004**, *92*, 147–162. [CrossRef] [PubMed]
46. Nair, J.J.; van Staden, J. Pharmacological and toxicological insights to the South African Amaryllidaceae. *Food Chem. Toxicol.* **2013**, *62*, 262–275. [CrossRef] [PubMed]
47. Govaerts, R. World Checklist of Selected Plant Species. Facilitated by the Royal Botanic Gardens, Kew. 2015. Available online: https://wcsp.science.kew.org/about.do (accessed on 25 March 2022).
48. Kubec, R.; Velíšek, J.; Musah, R.A. The amino acid precursors and odor formation in society garlic (*Tulbaghia violacea* Harv.). *Phytochemistry* **2002**, *60*, 21–25. [CrossRef]
49. Dillon, H.; Nelson, E.C. Tulbaghia leucantha: Alliaceae. *Kew Mag.* **1991**, *8*, 12–15. [CrossRef]
50. Makunga, N.P. *Medicinal Plants of South Africa*; Briza Publications: Pretoria, South Africa, 2010; Volume 105.
51. Van Wyk, B.E. The potential of South African plants in the development of new food and beverage products. *S. Afr. J. Bot.* **2011**, *77*, 857–868. [CrossRef]
52. Raji, I.A.; Obikeze, K.; Mugabo, P.E. Potential beneficial effects of tulbaghia violacea william henry harvey (Alliaceae) on cardiovascular system—A Review. *Trop. J. Pharm. Res.* **2015**, *14*, 1111–1117. [CrossRef]
53. Pooley, E. A Field Guide to the Wild Flowers of KwaZulu-Natal and the Eastern Region. *Natal Flora Publ. Trust. Pg* **2005**, *93*, 630.

54. Sander, T.; Freyss, J.; Von Korff, M.; Rufener, C. DataWarrior: An open-source program for chemistry aware data visualization and analysis. *J. Chem. Inf. Model.* **2015**, *55*, 460–473. [CrossRef]
55. Pino, J.A.; Quijano-Celís, C.E.; Fuentes, V. Volatile compounds of tulbaghia violacea harv. *J. Essent. Oil-Bear. Plants* **2008**, *11*, 203–207. [CrossRef]
56. Ranglová, K.; Krejčová, P.; Kubec, R. The effect of storage and processing on antimicrobial activity of Tulbaghia violacea. *S. Afr. J. Bot.* **2015**, *97*, 159–164. [CrossRef]
57. Smith, S.; Stansbie, J. *Flora of Tropical East Africa. Crown Agents for Oversea Governments and Administration*; CRC Press: Boca Raton, FL, USA, 2003; p. 230.
58. Takaidza, S.; Mtunzi, F.; Pillay, M. Analysis of the phytochemical contents and antioxidant activities of crude extracts from Tulbaghia species. *J. Tradit. Chin. Med.* **2018**, *38*, 272–279. [CrossRef]
59. Staffa, P.; Nyangiwe, N.; Msalya, G.; Nagagi, Y.P.; Nchu, F. The effect of Beauveria bassiana inoculation on plant growth, volatile constituents, and tick (Rhipicephalus appendiculatus) repellency of acetone extracts of Tulbaghia violacea. *Vet. World* **2020**, *13*, 1159–1166. [CrossRef] [PubMed]
60. Devi, K.P.; Malar, D.S.; Nabavi, S.F.; Sureda, A.; Xiao, J.; Nabavi, S.M.; Daglia, M. Kaempferol and inflammation: From chemistry to medicine. *Pharmacol. Res.* **2015**, *99*, 1–10. [CrossRef] [PubMed]
61. Teffo, L.S.; Aderogba, M.A.; Eloff, J.N. Antibacterial and antioxidant activities of four kaempferol methyl ethers isolated from Dodonaea viscosa Jacq. var. angustifolia leaf extracts. *S. Afr. J. Bot.* **2010**, *76*, 25–29. [CrossRef]
62. Yang, C.; Yang, W.; He, Z.; Guo, J.; Yang, X.; Wang, R.; Li, H. Kaempferol Alleviates Oxidative Stress and Apoptosis Through Mitochondria-dependent Pathway During Lung Ischemia-Reperfusion Injury. *Front. Pharmacol.* **2021**, *12*, 11. [CrossRef]
63. Murray, C.J. Global burden of bacterial antimicrobial resistance in 2019: A systematic analysis. *Lancet* **2022**, *388*, 629–655. [CrossRef]
64. Anand, U.; Jacobo-Herrera, N.; Altemimi, A.; Lakhssassi, N. A comprehensive review on medicinal plants as antimicrobial therapeutics: Potential avenues of biocompatible drug discovery. *Metabolites* **2019**, *9*, 258. [CrossRef]
65. Kokoska, L.; Kloucek, P.; Leuner, O.; Novy, P. Plant-Derived Products as Antibacterial and Antifungal Agents in Human Health Care. *Curr. Med. Chem.* **2018**, *26*, 5501–5541. [CrossRef]
66. Salam, A.M.; Quave, C.L. Opportunities for plant natural products in infection control. *Curr. Opin. Microbiol.* **2018**, *45*, 189–194. [CrossRef]
67. Krstin, S.; Sobeh, M.; Braun, M.S.; Wink, M. Tulbaghia violacea and Allium ursinum extracts exhibit anti-parasitic and antimicrobial activities. *Molecules* **2018**, *23*, 313. [CrossRef] [PubMed]
68. Eid, H.H.; Metwally, G.F. Phytochemical and biological study of callus cultures of Tulbaghia violacea Harv. Cultivated in Egypt. *Nat. Prod. Res.* **2017**, *31*, 1717–1724. [CrossRef] [PubMed]
69. Kumar, P.; Mahato, D.K.; Kamle, M.; Mohanta, T.K.; Kang, S.G. Aflatoxins: A global concern for food safety, human health and their management. *Front. Microbiol.* **2017**, *7*, 2170. [CrossRef] [PubMed]
70. Belewa, V.; Baijnath, H.; Frost, C.; Somai, B.M. Tulbaghia violacea Harv. plant extract affects cell wall synthesis in Aspergillus flavus. *J. Appl. Microbiol.* **2017**, *122*, 921–931. [CrossRef]
71. Somai, B.M.; Belewa, V.; Frost, C. Tulbaghia violacea (Harv) Exerts its Antifungal Activity by Reducing Ergosterol Production in Aspergillus flavus. *Curr. Microbiol.* **2021**, *78*, 2989–2997. [CrossRef]
72. Pretorius, J.C. Extracts and Compounds from Tulbaghia Violacea and Their Use as Biological Plant Protecting Agents 2014. Google Patents US8697149B2, 15 April 2014.
73. Ncise, W.; Daniels, C.W.; Etsassala, N.G.E.R.; Nchu, F. Interactive effects of light intensity and ph on growth parameters of a bulbous species (Tulbaghia violacea l.) in hydroponic cultivation and its antifungal activities. *Med. Plants* **2021**, *13*, 442–451. [CrossRef]
74. Ncise, W.; Daniels, C.W.; Nchu, F. Effects of light intensities and varying watering intervals on growth, tissue nutrient content and antifungal activity of hydroponic cultivated Tulbaghia violacea L. under greenhouse conditions. *Heliyon* **2020**, *6*, 3906. [CrossRef] [PubMed]
75. Malungane, M.M.F.; Florah, M.M. *Effect of Crude Extracts of Tulbaghia violacea (Wild Garlic) on Growth of Tomato and Supression of Meloidogyne Species*; University of Limpopo: Mankweng, South Africa, 2014.
76. Kaushik, I.; Ramachandran, S.; Prasad, S.; Srivastava, S.K. Drug rechanneling: A novel paradigm for cancer treatment. In *Seminars in Cancer Biology*; Elsevier: Amsterdam, The Netherlands, 2021; Volume 68, pp. 279–290.
77. Cragg, G.M.; Grothaus, P.G.; Newman, D.J. Impact of natural products on developing new anti-cancer agents. *Chem. Rev.* **2009**, *109*, 3012–3043. [CrossRef]
78. Mthembu, N.N.; Motadi, L.R. Apoptotic potential role of Agave palmeri and Tulbaghia violacea extracts in cervical cancer cells. *Mol. Biol. Rep.* **2014**, *41*, 6143–6155. [CrossRef]
79. Motadi, L.R.; Choene, M.S.; Mthembu, N.N. Anticancer properties of Tulbaghia violacea regulate the expression of p53-dependent mechanisms in cancer cell lines. *Sci. Rep.* **2020**, *10*, 12924. [CrossRef]
80. Rivas-García, L.; Romero-Márquez, J.M.; Navarro-Hortal, M.D.; Esteban-Muñoz, A.; Giampieri, F.; Sumalla-Cano, S.; Battino, M.; Quiles, J.L.; Llopis, J.; Sánchez-González, C. Unravelling potential biomedical applications of the edible flower Tulbaghia violacea. *Food Chem.* **2022**, *381*, 132096. [CrossRef]

81. Bianchini, G.; Balko, J.M.; Mayer, I.A.; Sanders, M.E.; Gianni, L. Triple-negative breast cancer: Challenges and opportunities of a heterogeneous disease. *Nat. Rev. Clin. Oncol.* **2016**, *13*, 674–690. [CrossRef] [PubMed]
82. Dlamini, Z.; Alouna, M.; Hull, R.; Penny, C. Abstract 2843: The effects of extracts of the indigenous South African plant, Tulbaghia violacea, on triple negative breast cancer cells. In Proceedings of the NCRI Cancer Conference, London, UK, 8–12 November 2021.
83. Deepak, K.G.K.; Vempati, R.; Nagaraju, G.P.; Dasari, V.R.; Nagini, S.; Rao, D.N.; Malla, R.R. Tumor microenvironment: Challenges and opportunities in targeting metastasis of triple negative breast cancer. *Pharmacol. Res.* **2020**, *153*, 104683. [CrossRef] [PubMed]
84. Takaidza, S.; Kumar, A.M.; Ssemakalu, C.C.; Natesh, N.S.; Karanam, G.; Pillay, M. Anticancer activity of crude acetone and water extracts of Tulbaghia violacea on human oral cancer cells. *Asian Pac. J. Trop. Biomed.* **2018**, *8*, 456–462. [CrossRef]
85. Lyantagaye, S.L. Two new pro-apoptotic glucopyranosides from Tulbaghia violacea. *J. Med. Plants Res.* **2013**, *7*, 2214–2220. [CrossRef]
86. Lyantagaye, S. Characterization of the Biochemical Pathway of Apoptosis Induced by D-glucopyranoside Derivatives from Tulbaghia violacea. *Annu. Res. Rev. Biol.* **2014**, *4*, 962–977. [CrossRef]
87. Lushchak, V.I. Free radicals, reactive oxygen species, oxidative stress and its classification. *Chem. Biol. Interact.* **2014**, *224*, 164–175. [CrossRef]
88. Thorpe, G.W.; Fong, C.S.; Alic, N.; Higgins, V.J.; Dawes, I.W. Cells have distinct mechanisms to maintain protection against different reactive oxygen species: Oxidative-stress-response genes. *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 6564–6569. [CrossRef]
89. Lourenço, S.C.; Moldão-Martins, M.; Alves, V.D. Antioxidants of natural plant origins: From sources to food industry applications. *Molecules* **2019**, *24*, 4132. [CrossRef]
90. Madike, L.N.; Pillay, M.; Popat, K.C. Antithrombogenic properties of Tulbaghia violacea–loaded polycaprolactone nanofibers. *J. Bioact. Compat. Polym.* **2020**, *35*, 102–116. [CrossRef]
91. Arhin, I.; Depika, D.; Ajay, B.; Delon, N.; Irene, M. Biochemical, phytochemical profile and angiotensin-1 converting enzyme inhibitory activity of the hydro-methanolic extracts of Tulbaghia acutiloba harv. *J. Nat. Remedies* **2019**, *19*, 221–235. [CrossRef]
92. Madike, L.N.; Pillay, M.; Popat, K.C. Antithrombogenic properties of: Tulbaghia violacea aqueous leaf extracts: Assessment of platelet activation and whole blood clotting kinetics. *RSC Adv.* **2021**, *11*, 30455–30464. [CrossRef] [PubMed]
93. Glovaci, D.; Fan, W.; Wong, N.D. Epidemiology of Diabetes Mellitus and Cardiovascular Disease. *Curr. Cardiol. Rep.* **2019**, *21*, 1–8. [CrossRef] [PubMed]
94. Wild, S.; Roglic, G.; Green, A.; Sicree, R.; King, H. Global Prevalence of Diabetes: Estimates for the year 2000 and projections for 2030. *Diabetes Care* **2004**, *27*, 1047–1053. [CrossRef]
95. Matheus, A.S.D.M.; Tannus, L.R.M.; Cobas, R.A.; Palma, C.C.S.; Negrato, C.A.; Gomes, M.D.B. Impact of diabetes on cardiovascular disease: An update. *Int. J. Hypertens.* **2013**, *2013*, 653789. [CrossRef] [PubMed]
96. Moodley, K.; Joseph, K.; Naidoo, Y.; Islam, S.; Mackraj, I. Antioxidant, antidiabetic and hypolipidemic effects of *Tulbaghia violacea* Harv. (wild garlic) rhizome methanolic extract in a diabetic rat model. *BMC Complement. Altern. Med.* **2015**, *15*, 408. [CrossRef] [PubMed]
97. Moodley, K.; Mackraj, I. Metabolic effects of tulbaghia violacea harv. In a diabetic model. *Afr. J. Tradit. Complement. Altern. Med.* **2016**, *13*, 113–122. [CrossRef]
98. Raji, I.; Obikeze, K.; Mugabo, P. Comparison of the acute effects of Tulbaghia violacea William Henry Harvey (Alliaceae) on blood pressure and heart rate of ageing male normotensive Wistar kyoto rats and adult male spontaneously hypertensive rats. *Trop. J. Pharm. Res.* **2016**, *15*, 2429–2434. [CrossRef]
99. Moodley, K.; Naidoo, Y.; Mackraj, I. Effects of *Tulbaghia violacea* Harv. (Alliaceae) rhizome methanolic extract on kidney function and morphology in Dahl salt-sensitive rats. *J. Ethnopharmacol.* **2014**, *155*, 1194–1203. [CrossRef]
100. Navar, L.G. The role of the kidneys in hypertension. *J. Clin. Hypertens.* **2005**, *7*, 542–549. [CrossRef]
101. Davì, G.; Patrono, C. Platelet Activation and Atherothrombosis. *N. Engl. J. Med.* **2007**, *357*, 2482–2494. [CrossRef] [PubMed]
102. Masoud, K.A.A.; Okobi, E.; Ekpo, G.J. Amabeoku Investigation of Some Possible Mechanisms Involved in the Anticonvulsant Activity of *Tulbaghia violacea* Harv. *J. Pharm. Pharmacol.* **2017**, *5*. [CrossRef]
103. Madike, L.N.; Takaidza, S.; Ssemakalu, C.; Pillay, M. Genotoxicity of aqueous extracts of Tulbaghia violacea as determined through an Allium cepa assay. *S. Afr. J. Sci.* **2019**, *115*, 1–6. [CrossRef]
104. Madike, L.N.; Takaidza, S.; Ssemakalu, C.C.; Pillay, M. The effect of extracts of Tulbaghia violacea on the proliferation of a murine macrophage cell line. *S. Afr. J. Bot.* **2020**, *130*, 185–197. [CrossRef]
105. Stavělíková, H. Morphological characteristics of garlic (Allium sativum L.) genetic resources collection—Information. *Hortic. Sci.* **2008**, *35*, 130–135. [CrossRef]
106. Wheeler, E.J.; Mashayekhi, S.; Mcneal, D.W.; Travis Columbus, J.; Chris Pires, J. Molecular systematics of Allium subgenus Amerallium (Amaryllidaceae) in North America. *Am. J. Bot.* **2013**, *100*, 701–711. [CrossRef]
107. Fernandes, S.; Gois, A.; Mendes, F.; Perestrelo, R.; Medina, S.; Câmara, J.S. Typicality Assessment of Onions (*Allium cepa*) from Different Geographical Regions Based on the Volatile Signature and Chemometric Tools. *Foods* **2020**, *9*, 375. [CrossRef]
108. Jo, J.; Purushotham, P.M.; Han, K.; Lee, H.-R.; Nah, G.; Kang, B.-C. Development of a Genetic Map for Onion (*Allium cepa* L.) Using Reference-Free Genotyping-by-Sequencing and SNP Assays. *Front. Plant Sci.* **2017**, *8*, 1342. [CrossRef]
109. Najeebullah, S.; Shinwari, Z.K.; Jan, S.A.; Khan, I.; Ali, M. Ethno medicinal and phytochemical properties of genus Allium: A review of recent advances. *Pak. J. Bot.* **2021**, *53*, 135–144. [CrossRef]
110. Lawande, K.E. Onion. In *Handbook of Herbs and Spices*; Elsevier: Amsterdam, The Netherlands, 2012; pp. 417–429.

111. Debin, W.; Jiande, G.; Guangshu, L. General situation of Allium crops in China. In Proceedings of the IV International Symposium on Edible Alliaceae 688, Beijing, China, 21–26 April 2004; pp. 327–332.
112. Food and Agriculture Organization of the United Nations. Available online: http://www.fao.org/faostat/en/#data (accessed on 26 March 2022).
113. Bartolucci, F.; Iocchi, M.; De Castro, O.; Conti, F. Allium ducissae (A. subgen. Polyprason, Amaryllidaceae) a New Species from the Central Apennines (Italy). *Plants* **2022**, *11*, 426. [CrossRef]
114. Friesen, N. The genus *Allium* L. in the flora of Mongolia. *Feddes Repert.* **1995**, *106*, 59–81. [CrossRef]
115. Sinitsyna, T.A. Genus *Allium* L.(Alliaceae) in Siberia. *Vavilovia* **2020**, *2*, 3–22. [CrossRef]
116. Temperate Plants Database, Ken Fern. Available online: https://temperate.theferns.info/ (accessed on 26 March 2022).
117. Kawano, S.; Nagai, Y. Life-history monographs of Japanese plants. 4: *Allium victorialis* L. ssp. platyphyllum (Makino) Hultén (Alliaceae) Syn. *Allium victorialis* L. var. platyphyllum Makino; A. latissimum Prokh. *Plant Species Biol.* **2005**, *20*, 219–225. [CrossRef]
118. Kitamura, S.; Murata, G.; Hori, M. *Coloured Illustrations of Herbaceous Plants of Japan*; Hoikusha Publishing Co.: Osaka, Japan, 1958.
119. Arifin, N.S.; Okudo, H. Geographical distribution of allozyme patterns in shallot (*Allium cepa* var. ascalonicum Backer) and wakegi onion (A. × wakegi Araki). *Euphytica* **1996**, *91*, 305–313. [CrossRef]
120. Bah, A.A.; Wang, F.; Huang, Z.; Shamsi, I.H.; Zhang, Q.; Jilani, G.; Hussain, S.; Hussain, N.; Ali, E. Biology Phyto-characteristics, Cultivation and Medicinal Prospects of Chinese Jiaotou (*Allium chinense*). *Int. J. Agric. Biol.* **2012**, *14*, 650–657.
121. Blattner, F.R.; Friesen, N. *Relationship between Chinese Chive (Allium tuberosum) and Its Putative Progenitor A. Ramosum as Assessed by Random Amplified Polymorphic DNA (RAPD)*; California University Press: Los Angeles, CA, USA, 2006; pp. 134–142.
122. Pandey, A.; Pradheep, K.; Gaikwad, A.B.; Gupta, R.; Malav, P.K.; Rai, M. Systematics study on a morphotype of Allium tuberosum Rottler ex Spreng. (*Alliaceae*) from Ladakh, India. *Indian J. Plant Genet. Resour.* **2019**, *32*, 223–231. [CrossRef]
123. Sajad, M.A.; Khan, M.S.; Bahadur, S.; Naeem, A.; Ali, H.; Batool, F.; Shuaib, M.; Khan, M.A.S.; Batool, S. Evaluation of chromium phytoremediation potential of some plant species of Dir Lower, Khyber Pakhtunkhwa, Pakistan. *Acta Ecol. Sin.* **2020**, *40*, 158–165. [CrossRef]
124. Keusgen, M.; Fritsch, R.M.; Hisoriev, H.; Kurbonova, P.A.; Khassanov, F.O. Wild Allium species (Alliaceae) used in folk medicine of Tajikistan and Uzbekistan. *J. Ethnobiol. Ethnomed.* **2006**, *2*, 18. [CrossRef] [PubMed]
125. Ijaz, F.; Iqbal, Z.; Rahman, I.U.; Alam, J.; Khan, S.M.; Shah, G.M.; Khan, K.; Afzal, A. Investigation of traditional medicinal floral knowledge of Sarban Hills, Abbottabad, KP, Pakistan. *J. Ethnopharmacol.* **2016**, *179*, 208–233. [CrossRef]
126. Ajaib, M.; Ishtiaq, M.; Bhatti, K.H.; Hussain, I.; Maqbool, M.; Hussain, T.; Mushtaq, W.; Ghani, A.; Azeem, M.; Khan, S.M.R.; et al. Inventorization of traditional ethnobotanical uses of wild plants of Dawarian and Ratti Gali areas of District Neelum, Azad Jammu and Kashmir Pakistan. *PLoS ONE* **2021**, *16*, e0255010. [CrossRef]
127. Islam, M.; Inamullah, A.I.; Akhtar, N.; Alam, J.; Razzaq, A.; Mohammad, K.; Mahmood, T.; Khan, F.U.; Muhammad Khan, W.; Ishtiaq, A.; et al. Medicinal plants resources of Western Himalayan Palas Valley, Indus Kohistan, Pakistan: Their uses and degrees of risk of extinction. *Saudi J. Biol. Sci.* **2021**, *28*, 3076–3093. [CrossRef] [PubMed]
128. Amjad, M.S.; Qaeem, M.F.; Ahmad, I.; Khan, S.U.; Chaudhari, S.K.; Malik, N.Z.; Shaheen, H.; Khan, A.M. Descriptive study of plant resources in the context of the ethnomedicinal relevance of indigenous flora: A case study from Toli Peer National Park, Azad Jammu and Kashmir, Pakistan. *PLoS ONE* **2017**, *12*, e0171896. [CrossRef] [PubMed]
129. Tavares, L.; Santos, L.; Zapata Noreña, C.P. Bioactive compounds of garlic: A comprehensive review of encapsulation technologies, characterization of the encapsulated garlic compounds and their industrial applicability. *Trends Food Sci. Technol.* **2021**, *114*, 232–244. [CrossRef]
130. Zhao, X.X.; Lin, F.J.; Li, H.; Li, H.B.; Wu, D.T.; Geng, F.; Ma, W.; Wang, Y.; Miao, B.H.; Gan, R.Y. Recent Advances in Bioactive Compounds, Health Functions, and Safety Concerns of Onion (*Allium cepa* L.). *Front. Nutr.* **2021**, *8*, 463. [CrossRef] [PubMed]
131. Beretta, H.V.; Bannoud, F.; Insani, M.; Berli, F.; Hirschegger, P.; Galmarini, C.R.; Cavagnaro, P.F. Relationships Between Bioactive Compound Content and the Antiplatelet and Antioxidant Activities of Six Allium Vegetable Species. *Food Technol. Biotechnol.* **2017**, *55*, 266–275. [CrossRef]
132. Majewski , M. Allium sativum: Facts and myths regarding human health. *Rocz Panstw Zakl Hig.* **2014**, *65*, 1–8. [PubMed]
133. Marrelli, M.; Amodeo, V.; Statti, G.; Conforti, F. Biological Properties and Bioactive Components of *Allium cepa* L.: Focus on Potential Benefits in the Treatment of Obesity and Related Comorbidities. *Molecules* **2019**, *24*, 119. [CrossRef]
134. Teshika, J.D.; Zakariyyah, A.M.; Zaynab, T.; Zengin, G.; Rengasamy, K.R.; Pandian, S.K.; Fawzi, M.M. Traditional and modern uses of onion bulb (*Allium cepa* L.): A systematic review. *Crit. Rev. Food Sci. Nutr.* **2019**, *59*, S39–S70. [CrossRef]
135. Turati, F.; Pelucchi, C.; Guercio, V.; La Vecchia, C.; Galeone, C. Allium vegetable intake and gastric cancer: A case-control study and meta-analysis. *Mol. Nutr. Food Res.* **2015**, *59*, 171–179. [CrossRef]
136. Zhou, X.F.; Ding, Z.S.; Liu, N.B. Allium vegetables and risk of prostate cancer: Evidence from 132,192 subjects. *Asian Pac. J. Cancer Prev.* **2013**, *14*, 4131–4134. [CrossRef]
137. Turati, F.; Guercio, V.; Pelucchi, C.; La Vecchia, C.; Galeone, C. Colorectal cancer and adenomatous polyps in relation to allium vegetables intake: A meta-analysis of observational studies. *Mol. Nutr. Food Res.* **2014**, *58*, 1907–1914. [CrossRef] [PubMed]
138. Guercio, V.; Turati, F.; La Vecchia, C.; Galeone, C.; Tavani, A. Allium vegetables and upper aerodigestive tract cancers: A meta-analysis of observational studies. *Mol. Nutr. Food Res.* **2016**, *60*, 212–222. [CrossRef] [PubMed]
139. Kuete, V. Moringa oleifera, in Medicinal Spices and Vegetables from Africa. *Med. Spices Veg. Afr.* **2017**, *43*, 605–610.

140. Peltola, R. Allium victoralis. Available online: https://portal.mtt.fi/portal/page/portal/mtt/hankkeet/BARENTSPEC (accessed on 20 March 2022).
141. Shafakatullah, N.; Chandra, M. Isolation of lactic acid bacteria from Allium cepa var. aggregatum and study of their probiotic properties. *Int. J. Pharma Sci. Res.* **2015**, *6*, 749–752.
142. Lawless, J.W.; Latham, M.C.; Stephenson, L.S.; Kinoti, S.N.; Pertet, A.M. Iron supplementation improves appetite and growth in anemic Kenyan primary school children. *J. Nutr.* **1994**, *124*, 645–654. [CrossRef]
143. Lee, Y.M.; Lim, D.Y.; Choi, H.J.; Jung, J.I.; Chung, W.Y.; Park, J.H.Y. Induction of cell cycle arrest in prostate cancer cells by the dietary compound isoliquiritigenin. *J. Med. Food* **2009**, *12*, 8–14. [CrossRef]
144. Kaiser, P.; Youssouf, M.S.; Tasduq, S.A.; Singh, S.; Sharma, S.C.; Singh, G.D.; Gupta, V.K.; Gupta, B.D.; Johri, R.K. Anti-allergic effects of herbal product from Allium cepa (bulb). *J. Med. Food* **2009**, *12*, 374–382. [CrossRef]
145. Mohammadi-Motlagh, H.R.; Mostafaie, A.; Mansouri, K. Anticancer and anti-inflammatory activities of shallot (Allium ascalonicum) extract. *Arch. Med. Sci.* **2011**, *7*, 38–44. [CrossRef]
146. *Handbook of Chinese Herbs and Formulas*; Yeung, H., Ed.; Institute of Chinese Medicine: London, UK, 1985; Volume 1.
147. Jannat, K.; Rahman, T.; Rahmatullah, M. Traditional uses, phytochemicals and pharmacological properties of Allium tuberosum Rottler ex spreng. *J. Med. Plants Stud.* **2019**, *7*, 214–220.
148. Sabha, D.; Hiyasat, B.; Grtzinger, K.; Hennig, L.; Schlegel, F.; Mohr, F.W.; Rauwald, H.W.; Dhein, S. Allium ursinum L.: Bioassay-guided isolation and identification of a galactolipid and a phytosterol exerting antiaggregatory effects. *Pharmacology* **2012**, *89*, 260–269. [CrossRef]
149. Carotenuto, A.; De Feo, V.; Fattorusso, E.; Lanzotti, V.; Magno, S.; Cicala, C. The flavonoids of Allium ursinum. *Phytochemistry* **1996**, *41*, 531–536. [CrossRef]
150. Sobolewska, D.; Podolak, I.; Makowska-Wąs, J. *Allium ursinum*: Botanical, phytochemical and pharmacological overview. *Phytochem. Rev.* **2015**, *14*, 81–97. [CrossRef] [PubMed]
151. Ivanova, A.; Mikhova, B.; Najdenski, H.; Tsvetkova, I.; Kostova, I. Chemical composition and antimicrobial activity of wild garlic Allium ursinum of Bulgarian origin. *Nat. Prod. Commun.* **2009**, *4*, 1059–1062. [CrossRef] [PubMed]
152. Dong, Y.; Ruan, J.; Ding, Z.; Zhao, W.; Hao, M.; Zhang, Y.; Jiang, H.; Zhang, Y.; Wang, T. molecules Phytochemistry and Comprehensive Chemical Profiling Study of Flavonoids and Phenolic Acids in the Aerial Parts of Allium Mongolicum Regel and Their Intestinal Motility Evaluation. *Molecules* **2020**, *25*, 577. [CrossRef]
153. Marefati, N.; Ghorani, V.; Shakeri, F.; Boskabady, M.; Kianian, F.; Rezaee, R.; Boskabady, M.H. A review of anti-inflammatory, antioxidant, and immunomodulatory effects of Allium cepa and its main constituents. *Pharm. Biol.* **2021**, *59*, 287–302. [CrossRef]
154. Fossen, T.; Slimestad, R.; Andersen, Ø.M. Anthocyanins with 4′-glucosidation from red onion, *Allium cepa*. *Phytochemistry* **2003**, *64*, 1367–1374. [CrossRef]
155. Xiao, H.; Parkin, K.L. Isolation and identification of potential cancer chemopreventive agents from methanolic extracts of green onion (*Allium cepa*). *Phytochemistry* **2007**, *68*, 1059–1067. [CrossRef]
156. Fossen, T.; Andersen, Ø.M. Anthocyanins from red onion, *Allium cepa*, with novel aglycone. *Phytochemistry* **2003**, *62*, 1217–1220. [CrossRef]
157. Lanzotti, V.; Romano, A.; Lanzuise, S.; Bonanomi, G.; Scala, F. Antifungal saponins from bulbs of white onion, *Allium cepa* L. *Phytochemistry* **2012**, *74*, 133–139. [CrossRef]
158. Nile, A.; Nile, S.H.; Cespedes-Acuña, C.L.; Oh, J.W. Spiraeoside extracted from red onion skin ameliorates apoptosis and exerts potent antitumor, antioxidant and enzyme inhibitory effects. *Food Chem. Toxicol.* **2021**, *154*, 112327. [CrossRef]
159. Nohara, T.; Fujiwara, Y.; El-Aasr, M.; Ikeda, T.; Ono, M.; Nakano, D.; Kinjo, J. Thiolane-type sulfides from garlic, onion, and Welsh onion. *J. Nat. Med.* **2021**, *75*, 741–751. [CrossRef] [PubMed]
160. El-Aasr, M.; Fujiwara, Y.; Takeya, M.; Ikeda, T.; Tsukamoto, S.; Ono, M.; Nakano, D.; Okawa, M.; Kinjo, J.; Yoshimitsu, H.; et al. Onionin A from *Allium cepa* inhibits macrophage activation. *J. Nat. Prod.* **2010**, *73*, 1306–1308. [CrossRef] [PubMed]
161. Terahara, N.; Yamaguchi, M.; Honda, T. Malonylated anthocyanins from bulbs of red onion, *Allium cepa* L. *Biosci. Biotechnol. Biochem.* **1994**, *58*, 1324–1325. [CrossRef]
162. Pontin, M.; Bottini, R.; Burba, J.L.; Piccoli, P. *Allium sativum* produces terpenes with fungistatic properties in response to infection with Sclerotium cepivorum. *Phytochemistry* **2015**, *115*, 152–160. [CrossRef]
163. Lanzotti, V.; Barile, E.; Antignani, V.; Bonanomi, G.; Scala, F. Antifungal saponins from bulbs of garlic, *Allium sativum* L. var. Voghiera. *Phytochemistry* **2012**, *78*, 126–134. [CrossRef] [PubMed]
164. Okuyama, T.; Fujita, K.; Shibata, S.; Hoson, M.; Kawada, T.; Masaki, M.; Yamate, N. Effects of Chinese drugs "xiebai" and "dasuan" on human platelet aggregation (*Allium bakeri*, A. sativum). *Planta Med.* **1989**, *55*, 242–244. [CrossRef]
165. Timité, G.; Mitaine-Offer, A.C.; Miyamoto, T.; Tanaka, C.; Mirjolet, J.F.; Duchamp, O.; Lacaille-Dubois, M.A. Structure and cytotoxicity of steroidal glycosides from Allium schoenoprasum. *Phytochemistry* **2013**, *88*, 61–66. [CrossRef]
166. Fossen, T.; Slimestad, R.; Øvstedal, D.O.; Andersen, Ø.M. Covalent anthocyanin-flavonol complexes from flowers of chive, Allium schoenoprasum. *Phytochemistry* **2000**, *54*, 317–323. [CrossRef]
167. Barile, E.; Bonanomi, G.; Antignani, V.; Zolfaghari, B.; Sajjadi, S.E.; Scala, F.; Lanzotti, V. Saponins from Allium minutiflorum with antifungal activity. *Phytochemistry* **2007**, *68*, 596–603. [CrossRef]
168. Carotenuto, A.; Fattorusso, E.; Lanzotti, V.; Magno, S.; De Feo, V.; Cicala, C. The flavonoids of Allium neapolitanum. *Phytochemistry* **1997**, *44*, 949–957. [CrossRef]

169. Chehri, Z.; Zolfaghari, B.; Sadeghi Dinani, M. Isolation of Cinnamic Acid Derivatives from the Bulbs of Allium tripedale. *Adv. Biomed. Res.* **2018**, *7*, 60. [CrossRef]
170. Jan, K.; Michael, K. Cysteine sulfoxides and volatile sulfur compounds from Allium tripedale. *J. Agric. Food Chem.* **2010**, *58*, 1129–1137. [CrossRef]
171. Fattorusso, E.; Lanzotti, V.; Taglialatela-Scafati, O.; Cicala, C. The flavonoids of leek, *Allium porrum*. *Phytochemistry* **2001**, *57*, 565–569. [CrossRef]
172. Carotenuto, A.; Fattorusso, E.; Lanzotti, V.; Magno, S. Spirostanol saponins of *Allium porrum* L. *Phytochemistry* **1999**, *51*, 1077–1082. [CrossRef]
173. Peng, J.P.; Yao, X.S.; Tezuka, Y.; Kikuchi, T. Furostanol glycosides from bulbs of Allium chinense. *Phytochemistry* **1996**, *41*, 283–285. [CrossRef]
174. Kuroda, M.; Mimaki, Y.; Kameyama, A.; Sashida, Y.; Nikaido, T. Steroidal saponins from Allium chinense and their inhibitory activities on cyclic AMP phosphodiesterase and Na^+/K^+ ATPase. *Phytochemistry* **1995**, *40*, 1071–1076. [CrossRef]
175. Baba, M.; Ohmura, M.; Kishi, N.; Okada, Y.; Shibata, S.; Peng, J.; Yao, S.S.; Nishino, H.; Okuyama, T. Saponins isolated from Allium chinense G. Don and antitumor-promoting activities of isoliquiritigenin and laxogenin from the same drug. *Biol. Pharm. Bull.* **2000**, *23*, 660–662. [CrossRef]
176. Peng, J.; Yao, X.; Kobayashi, H.; Ma, C. Novel furostanol glycosides from Allium macrostemon. *Planta Med.* **1995**, *61*, 58–61. [CrossRef]
177. Peng, J.P.; Wu, Y.; Yao, X.S.; Okuyama, T.; Narui, T. Two new steroidal saponins from Allium macrostemon. *Yao Xue Xue Bao* **1992**, *27*, 918–922. [PubMed]
178. Peng, J.P.; Wang, X.; Yao, X.S. Studies on two new furostanol glycosides from Allium macrostemon Bunge. *Yao Xue Xue Bao* **1993**, *28*, 526–531.
179. Usui, A.; Matsuo, Y.; Tanaka, T.; Ohshima, K.; Fukuda, S.; Mine, T.; Yakashiro, I.; Ishimaru, K. Ferulic acid esters of glucosylglucose from *Allium macrostemon* Bunge. *J. Asian Nat. Prod. Res.* **2017**, *19*, 215–221. [CrossRef]
180. Kawashima, K.; Mimaki, Y.; Sashida, Y. Steroidal saponins from the bulbs of *Allium schubertii*. *Phytochemistry* **1993**, *32*, 1267–1272. [CrossRef]
181. Zou, Z.M.; Yu, D.Q.; Cong, P.Z. A steroidal saponin from the seeds of *Allium tuberosum*. *Phytochemistry* **2001**, *57*, 1219–1222. [CrossRef]
182. Sang, S.; Zou, M.; Xia, Z.; Lao, A.; Chen, Z.; Ho, C.T. New spirostanol saponins from Chinese chives (*Allium tuberosum*). *J. Agric. Food Chem.* **2001**, *49*, 4780–4783. [CrossRef] [PubMed]
183. Sang, S.M.; Zou, M.L.; Zhang, X.W.; Lao, A.N.; Chen, Z.L. Tuberoside M, a new cytotoxic spirostanol saponin from the seeds of *Allium tuberosum*. *J. Asian Nat. Prod. Res.* **2002**, *4*, 67–70. [CrossRef] [PubMed]
184. Mimaki, Y.; Kawashima, K.; Kanmoto, T.; Sashida, Y. Steroidal glycosides from *Allium albopilosum* and *A. ostrowskianum*. *Phytochemistry* **1993**, *34*, 799–805. [CrossRef]
185. Zolfaghari, B.; Yazdiniapour, Z.; Sadeghi, M.; Akbari, M.; Troiano, R.; Lanzotti, V. Cinnamic acid derivatives from welsh onion (*Allium fistulosum*) and their antibacterial and cytotoxic activities. *Phytochem. Anal.* **2021**, *32*, 84–90. [CrossRef]
186. Sang, S.; Lao, A.; Wang, Y.; Chin, C.K.; Rosen, R.T.; Ho, C.T. Antifungal constituents from the seeds of *Allium fistulosum* L. *J. Agric. Food Chem.* **2002**, *50*, 6318–6321. [CrossRef]
187. Tsuruoka, T.; Ishikawa, K.; Hosoe, T.; Davaajab, D.; Duvjir, S.; Surenjav, U. A new cinnamoylphenethylamine derivative from a Mongolian *Allium* species, *Allium carolinianum*. *J. Nat. Med.* **2018**, *72*, 332–334. [CrossRef]
188. Zamri, N.; Hamid, H.A. Comparative Study of Onion (*Allium cepa*) and Leek (*Allium ampeloprasum*): Identification of Organosulphur Compounds by UPLC-QTOF/MS and Anticancer Effect on MCF-7 Cells. *Plant Foods Hum. Nutr.* **2019**, *74*, 525–530. [CrossRef]
189. Kang, L.-P.; Liu, Z.-J.; Zhang, L.; Tan, D.-W.; Zhao, Y.; Zhao, Y.; Chen, H.-B.; Ma, B.-P. New furostanol saponins from *Allium ascalonicum* L. *Magn. Reson. Chem. Magn. Reson. Chem* **2007**, *45*, 725–733. [CrossRef] [PubMed]
190. Kubec, R.; Cody, R.B.; Dane, A.J.; Musah, R.A.; Schraml, J.; Vattekkatte, A.; Block, E. Applications of direct analysis in real time-mass spectrometry (DART-MS) in Allium chemistry. (Z)-butanethial S-oxide and 1-butenyl thiosulfinates and their S-(E)-1-butenylcysteine S-oxide precursor from *Allium siculum*. *J. Agric. Food Chem.* **2010**, *58*, 1121–1128. [CrossRef]
191. Hu, X.-P.; Zhou, H.; Du, Y.-M.; Ou, S.-Y.; Yan, R.; Wang, Y. Two new flavonoids from the bark of Allium chrysanthum. *J. Asian Nat. Prod. Res.* **2017**, *19*, 229–234. [CrossRef] [PubMed]
192. Kusterer, J.; Vogt, A.; Keusgen, M. Isolation and identification of a new cysteine sulfoxide and volatile sulfur compounds from Allium subgenus Melanocrommyum. *J. Agric. Food Chem.* **2010**, *58*, 520–526. [CrossRef] [PubMed]
193. Morita, T.; Ushiroguchi, T.; Hayashi, N.; Matsuura, H.; Itakura, Y.; Fuwa, T. Steroidal saponins from elephant garlic, bulbs of *Allium ampeloprasum* L. *Chem. Pharm. Bull.* **1988**, *36*, 3480–3486. [CrossRef]
194. Lee, K.T.; Choi, J.H.; Kim, D.H.; Son, K.H.; Kim, W.B.; Kwon, S.H.; Park, H.J. Constituents and the antitumor principle *of Allium victorialis* var. platyphyllum. *Arch. Pharm. Res.* **2001**, *24*, 44–50. [CrossRef]
195. Akhov, L.S.; Musienko, M.M.; Piacente, S.; Pizza, C.; Oleszek, W. Structure of steroidal saponins from underground parts of *Allium nutans* L. *J. Agric. Food Chem.* **1999**, *47*, 3193–3196. [CrossRef]
196. Mimaki, Y.; Matsumoto, K.; Sashida, Y.; Nikaido, T.; Ohmoto, T. New steroidal saponins from the bulbs of *Allium giganteum* exhibiting potent inhibition of cAMP phosphodiesterase activity. *Chem. Pharm. Bull.* **1994**, *42*, 710–714. [CrossRef]

197. Ren, L.; Yaun-Fei, W.; Qian, S.; Hua-Bin, H. Chemical composition and antimicrobial activity of the essential oil from *Allium hookeri* consumed in Xishuangbanna, Southwest China. *Nat. Prod. Commun.* **2014**, *9*, 863–864.
198. El-Saber Batiha, G.; Magdy Beshbishy, A.; Wasef, L.G.; Elewa, Y.H.A.; Al-Sagan, A.; Abd El-Hack, M.E.; Taha, A.E.; Abd-Elhakim, M.Y.; Prasad Devkota, H. Chemical Constituents and Pharmacological Activities of Garlic (*Allium sativum* L.): A Review. *Nutrients* **2020**, *12*, 872. [CrossRef]
199. Kuda, T.; Iwai, A.; Yano, T. Effect of red pepper Capsicum annuum var. conoides and garlic Allium sativum on plasma lipid levels and cecal microflora in mice fed beef tallow. *Food Chem. Toxicol.* **2004**, *42*, 1695–1700. [CrossRef] [PubMed]
200. Wallock-Richards, D.; Doherty, C.J.; Doherty, L.; Clarke, D.J.; Place, M.; Govan, J.R.W.; Campopiano, D.J. Garlic revisited: Antimicrobial activity of allicin-containing garlic extracts against Burkholderia cepacia complex. *PLoS ONE* **2014**, *9*, e112726. [CrossRef] [PubMed]
201. Ross, Z.M.; O'Gara, E.A.; Hill, D.J.; Sleightholme, H.V.; Maslin, D.J. Antimicrobial properties of garlic oil against human enteric bacteria: Evaluation of methodologies and comparisons with garlic oil sulfides and garlic powder. *Appl. Environ. Microbiol.* **2001**, *67*, 475–480. [CrossRef] [PubMed]
202. Pârvu, M.; Moţ, C.A.; Pârvu, A.E.; Mircea, C.; Stoeber, L.; Roşca-Casian, O.; Ţigu, A.B. Allium sativum Extract Chemical Composition, Antioxidant Activity and Antifungal Effect against Meyerozyma guilliermondii and Rhodotorula mucilaginosa Causing Onychomycosis. *Molecules* **2019**, *24*, 3958. [CrossRef]
203. Fufa, B.K. Anti-bacterial and Anti-fungal Properties of Garlic Extract (*Allium sativum*): A Review. *Microbiol. Res. J. Int.* **2019**, *28*, 1–5. [CrossRef]
204. Zhen, H.; Fang, F.; Ye, D.; Shu, S.; Zhou, Y.; Dong, Y.; Nie, X.; Li, G. Experimental study on the action of allitridin against human cytomegalovirus in vitro: Inhibitory effects on immediate-early genes. *Antivir. Res.* **2006**, *72*, 68–74. [CrossRef]
205. Danquah, C.A.; Tetteh, M.; Amponsah, I.K.; Mensah, A.Y.; Buabeng, K.O.; Gibbons, S.; Bhakta, S. Investigating ghanaian Allium species for anti-infective and resistance-reversal natural product leads to mitigate multidrug-resistance in tuberculosis. *Antibiotics* **2021**, *10*, 902. [CrossRef]
206. Satvati, S.A.R.; Shooriabi, M.; Amin, M.; Shiezadeh, F. Evaluation of the Antimicrobial Activity of Tribulus terrestris, Allium sativum, Salvia officinalis, and Allium hirtifolium Boiss Against Enterococcus faecalis. *Int. J. Enteric. Pathog.* **2017**, *5*, 63–67. [CrossRef]
207. Abdel-Hafeez, E.H.; Ahmad, A.K.; Kamal, A.M.; Abdellatif, M.Z.M.; Abdelgelil, N.H. In vivo antiprotozoan effects of garlic (*Allium sativum*) and ginger (*Zingiber officinale*) extracts on experimentally infected mice with Blastocystis spp. *Parasitol. Res.* **2015**, *114*, 3439–3444. [CrossRef]
208. Gruhlke, M.C.H.; Nicco, C.; Batteux, F.; Slusarenko, A.J. The Effects of Allicin—A Reactive Sulfur Species from Garlic, on a Selection of Mammalian Cell Lines. *Antioxidants* **2016**, *6*, 1. [CrossRef]
209. Danquah, C.A.; Kakagianni, E.; Khondkar, P.; Maitra, A.; Rahman, M.; Evangelopoulos, D.; McHugh, T.D.; Stapleton, P.; Malkinson, J.; Bhakta, S.; et al. Analogues of Disulfides from Allium stipitatum Demonstrate Potent Anti-tubercular Activities through Drug Efflux Pump and Biofilm Inhibition. *Sci. Rep.* **2018**, *8*, 1150. [CrossRef] [PubMed]
210. Asdaq, S.M.B.; Inamdar, M.N. Pharmacodynamic and Pharmacokinetic Interactions of Propranolol with Garlic (*Allium sativum*) in Rats. *Evid. Based. Complement. Alternat. Med.* **2011**, *2011*, 824042. [CrossRef] [PubMed]
211. Jang, H.-J.; Lee, H.-J.; Yoon, D.-K.; Ji, D.-S.; Kim, J.-H.; Lee, C.-H. Antioxidant and antimicrobial activities of fresh garlic and aged garlic by-products extracted with different solvents. *Food Sci. Biotechnol.* **2018**, *27*, 219–225. [CrossRef] [PubMed]
212. Abdel-Daim, M.M.; Shaheen, H.M.; Abushouk, A.I.; Toraih, E.A.; Fawzy, M.S.; Alansari, W.S.; Aleya, L.; Bungau, S. Thymoquinone and diallyl sulfide protect against fipronil-induced oxidative injury in rats. *Environ. Sci. Pollut. Res. Int.* **2018**, *25*, 23909–23916. [CrossRef]
213. Putnoky, S.; Caunii, A.; Butnariu, M. Study on the stability and antioxidant effect of the Allium ursinumwatery extract. *Chem. Cent. J.* **2013**, *7*, 21. [CrossRef]
214. Asgarpanah, J.; Ghanizadeh, B. Pharmacologic and medicinal properties of Allium hirtifolium Boiss. *Afr. J. Pharm. Pharmacol.* **2012**, *6*, 1809–1814. [CrossRef]
215. Ahmad, T.A.; El-Sayed, B.A.; El-Sayed, L.H. Development of immunization trials against *Eimeria* spp. *Trials Vaccinol.* **2016**, *5*, 38–47. [CrossRef]
216. Hobauer, R.; Frass, M.; Gmeiner, B.; Kaye, A.D.; Frost, E.A. Garlic extract (*Allium sativum*) reduces migration of neutrophils through endothelial cell monolayers. *Middle East J. Anaesthesiol.* **2000**, *15*, 649–658.
217. Gu, X.; Wu, H.; Fu, P. Allicin attenuates inflammation and suppresses HLA-B27 protein expression in ankylosing spondylitis mice. *Biomed. Res. Int.* **2013**, *2013*, 171573. [CrossRef]
218. Jeong, Y.Y.; Ryu, J.H.; Shin, J.-H.; Kang, M.J.; Kang, J.R.; Han, J.; Kang, D. Comparison of Anti-Oxidant and Anti-Inflammatory Effects between Fresh and Aged Black Garlic Extracts. *Molecules* **2016**, *21*, 430. [CrossRef]
219. Jin, P.; Kim, J.-A.; Choi, D.-Y.; Lee, Y.-J.; Jung, H.S.; Hong, J.T. Anti-inflammatory and anti-amyloidogeniceffects of a small molecule, 2,4-bis(p-hydroxyphenyl)-2-butenal in Tg2576 Alzheimer'sdisease mice model. *J. Neuroinflammation* **2013**, *10*, 767. [CrossRef] [PubMed]
220. Krejčová, P.; Kučerová, P.; Stafford, G.I.; Jäger, A.K.; Kubec, R. Antiinflammatory and neurological activity of pyrithione and related sulfur-containing pyridine N-oxides from Persian shallot (*Allium stipitatum*). *J. Ethnopharmacol.* **2014**, *154*, 176–182. [CrossRef] [PubMed]

221. Karunanidhi, A.; Ghaznavi-Rad, E.; Jeevajothi Nathan, J.; Abba, Y.; van Belkum, A.; Neela, V. *Allium stipitatum* Extract Exhibits In Vivo Antibacterial Activity against Methicillin-Resistant *Staphylococcus aureus* and Accelerates Burn Wound Healing in a Full-Thickness Murine Burn Model. *Evid. Based Complement. Altern. Med.* **2017**, *2017*, 1914732. [CrossRef]
222. Kim, J.E.; Park, K.M.; Lee, S.Y.; Seo, J.H.; Yoon, I.S.; Bae, C.S.; Yoo, J.C.; Bang, M.A.; Cho, S.S.; Park, D.H. Anti-inflammatory effect of Allium hookeri on carrageenan-induced air pouch mouse model. *PLoS ONE* **2017**, *12*, e0190305. [CrossRef] [PubMed]
223. Li, Z.; Le, W.; Cui, Z. A novel therapeutic anticancer property of raw garlic extract via injection but not ingestion. *Cell Death Discov.* **2018**, *4*, 108. [CrossRef] [PubMed]
224. Chhabria, S.V.; Akbarsha, M.A.; Li, A.P.; Kharkar, P.S.; Desai, K.B. In situ allicin generation using targeted alliinase delivery for inhibition of MIA PaCa-2 cells via epigenetic changes, oxidative stress and cyclin-dependent kinase inhibitor (CDKI) expression. *Apoptosis* **2015**, *20*, 1388–1409. [CrossRef]
225. Fleischauer, A.T.; Arab, L. Garlic and cancer: A critical review of the epidemiologic literature. *J. Nutr.* **2001**, *131*, 1032S–1040S. [CrossRef]
226. Piscitelli, S.C.; Burstein, A.H.; Welden, N.; Gallicano, K.D.; Falloon, J. The effect of garlic supplements on the pharmacokinetics of saquinavir. *Clin. Infect. Dis.* **2002**, *34*, 234–238. [CrossRef]
227. Dall'Acqua, S.; Maggi, F.; Minesso, P.; Salvagno, M.; Papa, F.; Vittori, S.; Innocenti, G. Identification of non-alkaloid acetylcholinesterase inhibitors from Ferulago campestris (Besser) Grecescu (Apiaceae). *Fitoterapia* **2010**, *81*, 1208–1212. [CrossRef]
228. Szychowski, K.A.; Rybczyńska-Tkaczyk, K.; Gaweł-Bęben, K.; Świeca, M.; Karaś, M.; Jakubczyk, A.; Matysiak, M.; Binduga, U.E.; Gmiński, J. Characterization of Active Compounds of Different Garlic (*Allium sativum* L.) Cultivars. *Pol. J. Food Nutr. Sci.* **2018**, *68*, 73–81. [CrossRef]
229. Lu, S.-H.; Wu, J.W.; Liu, H.-L.; Zhao, J.-H.; Liu, K.-T.; Chuang, C.-K.; Lin, H.-Y.; Tsai, W.-B.; Ho, Y. The discovery of potential acetylcholinesterase inhibitors: A combination of pharmacophore modeling, virtual screening, and molecular docking studies. *J. Biomed. Sci.* **2011**, *18*, 8. [CrossRef] [PubMed]
230. Mathew, B.; Biju, R. Neuroprotective effects of garlic a review. *Libyan J. Med.* **2008**, *3*, 23–33. [CrossRef] [PubMed]
231. Qidwai, W.; Ashfaq, T. Role of garlic usage in cardiovascular disease prevention: An evidence-based approach. *Evid. Based. Complement. Alternat. Med.* **2013**, *2013*, 125649. [CrossRef] [PubMed]
232. Ashraf, R.; Aamir, K.; Shaikh, A.R.; Ahmed, T. Effects of garlic on dyslipidemia in patients with type 2 diabetes mellitus. *J. Ayub Med. Coll. Abbottabad* **2005**, *17*, 60–64.
233. Zhai, B.; Zhang, C.; Sheng, Y.; Zhao, C.; He, X.; Xu, W.; Huang, K.; Luo, Y. Hypoglycemic and hypolipidemic effect of S-allylcysteine sulfoxide (alliin) in DIO mice. *Sci. Rep.* **2018**, *8*, 3527. [CrossRef]
234. Lee, M.-S.; Kim, I.-H.; Kim, C.-T.; Kim, Y. Reduction of body weight by dietary garlic is associated with an increase in uncoupling protein mRNA expression and activation of AMP-activated protein kinase in diet-induced obese mice. *J. Nutr.* **2011**, *141*, 1947–1953. [CrossRef]
235. Sobenin, I.; Andrianova, I.; Ionova, V.; Karagodin, V.; Orekhov, A. Anti-aggregatory and fibrinolytic effects of time-released garlic powder tablets. *Med. Heal. Sci. J.* **2012**, *10*, 47–51. [CrossRef]
236. Embuscado, M.E. Bioactives from culinary spices and herbs: A review. *J. Food Bioact.* **2019**, *6*. [CrossRef]
237. Mohammadi-rika, A.; Beigi-boroujeni, M.; Rajabzadeh, A.; Zarei, L. Effect of Extract of Allium stipitatum on Excisional Wound Healing in Rats. *Iran. J. Vet. Surg.* **2021**, *16*, 5–11.
238. Velten, R.; Erdelen, C.; Gehling, M.; Ghrt, A.; Gondol, D.; Lenz, J.; Loekhoff, O.; Wachendorff, U.; Wendisch, D.; Cripowellin, A. Cripowellin A and B, Novel Type of Amaryllidaceae Alkaloid from Crinum powellii. *Tetrahedron Lett.* **1998**, *39*, 1737–1740. [CrossRef]
239. Zvetkova, E.; Wirleitner, B.; Tram, N.T.; Schennach, H.; Fuchs, D. Aqueous extracts of Crinum latifolium and Camellia sinensis show immunomodulatory properties in human peripheral blood mononuclear cells. *Sci. Pharm.* **2001**, *79*, 2143–2150. [CrossRef]
240. Ulrich, M.R.; Davies, F.T., Jr.; Koh, Y.C.; Duray, S.A.; Egilla, J.N. Micropropagation of Crinum 'Ellen Bosanquet' by tri-scales. *Sci. Hortic.* **1999**, *82*, 95–102. [CrossRef]
241. Thi Ngoc Tram, N.; Titorenkova, T.V.; Bankova, V.S.; Handjieva, N.V.; Popov, S.S. *Crinum* L. (Amaryllidaceae). *Fitoterapia* **2002**, *73*, 183–208. [CrossRef]
242. Singh, K.A.; Nayak, M.K.; Jagannadham, M.V.; Dash, D. Thrombolytic along with anti-platelet activity of crinumin, a protein constituent of Crinum asiaticum. *Blood Cells. Mol. Dis.* **2011**, *47*, 129–132. [CrossRef]
243. Ghosal, S.; Rao, P.H.; Jaiswal, D.K.; Kumar, Y.; Frahm, A.W. Alkaloids of Crinum pratense. *Phytochemistry* **2007**, *20*, 2003–2007. [CrossRef]
244. Yoshisuke, T.; Noriaki, K.; Vijaya, K. The Alkaloidal Constituents of Goda-Manel (*Crinum zeylanicum* L.), a Sri Lankan Folk Medicine. *Chem. Pharm. Bull.* **1984**, *32*, 3023–3027.
245. Nordal, I.; Wahlstrom, R. Studies in the Crinum zeylanicum complex in East Africa. *Nord. J. Bot.* **1982**, *2*, 465–473. [CrossRef]
246. Bastida, J.; Peeters, P.; Rubiralta, M.; Naturals, D.D.P.; De Farmficia, F.; Barcelona, U. De Alkaloids from crinum kirkii. *Phytochemistry* **1995**, *40*, 1291–1293. [CrossRef]
247. Nair, J.J.; Machocho, A.K.; Campbell, W.E.; Brun, R.; Viladomat, F.; Codina, C.; Bastida, J. Alkaloids from Crinum macowanii. *Phytochemistry* **2000**, *54*, 5. [CrossRef]
248. Elgorashi, E.E.; Drewes, S.E.; Staden, J. Van Alkaloids from Crinum bulbispermum. *Phytochemistry* **1999**, *52*, 533–536. [CrossRef]

249. Tallini, L.R.; Carrasco, A.; Acosta León, K.; Vinueza, D.; Bastida, J.; Oleas, N.H. Alkaloid Profiling and Cholinesterase Inhibitory Potential of Crinum × amabile Donn. (Amaryllidaceae) Collected in Ecuador. *Plants* **2021**, *10*, 2686. [CrossRef] [PubMed]
250. Tallini, L.R.; Torras-Claveria, L.; de Borges, W.S.; Kaiser, M.; Viladomat, F.; Zuanazzi, J.A.S.; Bastida, J. N-oxide alkaloids from Crinum amabile (Amaryllidaceae). *Molecules* **2018**, *23*, 1277. [CrossRef] [PubMed]
251. Panthong, K.; Ingkaninan, K. Amabiloid A from Crinum × amabile Donn ex Ker Gawl. *Nat. Prod. Res.* **2021**, *35*, 3220–3225. [CrossRef] [PubMed]
252. Bordoloi, M.; Kotoky, R.; Mahanta, J.J.; Sarma, T.C.; Kanjilal, P.B. Anti-genotoxic hydrazide from Crinum defixum. *Eur. J. Med. Chem.* **2009**, *44*, 2754–2757. [CrossRef]
253. Fennell, C.W.; Elgorashi, E.E.; Van Staden, J. Alkaloid production in Crinum moorei cultures. *J. Nat. Prod.* **2003**, *66*, 1524–1526. [CrossRef]
254. Masi, M.; Koirala, M.; Delicato, A.; Di Lecce, R.; Merindol, N.; Ka, S.; Seck, M.; Tuzi, A.; Desgagne-Penix, I.; Calabrò, V.; et al. Isolation and Biological Characterization of Homoisoflavanoids and the Alkylamide N-p-Coumaroyltyramine from *Crinum biflorum* Rottb., an Amaryllidaceae Species Collected in Senegal. *Biomolecules* **2021**, *11*, 1298. [CrossRef]
255. Elgorashi, E.; Drewes, S.E.; Van Staden, J. Alkaloids from Crinum moorei. *Phytochemistry* **2001**, *56*, 637–640. [CrossRef]
256. Yu, M.; Wang, B.; Qi, Z.; Xin, G.; Li, W. Response surface method was used to optimize the ultrasonic assisted extraction of flavonoids from Crinum asiaticum. *Saudi J. Biol. Sci.* **2019**, *26*, 2079–2084. [CrossRef]
257. Khumkhrong, P.; Piboonprai, K.; Chaichompoo, W.; Pimtong, W.; Khongkow, M.; Namdee, K.; Jantimaporn, A.; Japrung, D.; Asawapirom, U.; Suksamrarn, A.; et al. Crinamine Induces Apoptosis and Inhibits Proliferation, Migration, and Angiogenesis in Cervical Cancer SiHa Cells. *Biomolecules* **2019**, *9*, 494. [CrossRef]
258. Sun, Q.; Shen, Y.H.; Tian, J.M.; Tang, J.; Su, J.; Liu, R.H.; Li, H.L.; Xu, X.K.; Zhang, W.D. Chemical constituents of Crinum asiaticum L. var. sinicum Baker and their cytotoxic activities. *Chem. Biodivers.* **2009**, *6*, 1751–1757. [CrossRef]
259. Kim, S.C.; Kang, J.; Kim, M.K.; Hyun, J.H.; Boo, H.J.; Park, D.B.; Lee, Y.J.; Yoo, E.S.; Kim, Y.H.; Kim, Y.H.; et al. Promotion effect of norgalanthamine, a component of Crinum asiaticum, on hair growth. *Eur. J. Dermatol.* **2010**, *20*, 42–48. [CrossRef]
260. Kogure, N.; Katsuta, N.; Kitajima, M.; Takayama, H. Two new alkaloids from Crinum asiaticum var. sinicum. *Chem. Pharm. Bull.* **2011**, *59*, 1545–1548. [CrossRef] [PubMed]
261. Do, K.M.; Shin, M.K.; Kodama, T.; Win, N.N.; Prema, P.; Nguyen, H.M.; Hayakawa, Y.; Morita, H. Flavanols and Flavanes from Crinum asiaticum and their Effects on LPS Signaling Pathway through the Inhibition of NF-κB Activation. *Planta Med.* **2021**. [CrossRef] [PubMed]
262. Yu, M.; Chen, Y.; Liu, Y.; Xu, Y.; Wang, B. Efficient polysaccharides from *Crinum asiaticum* L.'s structural characterization and anti-tumor effect. *Saudi J. Biol. Sci.* **2019**, *26*, 2085–2090. [CrossRef] [PubMed]
263. Endo, Y.; Sugiura, Y.; Funasaki, M.; Kagechika, H.; Ishibashi, M.; Ohsaki, A. Two new alkaloids from Crinum asiaticum var. japonicum. *J. Nat. Med.* **2019**, *73*, 648–652. [CrossRef]
264. Min, B.S.; Gao, J.J.; Nakamura, N.; Kim, Y.H.; Hattori, M. Cytotoxic alkaloids and a flavan from the bulbs of Crinum asiaticum var. japonicum. *Chem. Pharm. Bull.* **2001**, *49*, 1217–1219. [CrossRef]
265. Kim, Y.H.; Park, E.J.; Park, M.H.; Badarch, U.; Woldemichael, G.M.; Beutler, J.A. Crinamine from Crinum asiaticum var. japonicum inhibits hypoxia inducible factor-1 activity but not activity of hypoxia inducible factor-2. *Biol. Pharm. Bull.* **2006**, *29*, 2140–2142. [CrossRef]
266. Machocho, A.K.; Bastida, J.; Codina, C.; Viladomat, F.; Brun, R.; Chhabra, S.C. Augustamine type alkaloids from Crinum kirkii. *Phytochemistry* **2004**, *65*, 3143–3149. [CrossRef]
267. Presley, C.C.; Du, Y.; Dalal, S.; Merino, E.F.; Butler, J.H.; Rakotonandrasana, S.; Rasamison, V.E.; Cassera, M.B.; Kingston, D.G.I. Isolation, structure elucidation, and synthesis of antiplasmodial quinolones from Crinum firmifolium. *Bioorganic Med. Chem.* **2017**, *25*, 4203–4211. [CrossRef]
268. Chen, M.X.; Huo, J.M.; Hu, J.; Xu, Z.P.; Zhang, X. Amaryllidaceae alkaloids from Crinum latifolium with cytotoxic, antimicrobial, antioxidant, and anti-inflammatory activities. *Fitoterapia* **2018**, *130*, 48–53. [CrossRef]
269. Tian, H.; Liu, Q.J.; Wang, J.T.; Zhang, L. Antimicrobial crinane-type alkaloids from the bulbs of Crinum latifolium. *J. Asian Nat. Prod. Res.* **2021**, *23*, 1023–1029. [CrossRef] [PubMed]
270. Nam, N.H.; Kim, Y.; You, Y.J.; Hong, D.H.; Kim, H.M.; Ahn, B.Z. New constituents from Crinum latifolium with inhibitory effects against tube-like formation of human umbilical venous endothelial cells. *Nat. Prod. Res.* **2004**, *18*, 485–491. [CrossRef]
271. N'Tamon, A.D.; Okpekon, A.T.; Bony, N.F.; Bernadat, G.; Gallard, J.F.; Kouamé, T.; Séon-Méniel, B.; Leblanc, K.; Rharrabti, S.; Mouray, E.; et al. Streamlined targeting of Amaryllidaceae alkaloids from the bulbs of Crinum scillifolium using spectrometric and taxonomically-informed scoring metabolite annotations. *Phytochemistry* **2020**, *179*, 112485. [CrossRef] [PubMed]
272. Berkov, S.; Romani, S.; Herrera, M.; Viladomat, F.; Codina, C.; Momekov, G.; Ionkova, I.; Bastida, J. Antiproliferative alkaloids from Crinum zeylanicum. *Phytother. Res.* **2011**, *25*, 1686–1692. [CrossRef] [PubMed]
273. Ka, S.; Masi, M.; Merindol, N.; Di Lecce, R.; Plourde, M.B.; Seck, M.; Górecki, M.; Pescitelli, G.; Desgagne-Penix, I.; Evidente, A. Gigantelline, gigantellinine and gigancrinine, cherylline- and crinine-type alkaloids isolated from Crinum jagus with anti-acetylcholinesterase activity. *Phytochemistry* **2020**, *175*, 112390. [CrossRef]
274. Cortes, N.; Sierra, K.; Alzate, F.; Osorio, E.H.; Osorio, E. Alkaloids of Amaryllidaceae as Inhibitors of Cholinesterases (AChEs and BChEs): An Integrated Bioguided Study. *Phytochem. Anal.* **2017**, *29*, 217–227. [CrossRef]

275. Abebe, B.; Tadesse, S.; Hymete, A.; Bisrat, D. Antiproliferative Effects of Alkaloids from the Bulbs of Crinum abyscinicum Hochst. ExA. Rich. *Evid. Based. Complement. Alternat. Med.* **2020**, *2020*, 2529730. [CrossRef]
276. Presley, C.C.; Krai, P.; Dalal, S.; Su, Q.; Cassera, M.; Goetz, M.; Kingston, D.G.I. New potently bioactive alkaloids from Crinum erubescens. *Bioorganic Med. Chem.* **2016**, *24*, 5418–5422. [CrossRef]
277. Abdel-Halim, O.B.; Marzouk, A.M.; Mothana, R.; Awadh, N. A new tyrosinase inhibitor from Crinum yemense as potential treatment for hyperpigmentation. *Pharmazie* **2008**, *63*, 405–407. [PubMed]
278. Abdel-Halim, O.B.; Morikawa, T.; Ando, S.; Matsuda, H.; Yoshikawa, M. New crinine-type alkaloids with inhibitory effect on induction of inducible nitric oxide synthase from Crinum yemense. *J. Nat. Prod.* **2004**, *67*, 1119–1124. [CrossRef]
279. Aboul-Ela, M.A.; El-Lakany, A.M.; Hammoda, H.M. Alkaloids from the bulbs of Crinum bulbispermum. *Pharmazie* **2004**, *59*, 894–896. [CrossRef] [PubMed]
280. Ramadan, M.A.; Kamel, M.S.; Ohtani, K.; Kasai, R.; Yamasaki, K. Minor phenolics from Crinum bulbispermum bulbs. *Phytochemistry* **2000**, *54*, 891–896. [CrossRef]
281. Ali, A.; Ramadan, M.; Frahm, A. Alkaloidal Constituents of Crinum bulbispermum III: Bulbispermine—A New Alkaloid of Crinum bulbispermum. *Planta Med.* **1984**, *50*, 424–427. [CrossRef] [PubMed]
282. Kissling, J.; Ioset, J.R.; Marston, A.; Hostettmann, K. Bio-guided isolation of cholinesterase inhibitors from the bulbs of Crinum x powellii. *Phytother. Res.* **2005**, *19*, 984–987. [CrossRef]
283. Niño, J.; Hincapié, G.M.; Correa, Y.M.; Mosquera, O.M. Alkaloids of Crinum x powellii "Album" (Amaryllidaceae) and their topoisomerase inhibitory activity. *Z. Naturforsch. C* **2007**, *62*, 223–226. [CrossRef] [PubMed]
284. Houghton, P.J.; Agbedahunsi, J.M.; Adegbulugbe, A. Choline esterase inhibitory properties of alkaloids from two Nigerian Crinum species. *Phytochemistry* **2004**, *65*, 2893–2896. [CrossRef]
285. Nkanwen, E.R.S.; Gatsing, D.; Ngamga, D.; Fodouop, S.P.C.; Tane, P. Antibacterial agents from the leaves of Crinum purpurascens herb (Amaryllidaceae). *Afr. Health Sci.* **2009**, *9*, 264–269. [CrossRef] [PubMed]
286. Refaat, J.; Kamel, M.S.; Ramadan, M.A.; Ali, A.A. Crinum; An endless source of bioactive principles: A Review. Part V. Biological Profile. *Int. J. Pharm. Sci. Res.* **2013**, *4*, 1239–1252.
287. Mahomoodally, M.F.; Sadeer, N.B.; Suroowan, S.; Jugreet, S.; Lobine, D.; Rengasamy, K.R.R. Ethnomedicinal, phytochemistry, toxicity and pharmacological benefits of poison bulb—*Crinum asiaticum* L. *S. Afr. J. Bot.* **2021**, *136*, 16–29. [CrossRef]
288. Kim, Y.H.; Kim, K.H.; Han, C.S.; Park, S.H.; Yang, H.C.; Lee, B.Y.; Eom, S.-Y.; Kim, Y.-S.; Kim, J.-H.; Lee, N.H. Anti-inflammatory activity of Crinum asiaticum Linne var. japonicum extract and its application as a cosmeceutical ingredient. *J. Cosmet. Sci.* **2008**, *59*, 419–430.
289. Samud, A.M.; Asmawi, M.Z.; Sharma, J.N.; Yusof, A.P.M. Anti-inflammatory activity of Crinum asiaticum plant and its effect on bradykinin-induced contractions on isolated uterus. *Immunopharmacology* **1999**, *43*, 311–316. [CrossRef]
290. Rahman, A.S.M.; Azad, H.; Nazim, U.A. Analgesic and anti-inflammatory effects of Crinum asiaticum leaf alcoholic extract in animal models. *Afr. J. Biotechnol.* **2013**, *12*, 212–218. [CrossRef]
291. Minkah, P.A.B.; Danquah, C.A. Anti-infective, anti-inflammatory and antipyretic activities of the bulb extracts of Crinum jagus (J. Thomps.) Dandy (Amaryllidaceae). *Sci. Afr.* **2021**, *12*, e00723. [CrossRef]
292. Ratnasooriya, W.D.; Deraniyagala, S.A.; Bathige, S.D.N.K.; Hettiarachchi, H.D.I. Leaf extract of Crinum bulbispermum has antinociceptive activity in rats. *J. Ethnopharmacol.* **2005**, *97*, 123–128. [CrossRef] [PubMed]
293. Ahmad, B. Chemical composition and antifungal, phytotoxic, brine shrimp cytotoxicity, insecticidal and antibacterial activities of the essential oils of Acacia modesta. *J. Med. Plants Res.* **2012**, *6*, 4653–4659. [CrossRef]
294. Alawode, T.T.; Lajide, L.; Owolabi, B.J.; Olaleye, M.T. Evaluation of Extracts of Leaves of *Crinum jagus* for Antimicrobial Properties. *J. Appl. Sci. Environ. Manag.* **2020**, *24*, 1197–1201. [CrossRef]
295. Nguyen, H.M.; Nguyen, N.Y.T.; Chau, N.T.N.; Nguyen, A.B.T.; Tran, V.K.T.; Hoang, V.; Le, T.M.; Wang, H.C.; Yen, C.H. Bioassay-guided discovery of potential partial extracts with cytotoxic effects on liver cancer cells from vietnamese medicinal herbs. *Processes* **2021**, *9*, 1956. [CrossRef]
296. Mannan, A.; Kawser, M.J.; Ahmed, A.M.A.; Islam, N.N.; Alam, S.M.M.; Emon, M.A.E.K.; Gupta, S. Das Assessment of antibacterial, thrombolytic and cytotoxic potential of cassia alata seed oil. *J. Appl. Pharm. Sci.* **2011**, *1*, 56–59.
297. Yui, S.; Mikami, M.; Kitahara, M.; Yamazaki, M. The inhibitory effect of lycorine on tumor cell apoptosis induced by polymorphonuclear leukocyte-derived calprotectin. *Immunopharmacology* **1998**, *40*, 151–162. [CrossRef]
298. Patel, D. *Crinum asiaticum* Linn: A Medicinal Herb as Well as Ornamental Plant in Central India. *Int. J. Environ. Sci. Nat. Resour.* **2017**, *6*, 1–7. [CrossRef]
299. Hyun, J.H.; Kang, J.; Kim, S.C.; Kim, E.; Kang, J.H.; Kwon, J.M.; Park, D.B.; Lee, Y.J.; Yoo, E.S.; Kang, H.K. The effects of crinum asiaticum on the apoptosis induction and the reversal of multidrug resistance in hl-60/mx2. *Toxicol. Res.* **2008**, *24*, 29–36. [CrossRef] [PubMed]
300. Yusoff, S.M. Anti-angiogenesis as a possible mechanism of action for anti-tumor (potential anti-cancer) activity of Crinum asiaticum leaf methanol extract. *J. Angiother.* **2017**, *1*, E012–E017. [CrossRef]
301. Tan, W.-N.; Shahbudin, F.N.; Mohamed Kamal, N.N.S.N.; Tong, W.-Y.; Leong, C.-R.; Lim, J.-W. Volatile Constituents of the Leaf Essential Oil of Crinum asiaticum and their Antimicrobial and Cytotoxic Activities. *J. Essent. Oil Bear. Plants* **2019**, *22*, 947–954. [CrossRef]

302. Lim, H.S.; Kim, Y.; Kim, Y.J.; Sohn, E.; Kim, J.H.; Jeong, S.J. The Effects of Crinum asiaticum var. japonicum Baker Seeds on Neuroprotection and Antineuroinflammation in Neuronal Cell Lines. *Nat. Prod. Commun.* **2020**, *15*, 10. [CrossRef]
303. Seoposengwe, K.; van Tonder, J.J.; Steenkamp, V. In vitro neuroprotective potential of four medicinal plants against rotenone-induced toxicity in SH-SY5Y neuroblastoma cells. *BMC Complement. Altern. Med.* **2013**, *13*, 353. [CrossRef] [PubMed]
304. Ofori, M.; Danquah, C.A.; Ativui, S.; Doe, P.; Asamoah, W.A. In-Vitro Anti-Tuberculosis, Anti-Efflux Pumps and Anti-Biofilm Effects of Crinum Asiaticum Bulbs. *Biomed. Pharmacol. J.* **2021**, *14*, 1905–1915. [CrossRef]
305. Goswami, S.; Das, R.; Ghosh, P.; Chakraborty, T.; Barman, A.; Ray, S. Comparative antioxidant and antimicrobial potentials of leaf successive extract fractions of poison bulb, *Crinum asiaticum* L. *Ind. Crops Prod.* **2020**, *154*, 112667. [CrossRef]
306. Fu, L.; Zheng, Y.; Zhang, P.; Zhang, H.; Xu, Y.; Zhou, J.; Zhang, H.; Karimi-Maleh, H.; Lai, G.; Zhao, S.; et al. Development of an electrochemical biosensor for phylogenetic analysis of Amaryllidaceae based on the enhanced electrochemical fingerprint recorded from plant tissue. *Biosens. Bioelectron.* **2020**, *159*, 112212. [CrossRef]
307. Min, B.S.; Kim, Y.H.; Tomiyama, M.; Nakamura, N.; Miyashiro, H.; Otake, T.; Hattori, M. Inhibitory effects of Korean plants on HIV-1 activities. *Phytother. Res.* **2001**, *15*, 481–486. [CrossRef]
308. Naira, J.J.; Van Staden, J.; Bonnet, S.L.; Wilhelm, A. Antibacterial properties of the family amaryllidaceae: Evaluation of plant extracts in vitro. *Nat. Prod. Commun.* **2017**, *12*, 1145–1151. [CrossRef]
309. Surain, P.; Aneja, K.R. Anticandidal potential of Crinum asiaticum leaves extract against selected oral and vaginal Candida pathogens. *J. Innov. Biol.* **2014**, *6473*, 27–30.
310. Noubissi, P.A.; Fokam Tagne, M.A.; Fankem, G.O.; Ngakou Mukam, J.; Wambe, H.; Kamgang, R. Effects of *Crinum jagus* Water/Ethanol Extract on *Shigella flexneri*-Induced Diarrhea in Rats. *Evid. -Based Complement. Altern. Med.* **2019**, *2019*, 9537603. [CrossRef] [PubMed]
311. Udegbunam, S.O.; Udegbunam, R.I.; Nnaji, T.O.; Anyanwu, M.U.; Kene, R.O.C.; Anika, S.M. Antimicrobial and antioxidant effect of methanolic Crinum jagus bulb extract in wound healing. *J. Intercult. Ethnopharmacol.* **2015**, *4*, 239–248. [CrossRef] [PubMed]
312. Azikiwe, C.; Amazu, L. The potential organo-toxicity safety of Morpholine and Crinum jagus in rats. *Discovery* **2015**, *10*, 113–120.
313. Akintola, A.O.; Kehinde, A.O.; Adebiyi, O.E.; Ademowo, O.G. Anti-tuberculosis activities of the crude methanolic extract and purified fractions of the bulb of Crinum jagus. *Niger. J. Physiol. Sci.* **2013**, *28*, 135–140.
314. Ka, S.; Merindol, N.; Sow, A.A.; Singh, A.; Landelouci, K.; Plourde, M.B.; Pépin, G.; Masi, M.; Di Lecce, R.; Evidente, A.; et al. Amaryllidaceae Alkaloid Cherylline Inhibits the Replication of Dengue and Zika Viruses. *Antimicrob. Agents Chemother.* **2021**, *65*, e0039821. [CrossRef]
315. Maroyi, A. A review of ethnoboatany, therapeutic value, phytochemistry and pharmacology of Crinum macowanii Baker: A highly traded bulbous plant in Southern Africa. *J. Ethnopharmacol.* **2016**, *194*, 595–608. [CrossRef]
316. Ilavenil, S.; Kaleeswaran, B.; Sumitha, P.; Tamilvendan, D.; Ravikumar, S. Protection of human erythrocyte using Crinum asiaticum extract and lycorine from oxidative damage induced by 2-amidinopropane. *Saudi J. Biol. Sci.* **2011**, *18*, 181–187. [CrossRef]
317. Uddin, Z.; Bin, T.; Kumar, A.; Jenny, A.; Dutta, M.; Morshed, M.; Kawsar, H. Anti-Inflammatory and Antioxidant Activity of Leaf extract of Crinum asiaticum. *J. Pharm. Res.* **2015**, *5*, 5553–5556.
318. Indradevi, S.; Ilavenil, S.; Kaleeswaran, B.; Srigopalram, S.; Ravikumar, S. Ethanolic extract of Crinum asiaticum attenuates hyperglycemia-mediated oxidative stress and protects hepatocytes in alloxan induced experimental diabetic rats. *J. King Saud. Univ. Sci.* **2015**, *24*, 171–177. [CrossRef]
319. Ghane, S.G.; Attar, U.A.; Yadav, P.B.; Lekhak, M.M. Antioxidant, anti-diabetic, acetylcholinesterase inhibitory potential and estimation of alkaloids (lycorine and galanthamine) from Crinum species: An important source of anticancer and anti-Alzheimer drug. *Ind. Crops Prod.* **2018**, *125*, 168–177. [CrossRef]
320. Alawode, T.T.; Lajide, L.; Owolabi, B.J.; Olaleye, M.T. Studies on In vitro Antioxidant and Anti-Inflammatory Activities of Crinum jagus Leaves and Bulb Extracts. *Int. J. Biochem. Res. Rev.* **2019**, *28*, 1–9. [CrossRef]
321. Adewusi, E.A.; Steenkamp, V. In vitro screening for acetylcholinesterase inhibition and antioxidant activity of medicinal plants from southern Africa. *Asian Pac. J. Trop. Med.* **2011**, *4*, 829–835. [CrossRef]
322. Chahal, S.; Lekhak, M.M.; Kaur, H.; Shekhawat, M. Unraveling the medicinal potential and conservation of Indian Crinum Unraveling the medicinal potential and conservation of Indian Crinum (Amaryllidaceae) species. *S. Afr. J. Bot.* **2020**, *136*, 7–15. [CrossRef]
323. Kang, J.; Choi, J.H.; Lee, J.G.; Yoo, E. The Mechanism of *Crinum asiaticum* var. japonicum on the Activation of Anagen. *Korean J. Pharmacogn.* **2017**, *48*, 148–154.
324. Jeong, Y.J.; Sohn, E.H.; Jung, Y.H.; Yoon, W.J.; Cho, Y.M.; Kim, I.; Lee, S.R.; Kang, S.C. Anti-obesity effect of Crinum asiaticum var. japonicum Baker extract in high-fat diet-induced and monogenic obese mice. *Biomed. Pharmacother.* **2016**, *82*, 35–43. [CrossRef]
325. Taiwe, G.S.; Tchoya, T.B.; Menanga, J.R.; Dabole, B.; De Waard, M. Anticonvulsant activity of an active fraction extracted from *Crinum jagus* L. (Amaryllidaceae), and its possible effects on fully kindled seizures, depression-like behaviour and oxidative stress in experimental rodent models. *J. Ethnopharmacol.* **2016**, *194*, 421–433. [CrossRef]
326. Heinrich, M. Galanthamine from Galanthus and other Amaryllidaceae–chemistry and biology based on traditional use. *Alkaloids. Chem. Biol.* **2010**, *68*, 157–165. [CrossRef]
327. Jilani, M.S.; Tagwireyi, D.; Gadaga, L.L.; Maponga, C.C.; Mutsimhu, C. Cognitive-Enhancing Effect of a Hydroethanolic Extract of *Crinum macowanii* against Memory Impairment Induced by Aluminum Chloride in BALB/c Mice. *Behav. Neurol.* **2018**, *2018*, 2057219. [CrossRef]

328. Snijman, D.A.; Meerow, A.W. Floral and macroecological evolution within Cyrtanthus (Amaryllidaceae): Inferences from combined analyses of plastid ndhF and nrDNA ITS sequences. *S. Afr. J. Bot.* **2010**, *76*, 217–238. [CrossRef]
329. Galley, C.; Bytebier, B.; Bellstedt, D.U.; Linder, H.P. The Cape element in the Afrotemperate flora: From Cape to Cairo? *Proc. R. Soc. B Biol. Sci.* **2007**, *274*, 535–543. [CrossRef]
330. Mucina, L.; Rutherford, M.C. *The Vegetation of South Africa, Lesotho and Swaziland*; South African National Biodiversity Institute: Cape Town, South Africa, 2006.
331. Born, J.; Linder, H.P.; Desmet, P. The Greater Cape Floristic Region. *J. Biogeogr.* **2007**, *34*, 147–162. [CrossRef]
332. Cowling, R.M.; Procheş, Ş.; Vlok, J.H.J. On the origin of southern African subtropical thicket vegetation. *S. Afr. J. Bot.* **2005**, *71*, 1–23. [CrossRef]
333. Bhat, R.B.; Jacobs, T.V. Traditional herbal medicine in Transkei. *J. Ethnopharmacol.* **1995**, *48*, 7–12. [CrossRef]
334. Nwude, N.; Ebong, O.O. Some plants used in the treatment of leprosy in Africa. *Lepr. Rev.* **1980**, *51*, 11–18. [CrossRef]
335. Rárová, L.; Ncube, B.; Van Staden, J.; Fürst, R.; Strnad, M.; Gruz, J. Identification of Narciclasine as an in Vitro Anti-Inflammatory Component of Cyrtanthus contractus by Correlation-Based Metabolomics. *J. Nat. Prod.* **2019**, *82*, 1372–1376. [CrossRef]
336. Hutchings, A.; Scott, A.H.; University of Zululand; National Botanical Institute (South Africa). *Zulu Medicinal Plants: An Inventory*; University of Natal Press: Scottsville, South Africa, 1996; ISBN 0869808931.
337. Nair, J.J.; Bastida, J.; Codina, C.; Viladomat, F.; Van Staden, J. Alkaloids of the South African amaryllidaceae: A review. *Nat. Prod. Commun.* **2013**, *8*, 1335–1350. [CrossRef]
338. Mahlangeni, N.T.; Moodley, R.; Jonnalagadda, S.B. Phytochemical analysis of Cyrtanthus obliquus bulbs from the informal street market of Kwazulu-Natal, South Africa. *Afr. J. Tradit. Complement. Altern. Med.* **2015**, *12*, 28–34. [CrossRef]
339. Brine, N.D.; Campbell, W.E.; Bastida, J.; Herrera, M.R.; Viladomat, F.; Codina, C.; Smith, P.J. A dinitrogenous alkaloid from Cyrtanthus obliquus. *Phytochemistry* **2002**, *61*, 443–447. [CrossRef]
340. Masi, M.; Mubaiwa, B.; Mabank, T.; Karakoyun; Cimmino, A.; Van Otterlo, W.A.L.; Green, I.R.; Evidente, A. Alkaloids isolated from indigenous South African Amaryllidaceae: Crinum buphanoides (Welw. ex Baker), Crinum graminicola (I. Verd.), Cyrtanthus mackenii (Hook. f) and Brunsvigia grandiflora (Lindl). *S. Afr. J. Bot.* **2018**, *118*, 188–191. [CrossRef]
341. Elgorashi, E.E.; Van Staden, J. Pharmacological screening of six Amaryllidaceae species. *J. Ethnopharmacol.* **2004**, *90*, 27–32. [CrossRef] [PubMed]
342. Elgorashi, E.E.; Van Staden, J. Alkaloids from Cyrtanthus falcatus. *S. Afr. J. Bot.* **2003**, *69*, 593–594. [CrossRef]
343. Weniger, B.; Italiano, L.; Beck, J.P.; Bastida, J.; Bergonon, S.; Codina, C.; Lobstein, A.; Anton, R. Cytotoxic activity of Amaryllidaceae alkaloids. *Planta Med.* **1995**, *61*, 77–79. [CrossRef] [PubMed]
344. Elgorashi, E.E.; Stafford, G.I.; Mulholland, D.; Van Staden, J. Isolation of captan from Cyrtanthus suaveolens: The effect of pesticides on the quality and safety of traditional medicine. *S. Afr. J. Bot.* **2004**, *70*, 512–514. [CrossRef]
345. Kim, H.W.; Wang, M.; Leber, C.A.; Nothias, L.F.; Reher, R.; Kang, K.B.; van der Hooft, J.J.J.; Dorrestein, P.C.; Gerwick, W.H.; Cottrell, G.W. NPClassifier: A Deep Neural Network-Based Structural Classification Tool for Natural Products. *J. Nat. Prod.* **2021**, *84*, 2795–2807. [CrossRef] [PubMed]