ETHNOPHARMACOLOGICAL AND PHYTOCHEMICAL REVIEW OF *ALLIUM* SPECIES (SWEET GARLIC) AND *TULBAGHIA* SPECIES (WILD GARLIC) FROM SOUTHERN AFRICA

SL Lyantagaye
Department of Molecular Biology and Biotechnology, College of Natural and Applied Sciences, University of Dar es Salaam, P.O. Box 35179, Dar es Salaam, Tanzania.
E-mail: slyantagaye@gmail.com, lyantagaye@amu.udsm.ac.tz, Phone: +255-787537030

ABSTRACT
Tulbaghia *(wild Garlic) is a plant genus most closely related to the genus* Allium *both in the family* Alliaceae *and is entirely indigenous to Southern Africa. Indigenous people use several species of the genus as food and medicine, and few species are commonly grown as ornamentals. Biological and pharmacological research on Tulbaghia species and their relationship with* Allium sativum *(sweet Garlic) are presented and critically evaluated. Informations from studies on the treatment of microbes-caused diseases as well as of cancer have been presented in ethnobotanical reports. Moreover, recent scientific studies have been performed on crude extracts for certain* Tulbaghia *species as reviewed in this article. This article gives a critical assessment of the literature to date and aims to show that the pharmaceutical potential of the members of the genus* Tulbaghia *is comparable to that of its close relative* A. sativum *but has been underestimated and deserves closer attention.*

Keywords: *Allium sativum,* Ethnobotany, Ethnopharmacology, Medicinal, Phytochemical, Southern Africa, *Tulbaghia*

INTRODUCTION
Tulbaghia (wild Garlic) is a plant genus belonging to the family Alliaceae and is a small plant genus of about 30 species all indigenous to the Southern Africa region (Williamson 1955, Vosa 1975, Tredgold 1986, van Wyk and Gericke 2000, Figure 1) and is very interesting from both biological and chemical perspective. Some member species have been able to adopt foreign environmental conditions as they are being grown in as far as Europe and America (Benham 1993). Most of its member species are closely related to *Allium sativum* (sweet Garlic) and hence commonly known as wild garlic. There are many chemical constituents that have been identified in the Alliaceae family. The strong onion or garlic smells are found in the *Tulbaghia* and *Allium* genera, while steroidal saponins are found in most of the species (Dahlgren et al. 1985). The medicinal uses of the *Allium* plants have been widely studied and recorded (Ross 2003). Only 3 of the 30 distinguished species of *Tulbaghia* have been reported in scientific literature as ethnobotanically used or phytochemically investigated. However, significant information on chemical profile is available only for one species, *Tulbaghia violaceae*, and has been found to be rich in sulfur–containing compounds; the compounds in most cases account for the characteristic odours and the medicinal properties of both the *Tulbaghia* and *Allium* species. This review will focus mainly on the genus *Tulbaghia* and its ethnopharmacological relationship with *Allium*.

The Alliaceae family
Alliaceae is a family of herbaceous perennial flowering plants, which are monocots in the order Asparagales. The family has been widely but not universally recognized, in the past, the plants involved were often treated as belonging to the family Liliaceae. The Angiosperm Phylogeny Group II system (APG II system) of 2003 recognizes the

family and places it in the order Asparagales in the clade monocots.

Figure 1: A map showing countries (Southern Africa) where *Tulbaghia* plants are indigenous.

The Alliaceae family has about 600 species in 30 genera and is a widely distributed family (APG 2003). The major places of distribution for the whole family are Mediterranean Europe, Asia, North and South America and Sub-Saharan Africa (APG 1998, APG 2003). The Sub-Saharan Africa genera are *Allium*, *Tulbaghia* and *Agapanthus* (Dahlgren *et al*. 1985). Probably the most popular genus is *Allium*, which includes several important food plants, including garlic (*A. sativum* and *A. scordoprasum*), onions (*Allium cepa*), chives (*A. schoenoprasum*), and leeks (*A. porrum*). A strong "oniony" odour is characteristic of the whole genus *Allium*, but not all members are equally flavorful (Kourounakis and Rekka 1991). *A. sativum* and *Allium cepa* are worldwide known for their medicinal use (Ross 2003).

Genetical relationship between the genera *Tulbaghia* and *Allium*

The physical ends of eukaryotic chromosomes are protected from being recognised and processed as DNA breaks by telomeres. Tandemly repeated short minisatellite motif of DNA is usually found in the telomeres and is called telomeric DNA repeats. Telomere repeats are remarkably conserved among eukaryotes, and sequence variation among most of the major taxonomic groups does not exceed one or two nucleotides (Li *et al*. 2000). In plants this particular motif (5'-TTTAGGG-3') was first characterised in *Arabidopsis thaliana* (Richards and Ausubel, 1988) and has since been found in the majority of plant species (Cox *et al.* 1993) and is now refered to as the Arabidopsis cap.

However, not all plants share the typical plant telomere sequence and recently the presence of this or its variation has been used to show genetic similarity. *Allium*, *Tulbaghia* and *Nothoscordum* (family Alliaceae) are devoid of the *Arabidopsis*-type telomeres (Fay and Chase 1996). *Aloe* (Asphodelaceae) and *Hyacinthella* (Hyacinthaceae), both belonging to Asparagales, possess human/vertebrate-type sequences (5'-TTAGGG-3') at their chromosome termini (Puizina *et al*. 2003, Weiss and Scherthan 2002). As all these genera are petaloid monocots in the Asparagales, it suggests that an absence of *Arabidopsis*-type telomeres may be characteristic of this related group of plants (Adams *et al*. 2000, Weiss-Schneeweiss *et al*. 2004). The only other plant genera so far reported without such telomeres are *Cestrum* and closely related genera *Vestia* and *Sessea* (Solanaceae) (Sykorova et al. 2003). *A. cepa* (Alliaceae) lacks both *Arabidopsis*-type and human-type telomeres; it possesses an unknown type of telomere. (Sykorova et al. 2006). However, there exist significant differences between members of *Allium* and that of *Tulbaghia.* For example, *A. sativum* has 2n = 3x = 24 and *T. violacea* has a non-bimodal karyotype (2n = 12) (Fay and Chase 1996), which is not suprising for different species.

Therapeutics of *Allium* species

The genus *Allium* has about 1250 species, making it one of the largest plant genera in the world (Dahlgren *et al*. 1985). The plants can vary in height between 5 cm and 150 cm. The flowers form an umbel at the top of a leafless stalk. *A. sativum* is indigenous to Asia and probably the most widely used herb in the world (Hyams 1971), but it has been grown in most of tropical and subtropical region. *A. sativum* has linear sheathing leaves, globose umbels of white or reddish flowers. The bulbs are composed of "cloves", which are wrapped in a shared whitish papery coat. The odour is weak when the plant is intact, when damaged the smell grows strong. They are perennial bulbous plants containing mostly organosulfur compounds, such as allyl sulfides, propionthiol and vinyl disulfide in their essential oils (Dahlgren *et al*. 1985).

A. sativum and its extracts have been widely recognized worldwide as agents for prevention and treatment of cardiovascular and other metabolic diseases, atherosclerosis, hyperlipidemia, thrombosis, hypertension, microbial infections, asthma, and diabetes (Reuter 1995, Reuter et al. 1996). The therapeutic properties of *A. sativum* have been through review in the book called Medicinal Plants of the World (Humana) by Ross (2003).

The chemistry of *Allium* species

The active components of *A. sativum* include antioxidants such as organosulfur compounds, free radicals scavenger flavonoids such as allixin, trace elements such as germanium (normalizer and immunostimulant), selenium (for optimal function of the antioxidant enzyme glutathione peroxidase), volatile oil containing sulfur compounds, amino acids and other bio-active compounds (Ross 2003). Garlic chemistry is complex, and a number of other compounds are also produced in the plant by the aging process. As simply stated, organosulfur compounds are organic molecules that contain the element sulfur. Depending on structure, the presence of sulfur in an organic molecule is often indicated by a distinctive and oftentimes unpleasant and 'loud' odour. However, organosulfur compounds can also confer pleasant odour characteristics, as is observed in garlic and onions. The aroma and flavor molecules in garlic and onions are derived from precursor compounds that are derivatives of the amino acid cysteine.

A. sativum and *A. cepa* (onion) both contain 1-5% dry weight of cysteine derivatives in which the proton at sulfur in cysteine is replaced with an alkyl or alkenyl substituent, and the sulfur atom is itself oxidized to the sulfoxide. The cysteine sulfoxide derivatives found in onions and garlic are indicated in (Figure 2, Scheme 1).

Onions contain propiin, isoalliin and methiin, whereas garlic contains isoalliin, methiin and alliin (Ichikawam *et al.* 2006, Horníckové *et al.* 2010). Alliin exhibits considerable biological activity (Kourounakis and Rekka 1991).

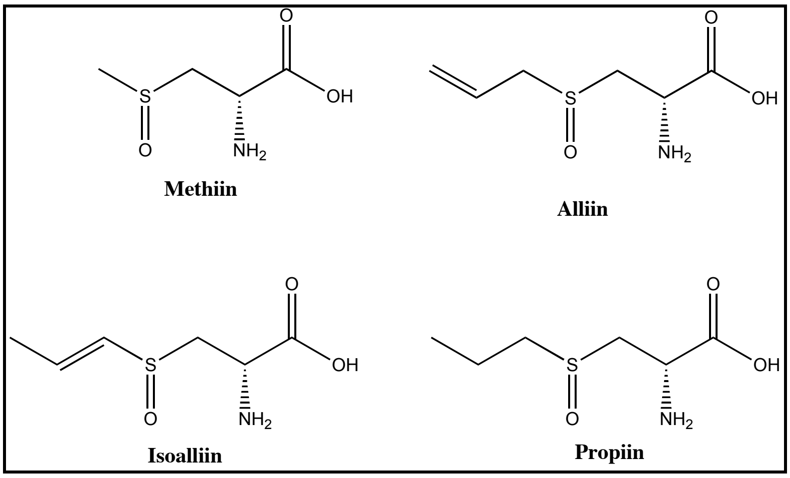
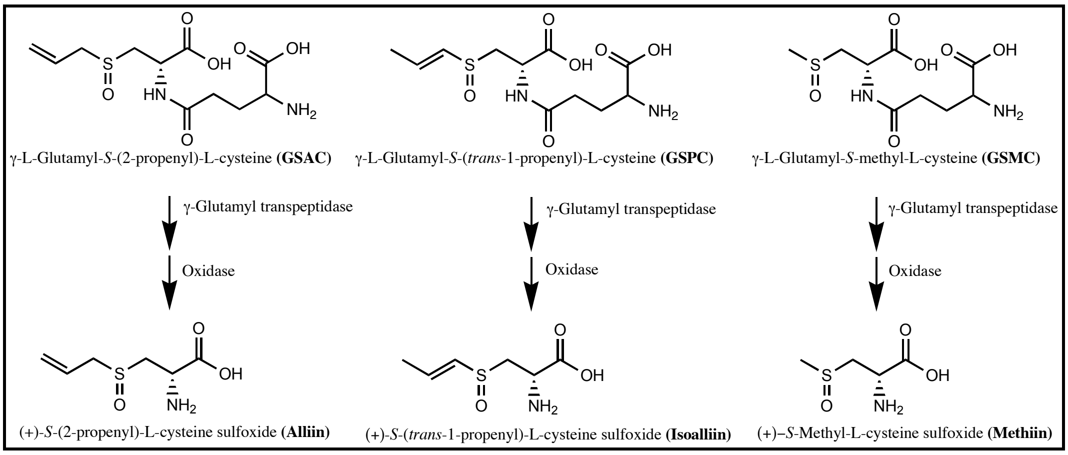
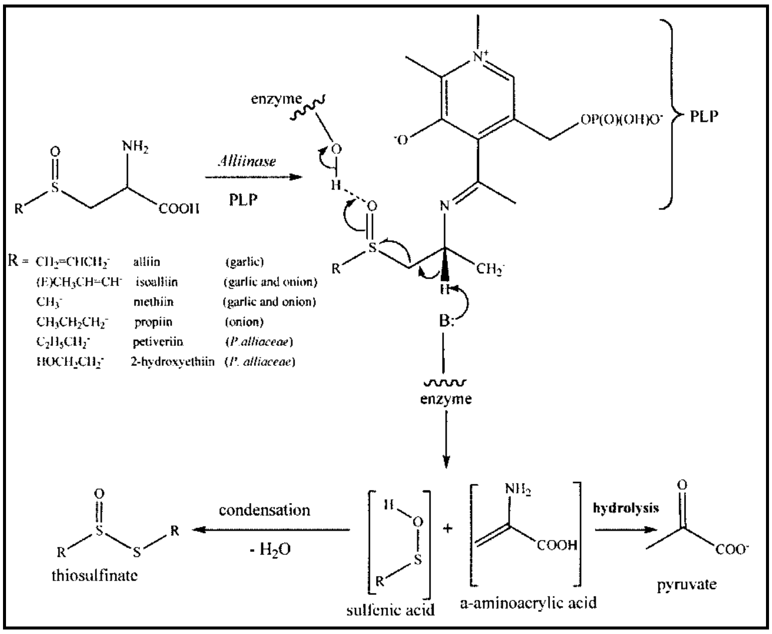


Figure 2: Cysteine sulfoxide (organosulfur) derivatives found in onions and garlic.



Scheme 1: Biosynthetic pathway of organosulfer compounds in garlic (Ichikawam *et al.* 2006).

The distinct flavors of garlic and onion reflect varying amounts of cysteine sulfoxides in each plant, most particularly isoalliin (higher amount in onion) and alliin (higher amount in garlic) (Fritsch and Keusgen 2006). Isoalliin is the precursor of thiopropanal S-oxide, the volatile sulfine in onion that causes tearing. The cysteine sulfoxide derivatives are contained in the cytoplasm of the plant cells. In the vacuoles of these cells is contained a class of enzymes known as C-S lyases. If the plant tissue is disrupted by cutting/slicing, chopping, chewing etc, the C-S lyase is released, and it subsequently acts upon the cysteine sulfoxide derivatives, cleaving the C-S bond between the b-carbon and sulfur (Scheme 2). This cleavage results in two fragments; a putative sulfenic acid intermediate, and a-aminoacrylic acid (Block 1992, Shimon *et al.* 2007). The latter compound spontaneously decomposes to ammonia and pyruvic acid while the former condenses with a second sulfenic acid molecule to form a class of compounds known as thiosulfinates (Block 1992, Shimon *et al.*, 2007). The importance of the thiosulfinates derivatives is from the fact that they have been shown to exhibit a variety of biological activities, including antibacterial, antifungal, antiviral and anticancer properties, among others (Ross 2003). Thiosulfinates also serve as the primary flavor and odour producing molecules in freshly prepared garlic and onion macerates. The thiosulfinates participate in a variety of subsequent reactions which afford a considerable number of organosulfur volatiles, such as sulfides, di- and trisulfides and dithiins (Figure 3). These compounds impart additional flavor, odour and biological activity characteristics to longer standing and/or heat-treated macerates.



Scheme 2.: Proposed general mechanism for the catalysis of C-S bond cleavage in Cys sulfoxide derivatives by alliinase (Block 1992, Shimon *et al.* 2007). Alliin, *S*-Allyl-L-Cys sulfoxide; 2-hydroxyethiin, *S*-2-hydroxyethyl-L-Cys sulfoxide; isoalliin, (*E*)-*S*-(1-propenyl)-L-Cys sulfoxide; methiin, *S*-methyl-L-Cys sulfoxide; petiveriin, *S*-benzyl-L-Cys sulfoxide; propiin, *S*-propyl-L-Cys sulfoxide.

Because earlier studies established that the aforementioned chemistry occurred in garlic and onions, and since both are members of the allium family, this chemistry is often referred to as 'allium chemistry'. However, there are numerous other plants unrelated to the *Allium* genus whose organo-leptic properties imply the presence of organosulfur compounds (Block 2010). Indeed, in the next sections it is shown that similar chemistry occurs in *T. violacea*.

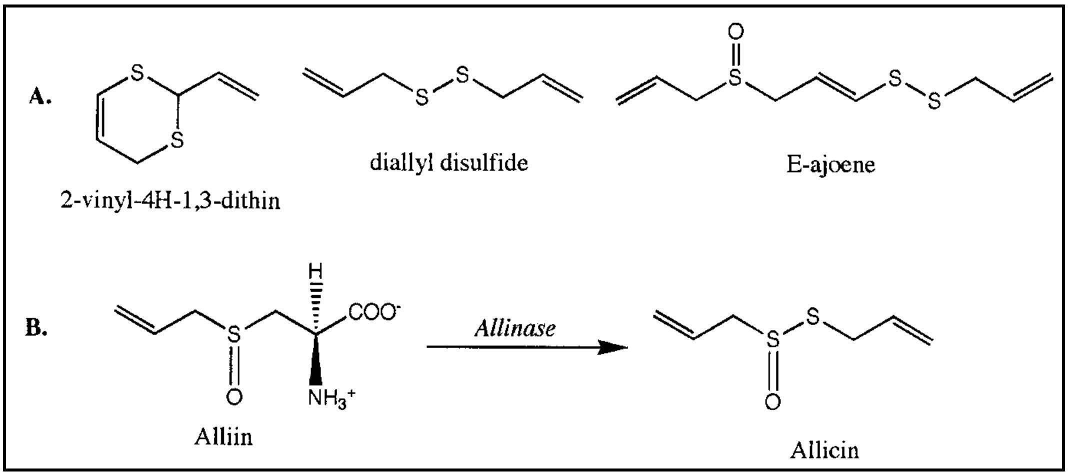


Figure 3: *A*, therapeutically active sulfur compounds from garlic; a representative for each of the three substance classes (allyl sulfides, dithiines, and ajoenes) is shown. *B*, the enzymatic reaction catalyzed by alliinase (Kuettner et al. 2002).

Tulbaghia species

Of all the members of the family Alliaceae, *Tulbaghia* is the genus most closely related to *Allium* and is entirely indigenous to Southern Africa (Figure 1). The natural distribution extends from Southern Tanzania to Malawi, Botswana, Zimbabwe, Mozambique, South Africa, Swaziland and Lesotho (Williamson 1955, Vosa 1975, Tredgold 1986, van Wyk and Gericke 2000, Vosa and Condy 2001). Indigenous people use several species as food and medicine, and few species are commonly grown as ornamentals (Vosa 1975, Vosa and Condy 2001). *T. violacea* is the most well known species as medicinal plant species in the genus, especially in the Eastern Cape and KwaZulu-Natal regions (Burton 1990, van Wyk *et al.* 2000). The presence of this species elsewhere is due to cultivation in gardens and in the commercial medicinal plant farms (van Wyk *et al*. 2000). A few species are reported in the UK, such as *T. violacea*, *T. cominsii, T. acutiloba, T. natalensis*, and *T. montana*, and also in the USA cultivated as decorative plants although most are rather tender and are best grown as warm greenhouse plants (Burbidge 1978, Watson and Dallwitz 1992). Typically, the *Tulbaghia* species are modest, unassuming plants with small flowers, grassy foliage, sometimes with a pungent skunky or alliaceous scent to the rhizomatous rootstalks. A new species of *Tulbaghia* (*T. pretoriensis*), sympatric to *Tulbaghia acutiloba* and found in and around Pretoria was the latest to be described in 2006. The two species differ from one another in their karyotype, flower morphology and scent, as well in their overall size (Vosa and Gillian 2006, Vosa 2007). Table 1 shows members on record of the small genus *Tulbaghia*, about 30 plants species.

Table 1: Plant species in the genus *Tulbaghia* (Burbidge 1978, Vosa 1980, Vosa 2000, Vosa and Condy 2006)

Species	**Common name [local names]**
Tulbaghia pretoriensis Vosa & Condy.	Wild Garlic
Tulbaghia acutiloba Harv.	Wild Garlic, Wildeknoffel [Afrikaans], sefothafotha [South Sotho], lisela [Swazi], ishaladi lezinyoka [Zulu].
Tulbaghia aequinoctialis Welw. ex Baker	Wild Garlic
Tulbaghia affinis Link	Wild Garlic
Tulbaghia alliacea L.f.	Wild Garlic
Tulbaghia bragae Engl.	Wild Garlic
Tulbaghia calcarea Engl. & K.Krause	Wild Garlic
Tulbaghia cameronii Baker	Wild Garlic
Tulbaghia capensis L.	Wild Garlic, Wildeknoffel [Afrikaans],
Tulbaghia coddii Vosa & Burb.	Wild Garlic
Tulbaghia cominsii Vosa	Wild Garlic
Tulbaghia dregeana Kunth	Wildelook, Ajuin [Afrikaans]
Tulbaghia friesii Suess.	Wild Garlic
Tulbaghia galpinii Schltr.	Wild Garlic
Tulbaghia hypoxidea Sm.	Wild Garlic
Tulbaghia leucantha Baker	Wild Garlic, sefothafotha [South Sotho]
Tulbaghia ludwigiana Harv.	Scented Wild Garlic, ingotjwa, sikwa [Swazi], umwelela-kweliphesheya [Zulu]
Tulbaghia luebbertiana Engl. & K.Krause	Wild Garlic
Tulbaghia macrocarpa Vosa	Wild Garlic
Tulbaghia montana Vosa	Wild Garlic
Tulbaghia natalensis Baker	Sweet Wild Garlic, iswele lezinyoka [Zulu]
Tulbaghia nutans Vosa	Wild Garlic
Tulbaghia pauciflora Baker	Wild Garlic
Tulbaghia rhodesica R.E.Fr.	Wild Garlic
Tulbaghia simmleri P.Beauv.	Wild Garlic
Tulbaghia tenuior K.Krause & Dinter	Wild Garlic
Tulbaghia transvaalensis Vosa	Wild Garlic
Tulbaghia verdoornia Vosa & Burb.	Wild Garlic
T. violacea Harv.	Wild Garlic, Wildeknoffel [Afrikaans], isihaqa [Zulu]
Tulbaghia x aliceae Vosa	Wild Garlic

T. violacea is a small perennial bulbous herb with corm-like rhizomes and narrowly linear, evergreen aromatic leaves. The flowers are tubular mauve or pale purple, occurring in groups of about ten at the tip of the slender stalk (Figure 4). The plant prefers partial shade or partial sun to full sun; and dry to moist soils. Mature height ranges from 30 cm to 120 cm depending on the environmental conditions. The plant can be grown successfully in a tub and transferred to a greenhouse or a frost-free place for the winter (Watson and Dallwitz 1992). The plant gives out a strong odour of onion or garlic when bruised (Watt and Breyer-Brandwijk 1962), hence its common names wild garlic (van Wyk et al. 2000) or society garlic (Watson and Dallwitz 1992). Inspite of its garlic-like flavor, the consumption of *T. violacea* is not accompanied by the development of bad breath as is in the case with the consumption of *A. sativum* and hence another common name "sweet garlic" (Kubec *et al*. 2002). This suggests that *T. violacea* and *A. sativum* may not contain exactly the same volatile chemical compositions. However, it was previously reported that *T. violacea* contain a carbon-sulfur lyase enzyme whose action is similar to that of lyases in the various *Allium* species (Jacobsen *et al*. 1968). The same study suggested the presence of sulfur compounds that corresponded with those found in *Allium* volatile compounds. Thus, suggesting that the garlic-like smell of the wild garlic is most likely due to the same or similar sulfur compounds (Burton 1990). It is, therefore, most likely that *T. violacea* may also contain the medicinal potential that is similar to its close relative *A. sativum* .

a

b

Figure 4: *Tulbaghia violacea;* a) whole plants, and b) flower,

Ethnobotany of *Tulbaghia* species

The traditional uses of *Tulbaghia* species are referred to in many folkloric and ethnobotanical studies performed in certain areas of South Africa, where like many other the poor Sub-Saharan Africa communities, plants are still the primary source of medicine.

According to van Wyk *et al*. (2000), *T. violacea* [common names: Wild garlic (English), Wildeknoffel (Afrikaans), Isihaqa (Zulu) and Moelela (Sotho)] is used in traditional medicine in the Eastern Cape and KwaZulu Natal for problems like fever, colds, asthma, tuberculosis, stomach-ache, and cancer of the oesophagus. The bulbs of *T. violacea* are used as a remedy for pulmonary tuberculosis and to destroy intestinal worms. The Zulu people use the bulb to make an aphrodisiac medicine. Some of the Rastafarians eat copious amounts of it and chili during winter allegedly "to keep the blood warm" and stop aches and pains. Bulbs and leaves soaked in water for a day can be used for rheumatism, arthritis and to bring down fever. The bulbs are also used for coughs, colds and flu. Zulu people also use the plant to repel snakes away from their houses. It is also used for the treatment of infant and mother in the case of depressed fontanelle. In the Eastern Cape *T. violacea* is used for colic, wind, restlessness, headache and fever, largely for young children. Like any drug, extensive use can give adverse symptoms such as abdominal pain, gastroenteritis, acute inflammation and sloughing of the intestinal mucosa, cessation of gastro-intestina peristalsis, contraction of the pupils and subdued reactions to stimuli. *Tulbaghia simmeleri* is often used as alternative for *T.*

violacea, where the latter is not available (Burton 1990, van Wyk *et al.* 2000).

Tulbaghia alliacea, has been reported as an early Cape remedy for fever, fits, rheumatism, and paralysis (Burton 1990). *T. alliacea* has the same common name as *T. violacea,* i.e., Wild garlic (English), Wildeknoffel (Afrikaans), Isihaqa (Zulu) and Moelela (Sotho). *T. alliacea* is an indigenous species in South Africa, growing particularly in the Eastern Cape and southern KwaZulu-Natal. It is a bulbous plant with long, narrow, hairless leaves arising from several white bases. Brownish green flowers occur in-groups of about 10 or more at the tip of a slender stalk (Robert 2001). Both the bulbs and leaves of *T. alliacea* are used medicinally. In Zimbabwe and South Africa the leaves of *Tulbaghia alliacea* are cooked as a relish, alone or with leaves of other plants, such as *Adenia* species. The rhizome is scraped clean and boiled with meat in stews or roasted as a vegetable. Young leaves are chopped and used to flavour soups, stews, pickles and omelettes as a substitute for shallot. In South Africa the bruised rhizome is used in baths for the relief of fever, rheumatism or paralysis. Small doses are used as a laxative (Williamson 1955, Vosa 1975, Tredgold 1986, van Wyk and Gericke 2000). The plant is used for fever and colds, asthma, pulmonary tuberculosis and stomach problems. In the Cape Dutch tradition, *T. alliacea* is used as a purgative and for fits, rheumatism and paralysis. Also tea can be made from chopped bulbs and roots and used as a purgative. Extracts of *T. alliacea* exhibit anti-infective activity against *Candida* species in vitro (Thamburan et al. 2006). The Khoikhoi and Basotho use the plant to make a brew from the chopped bulbs and roots (Robert 2001).

The bulbs of *Tulbaghia cepacea* are recommended for tuberculosis and as an anthelmintic (Watt and Breyer-Brandwijk 1962). Nothing has been reported in literature about the rest of the plant species, most probably they are used interchangeably with *T. violacea*, *T. simmleri,* and *T. alliacea*.

Chemical constituents of *Tulbaghia* species

Like in *Allium,* volatile sulfur-containing flavor compounds are responsible for the characteristic smell and taste of *Tulbaghia* species. Unlike *Allium* species, the closely related plant whose chemistry has been extensively studied, only few scientific articles about the chemical constituents of *T. violacea* have been published so far. Jacobsen *et al.* (1968) reported the presence of a C–S lyase and three unidentified *S*-substituted cysteine sulfoxide derivatives. Bate-Smith (1968) reported the presence in *T. violacea* of kaempferol (Figure 5). Burton and Kaye (1992) isolated 2,4,5,7-tetrathiaoctane-2,2-dioxide and 2,4,5,7-tetrathiaoctane from the leaves of *T. violacea*. Kubec *et al.* (2002) isolated 2,4,5,7-tetrathiaoctane-4-oxide and identified the three unknown cysteine derivatives that had been suggested by Jacobsen et al. (1968) as (*RSR*C)-*S*-(methylthiomethyl)cysteine-4-oxide (marasmin). (*SSR*C)-*S*-methyl- and (*SSR*C)-*S*-ethylcysteine sulfoxides (methiin, MCSO and ethiin, ECSO, respectively). Gmelin et al. (1976) were the first to propose that the enzymatic cleavage of marasmin is analogous to that of alliin (*S*-allylcysteine sulfoxide) in *A. sativum* and other alliaceous species. They suggested the formation of *S*-(methylthiomethyl) (methylthio) methanethiosulfinate (2,4,5,7-tetrathiaoctane-4-oxide, marasmicin, 2 in Sheme 3) from marasmin as the primary breakdown product.

The presence of a C–S lyase in *T. violacea* (Jacobsen et al. 1968), suggests the close genetic relationship with *Allium* species, also due to marasmicin being in close analogy to the alliin/allicin system, make it reasonable to assume that a similar mechanism is also operating in *T. violacea*.

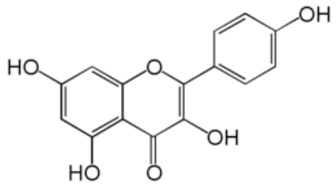


Figure 5: Kaempferol

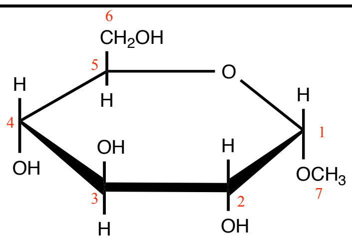
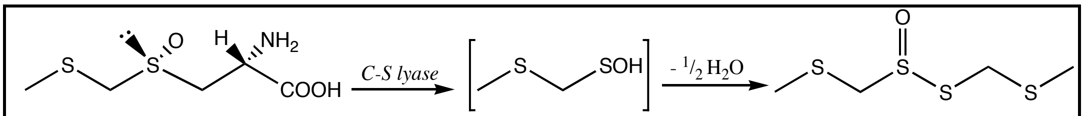


Figure 6. Methyl-α-D-glucopyranoside (MDG).



(R_SR_C)-S-(methylthiomethyl)cysteine-4-oxide, **1**

marasmicin, **2**

Scheme 3: Formation of marasmicin, 2, from (R_SR_C)-*S*-(methylthiomethyl)cysteine-4-oxide, 1, in *T. violacea*.

Marasmicin is unstable and further decomposes giving various sulphur-containing degradation products, e.g. 2,4,5,7-tetrathiaoctane, 2,4,5,7-tetrathiaoctane-2,2-dioxide, 2,4,5,7-tetrathiaoctane-4,4-dioxide, or 2,4,5,7-tetrathiaoctane-2,2,7,7-tetraoxide (Kubec et al. 2002). Other classes of compounds reported in *T. violacea* are flavonols e.g. kaempferol (Figure 5), and saponins/sapogenins, which are generally present in *Allium* and *Tulbaghia* (Watson and Dallwitz 1992). Burton (1990) identified free sugars including glucose, fructose, sucrose, maltose, arabinose, rhamnose, xylose and galactose, and glycosides from an aqueous extract of *T. violacea*. Lyantagaye and Rees (2003) and Lyantagaye et al. (2005) have reported the presence of glucopyranoside "Methyl-α-D-glucopyranoside (MDG)" (Figure 6) from *T. violacea* aqueous extracts.

S-alk(en)yl cysteine sulfoxides, thiosulfinates, polysulfides, fructose and glucose compounds have been found from the aqueous extract *T. alliacea*. Also, a furanoid compound [5-(hydroxymethyl)-2-furfuraldehyde] was identified as an artefact compound generated by the acid hydrolysis step. This compound occurs as a product from the acid-catalyzed dehydration of fructose (Maoela 2005).

Krest et al. (2000) reported the presence of S- methyl-L-cysteine sulfoxide (MCSO, methiin), S-propyl cysteine sulfoxide (PCSO, propiin), S-allyl-L-cysteine sulfoxide (ACSO, alliin) and S- (trans-1-propenyl)-L-cysteine sulfoxide (PeCSO, isoalliin) in considerable amounts in *T. acutiloba.* These compounds have been well known to occur in most *Allium* species. Also, the presence of lectin-like proteins have been reported more than once

(Gaidamashvili and van Staden 2002a, 2002b, 2006).

Bioactivity of *Tulbaghia* species extracts

The compounds 2,4,5,7-tetrathiaoctane-2,2-dioxide and 2,4,5,7-tetrathiaoctane from the leaves of *T. violacea*, reported by Burton and Kaye (1992), were found to have antibacterial activity (Burton 1990). Crude aqueous extracts from *T. violacea* have been shown to exhibit apoptosis inducing ability, and so the extacts contain potentially anticancer agents (Lyantagaye and Rees, 2003). Two years later, Lyantagaye et al. (2005) remarked on the promising anticancer activities of *T. violacea* - derived compounds containing a methyl-α-D-glucopyranoside (MDG) moiety in their structure (Figure 6). The MDG structure has been postulated to interfere with the bio-activities of *hexokinase*, as well to induce reactive oxygen species, which cause cellular damage and hence apoptotic cell death (Cohen et al. 2002, Pastorino et al. 2002, Lyantagaye 2005). This was the first time *T. violacea* – derived MDG was reported to kill cancer cells by inducing apoptosis in the cells. Current research efforts focus on understanding the exact mode of action of MDG and other related plants from the the plant extracts.

An *in vitro* study by Kowalski *et al*. (2005) showed that the flavonoid kaempferol inhibits monocyte chemoattractant protein (MCP-1). MCP-1 plays a role in the initial steps of atherosclerotic plaque formation. The kaempferol and quercetin seems to act synergistically in reducing cell proliferation of cancer cells, meaning that the combined treatments with quercetin and kaempferol are more effective than the additive effects of each flavonoid (Ackland et al. 2005). An 8-year study found that three flavonols (kaempferol, quercetin, and myricetin) reduced the risk of pancreatic cancer by 23 percent (Nöthlings *et al*. 2008). Many glycosides of kaempferol, such as kaemferitrin and astragalin, have been isolated as natural products from plants. Kaempferol consumption in tea and broccoli has been associated with reduced risk of heart disease (Park *et al*. 2006).

More studies have also shown that extracts from *Tulbaghia* species control plant fungal pathogens by inhibiting their growth (Lindsey and van Staden 2004, Vries *et al*. 2005, Nteso and Pretorius 2006). Gaidamashvili and van Staden (2002a, 2002b, 2006) reported the isolation of lectin-like proteins and their prostaglandin inhibitory activity and *Staphylococcus aureus* and *Bacillus subtilis* growth inhibition. There have also been roports on the potential anti-infective remedy for fungal infections (Motsei 2003, Bull *et al*. 2005, Thamburan *et al*. 2006). ACE inhibitor activity and lowering of blood pressure and down regulating of AT1a gene expression in a hypertensive rat model have been reported (Mackraj and Ramesar 2007, Mackraj et al. 2007). More recently, Ebrahim and Pool (2010) reported that *T. violacea* has androgenic properties; treatment of cells with *T. violacea* increased LH-induced testosterone production.

CONCLUSION

Plants are known to be important sources of therapeutic agents. This implies that compounds or mixture of compounds that have activity in mammalian cells are potential therapeutic agents and can be used as leads towards the development of new drugs. Only reports for biological activity of 4 of the 29 species of *Tulbaghia* exist, and significant phytochemical investigations have been conducted on only 1 of them. Sulfur-type compounds seem to be typical for the genus as they were found from several species. Among these compounds, kaempferol and other sulfur compounds are most remarkable and have received much scientific attention because of their anti-cancer potential. Clearly, members of the genus *Tulbaghia* possess significant pharmacological potential and promising activities of extracts in the context of ethnomedicinal knowledge, and therefore promote a high degree of interest in further studies. Knowledge obtained from such studies could also enhance the efficacy of already existing ethnomedicinal uses and, consequently, support the cultural value of these species. The *Tulbaghia* species described in this review do not appear limited in their availability and might serve as an important source of medicine among people living in the Southern Africa region. There is a necessity to attempt to investigate more possible specific targets involved in their mode of actions by the individual compounds isolated from *Tulbaghia* plant species using molecular biology techniques. It is therefore evident that the pharmaceutical potential of the members of the genus *Tulbaghia* has been underestimated and deserves closer attention.

ACKNOWLEDGEMENTS
It would not have been possible to produce the review without the financial support from the National Research Foundation (NRF) of South Africa, Triangle Pharmaceuticals, USA, South African Department of Trade and Industry, Cancer Association of South Africa, Carnegie-IAS - (RISE) USA and ACP-EU funding for POL-SABINA project, and the Sida/Sarec through core support component at the University of Dar es salaam.

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