Folk Medicine, Pharmacological and Biological Activities

Allium species have many bioactive constituents such as sulphur compounds, steroidal saponins, flavonoids, polysaccharides. They have the physiological functions of diminishing inflammation, preventing blood platelet conglomeration, antioxidation, reducing cholester, anticancer, antidiabetic effects and so on. Ingestion of onions may prevent certain cardiovascular diseases (e.g. Corea *et al*., 2005; Corzo-Martinez *et al*., 2007; Jacob *et al*., 2008; Bora and Sharma, 2009; El-Aasr *et al*., 2010). The research advances of bioactive constituents and pharmacological functions of *Allium* species were reviewed by several authors (e.g. Hanley and Fenwick, 1985; Rose *et al*., 2005; Benkeblia and Lanzotti, 2007; Liu *et al*., 2007; Jacob and Anwar, 2009).

Allium chinense has been used routinely in some traditional Chinese preparations for the treatment of stenocardia, arteriosclerosis, so-called stagnant blood (Peng *et al*., 1996a). *Allium ascalonicum* is used in Nigerian folk medicine for the treatment of migrating pain (Owoyele *et al*., 2004). *Allium giganetum* have been reported to prevent probably, a number of diseases such as carcinogenesis, atherosclerosis, pulmonary damages, liver necrosis, etc. (Štajner *et al*., 2006a,b). *Allium macrostemon* is a Chinese traditional medicine, used for the treatment of myocardial infarction (Peng *et al*., 1992b). The Cherokee Indians consumed leaves of ramp (*Allium tricocum* Ait.), also known as wild leek for colds and croup or as a spring tonic, while the warm juice of the leaves and bulbs was used for earaches; the Iroquois Indians gave a decoction of ramp to children for worms (Calvey *et al*., 1998). The seeds of the Chinese chive (*Allium tuberosum*) have been reputedly used as a traditional Chinese medicine for treating both impotence and nocturnal emissions (Hu *et al*., 2009). Štajner *et al*. (2008b) reported that *Allium ursinum* is particularly effective in reducing high blood pressure and blood cholesterol levels and therefore popular in traditional and official medicine.

The antibacterial properties of several *Allium* species and/or their sulphur compounds have been extensively investigated. The antibacterial principle of *Allium sativum,* alliicin, was first isolated, characterised, and its antibacterial action assessed by Cavallito and Bailey (1944) and Cavallito *et al.* (1945). Later, Feldberg *et al.* (1988) reported an *in vitro* mechanism of inhibition of bacterial cell growth by alliicin. They noted that alliicin delayed and inhibited partially DNA and protein synthesis, while inhibition of RNA synthesis was immediate and total, suggesting that this is the primary target of alliicin action (Benkeblia and Lanzotti, 2007). From a fundamental point of view, the antibacterial activity of *Allium* thiosulphinate-extracts have been extensively investigated, however, these investigations focused mainly on onion and garlic (cf 6.1.6 and 6.1.20). However, onion is not as potent as garlic since the sulphur compounds in onion are only about one-quarter the level found in garlic (Benkeblia and Lanzotti, 2007). An oil obtained from *Allium schoenoprasum* inhibited *Mycobacterium tuberculosis* (Gupta and Viswanathan, 1955). *Allium* extract has been considered a natural preservative or food additive and can be used for controlling pathogens (Whitmore and Naidu, 2000). Aqueous extract of *Allium tuberosum* showed antibacterial activity against *Escherichi coli* and *Micrococcus luteus*. The antibacterial substance may be enzymatically developed alliicin from alliin (Akema *et al*., 1987).

Comparatively to the extensive literature on the effect of *Allium* extracts on bacteria, little has been done on their effect on fungi. The first investigation was reported by Raghunandana *et al*. (1946). Later, Yamada and Azuma (1977) reported that alliicin was effective *in vitro* against *Candida*, *Cryptococcus*, *Trichophyton*, *Epidermophyton*, and *Microsporum*, however, decreased activity was demonstrated against *Aspergillus*. Neverthless, these authors noted that the minimum inhibitory concentration of alliicin was considerably affected by incubation time, inoculums size, type of medium, and medium pH. These authors also reported that alliicin induced morphological abnormalities in hyphae of *Trichophyton mentagrophytes* Morita, and the percent germination of spores of Morita strain greatly decreased (Benkeblia and Lanzotti, 2007). Nagawa *et al*. (1996) reported that ajoene also inhibited yeast growth at concentrations below 20 mg/ml, and that *Saccharomyces cerevisiae* was killed by 30 mg/ml of ajoene after 24 hours of cultivation. On the other hand, the antifungal activity and the minimal fungicidal concentration (MFC) of different *Allium* plants, namely garlic (*Allium sativum*), bakeri garlic (*Allium bakeri* L.), Chinese leek (*Allium odorum* L.), Chinese chive (*Allium tuberosum* Rottler), scallion (*Allium fistulosum* Auct.), onion bulb (*Allium cepa*) and shallot bulb (*Allium ascalonicum* L.), against *Aspergillus niger*, *Aspergillus flavus* and *Aspergillus fumigates* were investigated and the results have shown that all these *Allium* species possessed antifungal activity, with garlic showing the lowest MFC (Yin and Tsao, 1999; Benkeblia and Lanzotti, 2007). Fistulosin (octadecyl 3-hydroxyindole) isolated from the roots of *Allium fistulosum* showed high activity against *Fusarium oxysporum* primarily inhibiting protein synthesis (Phay *et al*., 1999). From the inner shoots of *Allium tuberosum*, a single-chained protein with a molecular weight of 36 kDa and and N-terminal sequence manifesting resemblance to chitinase, but lacking in cysteine residues characteristic of a cysteine-rich domain present in chitinases of other *Allium* species was purified. It exhibited antifungal activity against *Rhizoctonia solani*, *Fusarium oxysporum*, *Coprinus comatus*, *Mycosphaerella arachidicola* and *Botrytis cinerea* (Lam *et al*., 2000).

The antioxidant activities of *Allium* species have been of particular interest because of the relationship between oxidative stress and pathologies such as atherosclerosis, cancer, and aging, in which free radicals and reactive oxygen species are implicated as having a role (Cavalieri and Rogan, 1992; Haliwell *et al*., 1992; Salvemini and Botting, 1993). Later, investigations on antioxidant properties of *Allium* components have used crude extracts or other derivatives. However, due to the complexity of such preparations, some investigators have reached unequivocal conclusions (Kourounakis and Rekka, 1991; Rekka and Kouraunakis, 1994; Prasad *et al*., 1995) or have insinuated that the thiosulphinates or related organosulphur components are primarily responsible for the observed antioxidant effects (Augusti, 1990; Kim *et al*., 1997; Siegers *et al*., 1999a), although other endogenous components, such as phenolics, may have antioxidant properties (Yin and Cheng, 1998;

Benkeblia, 2005). Nevertheless, pure thiosulphinates and related organosulphur compounds have exhibited real antioxidant properties under specific conditions (Imai *et al*., 1994; Rabinkov *et al*., 1998). It was claimed that *S*-2-propenyl-L-cysteine sulphoxide is an effective antioxidant (Hirata and Matsushita, 1996), however, the case in point was the finding that pure alliin (*S*-allyl-L-cysteine sulphoxide) has no antioxidant activity in a linoleic acid emulsion and has only weak reducing power (Yin and Ching, 1998; Benkeblia and Lanzotti, 2007). Xiao and Parkin (2002) investigated the antioxidant properties of some pure thiosulphinates. Among them, some were not capable of scavenging hydrogen peroxide or superoxide anion. Relative to standard antioxidants (ascorbic acid, *n*-propyl gallate, butylated hydroxytoluene, Trolox, and reduced glutathione), these thiosulphinates were 1- to 3-fold less efficient at reducing DPPH (2,2-diphenyl-1-picrylhydrazyl) radical, 0.5-2-fold less efficient at quenching singlet oxygen, and about equally effective at scavenging hydroxyl radical, while alliicin was the most effective thiosulphinate in these assays. On the other hand, *in vitro* antioxidant activities of five *Allium* species extracts, namely of *Allium nevsehirense*, *Allium sivasicum, Allium dictyoprosum, Allium scrodoprosum* subsp. *rotundum* and *Allium atroviolaceum* were investigated by Tepe *et al*. (2005). The extracts were screened for their potential antioxidant activities. They reported that non-polar sub-fractions of the extracts did not show any antioxidant potential, while the polar sub-fractions exhibited marked activity. Among the polar ones, the most active one was *Allium atroviolaceum* (Benkeblia and Lanzotti, 2007).

Several other studies have been carried out on the antioxidant properties of *Allium* species, and a correlation between the phenolic contents and the antioxidant activity was reported. According to Nuutila *et al*. (2003), the linear correlation between antioxidant activity and polyphenol content underline the fact that the phenolic compounds of *Allium* plants contribute to their antioxidative effects. Nencini *et al*. (2007) examined the antioxidant activity of different parts of three wild *Allium* species *viz. Allium neapolitanum* Cyr, *Allium roseum* L. and *Allium subhirsutum* L., compared to garlic (*Allium sativum*). The flowers of species growing wild showed the higher antioxidant power. Interesting results were shown even by leaves, while the antioxidant capacity of the bulbs was lower. A correlation between the phenolic contents and the antioxidant activity was found. The antioxidant properties of several *Allium* species have been attributed to their content of antioxidant enzymes. Antioxidant activity of leaves of *Allium giganteum* L. is the highest, compared to bulb and stalk, due to high antioxidant enzyme activities and high quantities of all non-enzymic antioxidants (flavonoids, chlorophylls a and b, carotenoids and vitamin C) (Štajner *et al*., 2006a). The studies on the antioxidant activity of different *Allium* species e.g. *Allium fistulosum* L., *Allium nutans* L. and *Allium sphaerocephalum* L. and others showed that they possess antioxidant activities in all organs, but especially in the leaves which could be used mainly in salads (Štajner *et al*., 1998a,b, 1999, 2003, 2006b). Several *Allium* species both cultivated (*Allium nutans* L., *Allium fistulosum* L., *Allium vineale* L., *Allium pskemense* B. Fedtsch, *Allium schoenoprasum* L., *Allium cepa* L. and *Allium sativum* L.) and wild (*Allium flavum* L., *Allium sphaerocephalum* L., *Allium atroviolaceum* Boiss., *Allium vineale* L., *Allium ursinum* L., *Allium scorodoprasum* L., *Allium roseum* L. and *Allium subhirsutum* L.) were investigated by Štajner *et al*. (2008a). The obtained results showed that the investigated *Allium* species possess effective antioxidant properties indicating their possible nutritional and medicinal values. The bulbs could be used in the human diet as a source of natural antioxidants and also in the pharmaceutical and cosmetic industries. The high antioxidant activity is due to high antioxidant enzyme activities (SOD, CAT, GPx and GSH-Px) and non-enzymatic antioxidants (GSH and flavonoids) (Štajner *et al*., 2008a). Other studies have been reported about the antioxidant activities of *Allium* species, due to the activities of antioxidant enzymes e.g. *Allium flavum* (Štajner *et al*, 1998c), *Allium nutans* (Štajner *et al*., 1999), *Allium schoenoprasum* (Štajner *et al*., 2004), *Allium scorodoprasum* (Jang *et al*., 2008) and *Allium ursinum* (Štajner *et al*., 2008b). The protective effects of the steroidal glycosides (ACS) from *Allium chinense* against H_2O_2-induced oxidative stress in rat cardiac H9C2 cell, have been reported. Preliminary analysis of the structure- activity relationship indicated that ACS with a spirostane–type skeleton exhibited stronger protection than that with a furostane-type skeleton, and glycosylation of the steroids could substantially lower the protective activities (Ren *et al*., 2010).

Many of the steroidal glycosides, isolated from *Allium* species have been found to possess antitumour acivity. A cholestane glycoside isolated from *Allium jesdianum* was found to exhibit cytostatic and cytotoxic activities against malignant tumour cells (Mimaki *et al*., 1999a). Some of the steroidal saponins isolated from *Allium leucanthum* were found to be active with relatively similar IC_{50} values ranging from 3.7 to 5.8 μM for a lung cancer cell line (A 549) and 5.6 to 8.2 μM for a colon cancer cell line (DLD-1) (Mskhiladze *et al*., 2008). Chen *et al*. (2007) investigated the cytotoxic activities of the saponins from the bulbs of *Allium macrostemon* Bunge, on several cancer cell lines including solid tumour (HepG2, MCF-7, NCl-H460 and SF-268) and drug resistant tumour (R-HepG2). Five compounds showed diverse cytotoxicity to these cancer cell lines. Tuberoside M (isolated from the seeds of *Allium tuberosum*) showed a significant inhibitory effect on the growth of the human promyelocytic leukemia cell line (HL-60) with IC_{50} value of 6.8 μg/mL (Sang *et al*, 2002b). Also, the protein (a robust cysteine-deficient chitinase-like antifungal protein) from inner shoots of the edible chive *Allium tuberosum* exerted some cytotoxic effect on breast cancer cells and was inhibitory toward HIV-1 reverse transcriptase (Lam *et al*., 2000). The reduced of prostate cancer associated with intake of *Allium* vegetables (garlic, scallions, onions, chives and leeks) was reported. It was more pronounced for men with localized than with advanced prostrate cancer (Hsing *et al*., 2002).

N-*p*-Coumaroyltyramine (i) and *N*-*trans*-feruloyltyramine (ii) isolated from the Chinese drug "Xiebai" (*Allium bakeri*) had a pronounced inhibitory effect on platelet aggregation. Compound (ii) showed a strong inhibitory activity against the primary and secondary wave aggregation induced by 2 μM ADP (Adenosine diphosphate), whereas (i) was effective only against the primary aggregation (Okuyama *et al*., 1986). Macrostemanoside A (a steroidal saponin, isolated from *Allium macrostemon* showed remarkable inhibitory effect on rabbit platelet aggregation induced by ADP *in vitro* (C_{50} = 0.065 mmol) (Peng *et al*., 1992b). Both adenosine and 2,3,4,9-tetrahydro-1*H*-pyrido[3,4-b]indolo-3-carboxylic acid, isolated from the same species showed strong inhibitory activity on human platelet aggregation *in vitro* (Peng *et al*., 1995b). Thiosulphinates have been implicated as a principle source of antiplatelet property of raw onion and garlic juice. The study of Briggs *et al*. (2000) revealed that ethyl ethane thiosulphinate, propyl propane thiosulphinate and alliicine were significantly more potent platelet inhibitors than aspirin at nearly equivalent concentrations. Bulbus allii macrostomi (bulbs of *Allium macrostemon* Bunge) is usually used in clinical prevention and control in coronary artery disease in many combination formulas (Cheng *et al*., 2000; He *et al*., 2002). The chemical compositions of Bulbus macrostomi are mainly methyl allyl trisulphide, polysaccharide and saponins, and they work together to decrease the serum low density lipoprotein and lipid peroxides in rats, and also showed the efficacy of anticoagulation and calcium antagonistic (Li *et al*., 1994; Zhang and Gao, 2003; Liu *et al*., 2005). Liu *et al*. (2008) studied the effects of *Allium macrostemon* on clinical outcomes and oxidized low-density lipoprotein and plasminogen in unstable angina (UA) and non-ST-segment elevation myocardial infarcture (NSTEMI) patients. The results showed therapeutic effects with the use of Bulbus macrostomi for UA/NSTEMI, as well as a low rate of diverse effects, which confirmed the advantage of traditional Chinese medicine and led to the view that it could be a complementary therapy for patients with resistance or low sensitivity to Western drugs. The antithrombic and antisclerotic effects of *Allium ursinum* have been also reported (Richter, 1999). The butanol extract of *Allium bakeri* has an antiplatelet effect (Okuyama *et al*., 1989). A glucofructan, isolated from *Allium survorovii* exhibits a pronounced lipolipidemic activity in animals with hyperlipidemia and artherosclerosis (Khodzhaeva *et al*., 1998). Owoyela *et al*. (2004) studied the haematological effect of the ethanolic extract of *Allium ascalonicum* in male albino rats. The results showed that the extract decreased most of the parameters relating to red cells and increased most of those relating to white cells. It also decreased the total cholesterol, high density lipoprotein cholesterol (HDL) and low density lipoprotein cholesterol (LDL) with no significant effect on the triglyceride levels.

The cholinesterase and choline acetyltransferase activities of some *Allium* species have been reported e.g. *Allium altaicum* (Hadacova *et al*., 1981), *Allium tuberosum* (Kim *et al*., 2007) and others (e.g. Hadacova *et al*., 1983). Flavonol glycosides of *Allium tuberosum* possess antiallergy and fibrinolysis-inducing activities (Daiichi, 1983). The methanolic extract of *Allium tuberosum* exhibited significant lengthening of the barbiturate hypnosis (Choi *et al*., 1998).

Allelopathic active compounds from *Allium fistulosum* and their effect on growth of other crops have been investigated (Choi, 1993; Choi and Son, 1993, Choi *et al*., 1998). When summer chrysanthemums were transplanted near Welsh onion (*Allium fistulosum*), rooting and early growth of chrysanthemums were inhibited and plants wilted to death. Vanillic acid and β-sitosterol were identified as growth inhibitors of Compositae crops (chrysanthemums and lettuce). The activity of vanillic acid was reported higher than that of β-sitosterol (Choi *et al*., 1996). The study of the allelopathic activity of different extracts from underground parts of *Allium nutans* showed that the sum of steroidal glycosides possess the highest activity (Akhov *et al*., 2000).