a- Antibacterial Properties

It was observed that a freshly prepared infusion of ground garlic cloves possessed high antibacterial activity. A literature investigation showed that *Allium sativum* has been endowed with therapeutic varieties both in legend and in the scientific literature. Several investigators have observed antibacterial activity of garlic extracts and have attributed the activity to diallyl sulphide, unsatable sulphur in alky polysulphides, a bacteriophage, acrolein or some similar unsaturated aldehyde. The antibacterial principle of *Allium sativum*, alliicin, was first isolated, characterized, and its physical properties and antibacterial action assessed by Cavallito and Bailey (1944) and Cavallito *et al*. (1945). Both the extract and alliicin showed significant activity against all 20 tested bacteria (except *Pseudomonas*) while tested concentrations of ampicillin (10 µg) and kanamycin (25 µg) were found ineffective against a large number of bacteria (Ahsan and Islam, 1996). 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 syntheses, while inhibition of RNA synthesis was immediate and total, suggesting that this is the primary target of alliicin action (Benkeblia and Lanzotti, 2007). The antibacterial and antifungal activities against a variety of Gram-positive bacterial have been extensively investigated (Whitmore and Naidu, 2000). Han *et al*. (1995) reported that the antibiotic activity of 1 mg of alliicin has been equated to that of 15 IU of penicillin. Later investigations have also demonstrated an inhibitory effect by aqueous extracts on numerous bacterial species such as *Helicobacter pylori, Bacillus subtilis, Escherichia coli, Flavobacterium* sp., *Listeria monocytogenes, Pseudomonas aeruginosa, Salmonella typhimurium, Staphylococcus aureus* and *Vibrio parahaemolyticus* (Sivam *et al*., 1997, Hsieh *et al*., 2001; Ward *et al*, 2002; Benkeblia, 2004). However, these authors reported different minimum level of inhibition depending on the extraction method, the final content of thiosulphinates in the extracts and also the applied method for the assessment of the inhibitory effect (Benkeblia and Lanzotti, 2007).

Alliicin and allyl methyl plus methyl allyl thiosulphinates extracted from garlic have shown inhibition of the *in vitro* growth of *Helicobacter pylori* (Hp). The capacity and effectiveness of isolated natural thiosulphinates have been tested, and this has enabled the identification of the main compounds responsible for the bacteriostatic activity. Additionally, microbiological analyses have also shown that these compounds have a synergic effect on the inhibition of the *in vitro* growth of Hp (Cañizares *et al*., 2004). Similarly, this inhibition effect was also noted on *Staphylococcus aureus* and results showed a complete inhibition of all strains tested at a concentration of 6.5 mg/ml (Gnan and Demello, 1999). Furthermore, three thiosulphinates were isolated from oil-macerated garlic extract by Yoshida *et al*. (1998), and their antimicrobial activities against Gram-positive and Gram-negative bacteria were compared with alliicin. The results have shown that antimicrobial activity of two isolated thiosulphinates were comparable but lower than that of alliicin. They suggested that the antimicrobial activity were affected by alk-(en)-yl groups and the order for antimicrobial activity was: allyl ≥ methyl > propenyl. Among these numerous and abundant naturally

occurring compounds, *Allium* extract has been considered a natural preservative or food additive, and can be used as additional methods for controlling pathogens (Whitmore and Naidu, 2000; Bekeblia and Lanzotti, 2007). There are several other studies on the antibacterial activity of garlic (Lejnieks and Schwieger, 1956; Abdullaeva, 1959; Sharma *et al*, 1977; Patel *et al.*, 1986; Didry *et al*., 1987; Plummer, 1992; Koch, 1993; Ankri and Mirelman, 1999; O'Gara *et al*., 2000; Ross *et al.*, 2001; Harris *et al*, 2001; Sivam, 2001; Chaithradhyuthi *et al.*, 2009). Garlic as well as ajoene and allitridium have *in vitro* activity against 20 medical isolates of *Scedosporium prolificans* (Davis *et al.*, 2003).

b- Antifungal Properties

The antibiotic content of garlic varies according to the part of the plant [most in brood bulbs, less in true bulbs (garlic cloves), and least in stems and leaves], strain, origin, kind of cultivation, and vegetative maturity. Storage reduces this content but this varies considerably with storage conditions and type of garlic. Usually strong activity was noted against pathogenic yeasts, especially *Candida* species, even though garlic is rarely used in candidiases and other skin diseases, where less effective agents are commonly used. The antibiotic activity was 10-100 times greater in dermatophytes and yeasts than on bacteria, garlic (in 1:5 and 1:10 extracts stand at room temperature for 24 hours) was the most effective agent tried against *Candida albicans*; it was also very active against *Candida tropicalis* and *Candida pseudoutropicalis*, but somewhat less active against *Candida krusei*. Parakkel tests with nystatin, gentian violet, methylene blue, and 5 other antifungal agents showed garlic superior to all others, including alliicin. Best results were obtained in combination with oxidizing agents (H_2O_2), which aid the action of garlic due to its high content of catalase. The garlic bulb also contains soluble carbohydrates which aid in the growth of the bacteria, and decrease the antibiotic avtivity. These became more pronounced after storage for 6 months or more. The activity of the alliicin in garlic was decreased by reduction. It is also inactivated by cysteine and thiosulfate (Kabelik, 1970).

The volatiles from *Allium sativum* showed an excellent inhibition of spore germination of the fungi tested by Singh and Deshmurkh (1984). The antifungal activity of the essential oil of garlic (as mentioned above, cf. *Allium cepa*) gainst several fungi (e.g. *Aspergillus niger*, *Candida* spp., *Malassezia furfur* and *Penicillium cyclopium*) has been reported (Benkeblia, 2004; Shams-Ghahfarokhi *et al*., 2006). In contrast, López-Días *et al*. (2002) stated that garlic extract tested had no or a very little effect on the growth of *Penicillium nalgiovense* isolated from the surface of Spanich fermented meat sausage. However, Pyun and Shin (2006) stated that among the tested volatile oils from *Allium* plants, *Allium sativum* exhibited the strongest inhibition of growth of *Trichophyton rubrum* and *Trichophyton soudanense*. Possible uses of garlic extracts or essential oils in food industry as alternatives for protection of foods from fungal contamination are reported (Sovova and Sova, 2003). Lemar *et al*. (2005) found that allyl alcohol (a metabolic product that accumulates after trituration of garlic cloves) and garlic extract produce oxidative stress in *Candida albicans*. Allyl alcohol is produced from garlic in two ways: firstly by a self-condensation reaction of alliicin and secondly by the reaction between alliin, the precursor of alliicin and water (Lemar *et al*., 2005). It is released after ingestion of garlic (Egen-Schwind *et al*., 1992) and is present in exhaled air after ingestion of all garlic products; the highest concentration being after ingestion of freeze-dried garlic tablets (Laasko *et al*., 1989). Eruboside B, obtained by enzymic hydrolysis of protoeruboside B (a furostanol glycoside isolated from the bulbs of garlic) inhibited the growth of *Candida albicans in vitro* (Matsuura *et al*., 1988). Alliicin, in its pure form was found to exhibit antibacterial, antifungal and antiviral activities (Ankri and Mirelman, 1999).

c- Antioxidant Properties

The antioxidant and free-scavenging properties of garlic are well documented (Prasad *et al*., 1995; Helen *et al.*, 1999; Balasenthil *et al*., 2000; Borek, 2001; Wu *et al.*, 2001; Yoshiuchi *et al*., 2001; Banerjee *et al*., 2002, 2003; Dillon *et al*., 2003; Benkeblia, 2005; Aqil *et al*., 2006; Pedreza-Chaverri *et al*., 2007b; Štajner *et al*., 2008a; Chaithradhyuthi *et al*., 2009; Koseoglu *et al*., 2010), thus justifying their traditional use. Aquirrezábal *et al*. (2000) compared the antioxidant effect of garlic with a mixture of nitrate, nitrite and ascorbic acid in dry sausage, and they noted that garlic was as effective as the mixture of additives in inhibiting lipid oxidation. The antioxidant protection of diallyl sulphide (DAS), diallyl disulphide (DADS), *S*-ethyl cysteine, *N*-ethyl cysteine, *N*-acetyl cysteine in ground beef against lipid oxidation was studied by Yin and Cheng (2002). These authors found that the exogenous addition of these garlic-derived organosulphur compounds significantly delayed the oxymyoglobin and lipid oxidations ($P < 0.05$). The antioxidant protection from these organosulphur compounds was dose-dependent ($P < 0.05$), and showed significantly greater antioxidant avtivity than α-tocopherol ($P < 0.05$). The presence of DAS and DADS in ground beef significantly reduced aerobes and inhibited the growth of 5 inoculated pathogenic bacteria, *Salmonella typhimurium*, *Escherichia coli*, *Listeria monocytogenes*, *Staphylococcus aureus*, and *Campylobacter jejuni* ($P < 0.05$). These results suggested that the application of these organosulphur compounds in meat or other food systems could enhance color, lipid and microbial safety (Yin and Cheng, 2002). The antioxidant effects of different forms of garlic were investigated against lipid oxidation in raw chiken sausage during storage, and the antioxidant activity was also compared to BHA (butylated hdroxyanisole) (Sallam *et al*., 2004). The latter authors found that the addition of either garlic or BHA delayed the lipid oxidation, and fresh garlic showed the highest antioxidant activity followed by garlic powder, BHA and garlic oil. Pedraza-Chaverri *et al*. (2007b) analysed the potential hypochlorous (HOCl) scavenging ability of several garlic preparations with the purpose of determining whether heating is able to modify this scavenging ability. Garlic is normally consumed in cooked foods and it has been demonstrated that heating may affect several properties of garlic including the antioxidant properties. The heating treatment used by Pedraza-Chaverri *et al*. (2000) was applied by other authors (Ali, 1995; Prasad *ert al*., 1996; Yin and Cheng, 1998; Song and Milner, 1999; Pedraza-Chaverri *et al*., 2004, 2006, 2007a). Boiling garlic cloves for 15 minutes impaired significantly its ability to inhibit cyclooxygenase activity (Ali, 1995). In addition, heating garlic cloves for 1 minute in a microwave reduced its anticancer properties (Song and Milner, 1999) and heating garlic extract for 10 minutes at 100^{o}C reduced the ability to inhibit platelet aggregation (Ali *et al*., 1999). In contrast, the $OH^{\bullet}$ scavenging properties of garlic were essentially observed when garlic extracts were heated (Prasad *et al*., 1996; Pedraza-Chaverri *et al*., 2006). Shobana and Naidu (2000) found that the capacity of garlic to inhibit lipid peroxidation was not affected by boiling (30 minutes at 100^{o}C). In contrast, Yin and Cheng (1998) found that heating treatment (100^{o}C for 15 minutes in an oven) chopped garlic reduced the ability to inhibit lipid peroxidation. The data obtained by Pedraza-Chaverri *et al.* (2007b) showed that garlic is an effective HOCl scavenger which may contribute to the recognized antioxidant and medicinal properties of garlic. The presence of a 10% (vol./vol.) di-Et ether extract of aged garlic AGE significantly reduced $Cu^{2+}$and 15-lipoxy-genase-mediated lipid peroxidation of isolated LDL by 81 and 37%, respectively. In addition, it was found that AGE also had the capacity to chelate Cu ions. In contrast, the di-Et ether extract of AGE displayed no Cu binding capacity, but demonstrated distinct antioxidant properties. These results support the view that AGE inhibited the *in vitro* oxidation of isolated LDL by scavenging superoxide and inhibiting the formation of lipid peroxides. AGE was also shown to reduce LDL oxidation by the chelation of Cu^{2+}. Thus, AGE may have a

role to play in preventing the development and progression of atherosclerotic disease (Dillon *et al*., 2003). The study of Koscielny *et al.* (1999) substantiated that not only a preventive but possibly also a curative role in arteriosclerosis therapy (plaque regression) may be ascribed to garlic remedies. In addition, this scavenging ability is not eliminated by the heating before or after cutting suggesting that this capacity is independent of allinase activity (Pedraza-Chaverri *et al*., 2007b). A correlation between the phenolic constituents and the antioxidant activity was found (Tables 7-9) The leaves of *Allium sativum* seem to have higher antioxidant capability (Nencini *et al*., 2007).

In *in vitro* assay systems, tetrahydro-β-carboline derivatives in aged garlic showed strong hydrogen peroxide scavenging activities. Among the four compounds identified in aged garlic extract (AGE), (1*S*,3*S*)-1-methyl-1,2,3,4-tetrahydro-β-carboline-1,3-dicarboxylic acid was found to be stronger than the common antioxidant, ascorbic acid. These alkaloids also inhibited AAPH-induced lipid peroxidation and LPS-induced nitrite production from murine macrophages. These data demonstrate that not only organosulphur compounds but also these four alkaloids may contribute to the antioxidant activities of AGE, and suggesting that processing procedure such as natural aging process could play an important role in influencing medicinal functions of foodstuffs (Ide *et al*., 2003).

d- Anticarcenogenic Properties

Several epidemiological observations and a number of laboratory studies have indicated anticarcinogenic potential of garlic. The anticarcinogenic properties of garlic have been attributed to a wide variety of chemical compounds, present in garlic, but most studies have focused on specific thioallyl constituents. Garlic components have been found to block covalent binding of carcinogens to DNA, enhance degradation of carcinogens, have antioxidative and free radical scavenging properties and to regulate cell proliferation, apoptosis and immune responses. There are a number of mechanisms at work which jointly are responsible for eliciting the noted anticarcinogenic effects (Das, 2002). Several experimental studies on animals and cultured cells have demonstrated the anticarcinogenic effect of garlic and its chemical compounds. Oral feeding of garlic extracts has been shown to reduce the incidence and growth of transplantable and spontaneous tumours in experimental animals and the active components were found to influence a number of physiological and immunological functions which account for their anticarcenogenic and antitumour effects (Das, 2002).

When garlic was topically applied during the initiation phase of benzo(a)pyrene (BP) induced skin carcinogenesis in mice, a decline was noted in the incidence and multiplicity of tumours (Sadhana *et al.*, 1988). The results obtained by Singh and Shukla (1998) suggest that diallyl sulphide (a major flavor of garlic) has a protective effect in polycyclic aromatic hydrocarbon-induced mouse skin carcinogenesis. Oral administration of fresh water extract of garlic was shown to result in reduction of chemically induced cervical carcinomas in mice (Hussain, 1990). Garlic treatment inhibited development of murine transitional cell carcinomas significantly (Riggs *et al*., 1997) and an aqueous extract effectively suppressed dimethylbenz(a)anthracene (DMBA) induced oral carcinogensis in hamsters by modulation of lipid peroxidation and glutathione (GSH), glutathione-*S*-transferase (GST) and glutathione peroxidase (GPx) levels (Balasenthil *et al*., 1999). Selenium enriched garlic was found to suppress development of premalignant lesions and formation of adenocarcinomas in the mammary glands of carcinogens treated rats (Ip *et al*, 2000). It has been also observed that fresh garlic juice administered orally can prevent development of azoxymethane (AOM) induced aberrant crypt foci and adenocarcinoma in rat colon (Sengupta *et al*., 2002). Samaranayake *et al.* (2000) reported that garlic inhibited diethyl nitrosamine (DEN) induced

hepatocarcinogenesis in Wistar rats. Garlic juice given orally during exposure to DMBA could reduce clastogenecity in mice and also AOM induced micronuclei formation in the rat (Khanum *et al*., 1998; Das, 2002). It was demonstrated that diallyl sulphide (DAS), diallyl trisulphide (DAT), allyl methyl disulphide (AMD) and allyl methyl trisulphide (AMT) inhibit gastric malignancy induced by BP in mice (Sparnins *et al*., 1986, 1988). Wattenberg *et al.* (1989) reported that DAS, disulphide derivatives (DADS), AMT and *S*-allyl cysteine (SAC) could reduce nitroso compound induced for stomach tumours in mice. Wargovich *et al*. (1988) had noted that these compounds inhibited development of papilloma and squamous cell carcinoma in oesophageal tissue in rat. Fukushima *et al.* (1997) analysed the potential of several organosulphur compounds present in garlic and onion and observed inhibitory effect of DAS on renal and colon carcinogenesis in rat induced by diethyl nitrosamine (DEN). However, they observed that DAS, DAT and AMT enhanced formation of altered hepatocellular foci and commented that some of the organosulphur compounds may have promotional potential at certain sites. In another study, SAC failed to elicit any action during *N*-methyl nitrosourea induced mammary tumourigenesis in rat (Cohen *et al*., 1999), although Amagase and Milner (1993) reported that garlic components could prevent DMBA induced mutagenesis and tumourigenesis in mammary gland. Severl studies have indicated that allyl sulphide derivatives can inhibit growth of transplantable tumours (Sundaram and Milner,1996; Das, 2002), and can also ameliorate cardio and hepatotoxic effects of potent anticancer drug doxorubicin (Mostafa *et al*., 2000). It was suggested that clinical efficacy of doxorubicin could also be improved by using the anticancer drug with DADS which inhibited liver microsomal lipid peroxidation (Dwivedi *et al*., 1998). DADS was found to suppress growth of human colon tumour cell xenografts in athymic nude mice without apparent ill consequences in the host and could reduce toxicity of the antitumour agent 5-fluorouracil (Sundaram and Milner, 1996).

It has been noted that production of heterocyclic aromatic amines (HAA-s) during high temperature cooking of meat and fish could be significantly redcuced by marination with turmeric-garlic juice before cooking (Nerurkar *et al*., 1999). Production of *N*-nitrosomorpholine (NMOR), a known liver carcinogen, was reported to be reduced by water extracts of garlic and deodorized garlic powder (Dion *et al*., 1997). Das (2002) reported that investigations have revealed that garlic and its chemical compounds were able to influence cell proliferation and programmed cell death. Antiproliferative effect of naturally occurring garlic derivatives and synthetic *S*-cysteinyl compounds resembling garlic constituent was noted on human prostrate carcinoma cells-LNCaP and the effect was suggested to be by inhibition of polyamine synthesizing enzyme ornithine decarboxylase. Ajoene, a major compound of garlic was found to induce apoptosis in human leukaemic cells, but interestingly not in normal peripheral mononuclear cells from healthy subjects. The effect was dependant (Dirsch *et al*., 1998). Also, Qi and Wang (2003) found that ajoene, induced apoptosis in leukemic cells in addition to other blood cells of leukemic patients. A stable organosulphur compound of aged garlic extract, *S*-allyl mercapto cysteine (SAMC) produced DNA fragmentation compatible with apoptosis in two erythroleukaemia cell lines HEL and OCIM-1 (Sigounas *et al*., 1997). Exposure of cultured human nonplastic and neoplastic lung cells (A549 and MRC-S) for 24 hours to diallyl trisulphide (DATS) caused significant induction of apoptosis as indicated by increased DNA fragmentation (Sakamoto *et al*., 1997). Garlic oil has been shown to induce differentiation and apoptosis at BGC-823, a human gastric cancer line and p21 and p53 genes played an important role in the process (Li *et al*., 1998). Das (2002) reported that administration of fresh garlic juice during exposure to carcinogen AOM can inhibit proliferation as well induce apoptosis at the target site-colon. It was further noted that cycloxygenase-2 (COX2) expression in rat colon that was enhanced

following exposure to AOM, could be reduced by garlic juice administered orally (Das, 2002). Durak *et al*. (2003) found that consumption of garlic aqueous extract leads to significant improvement in patients with begining prostrate hyperplasia and prostrate cancer.

There are numerous studies to show an inverse relationship between garlic consumption and cancer risk although some populations based studies failed to associate use of garlic supplements with increased or decreased prevelance of lung, colon and rectal cancers (Das, 2002). Based on their studies in Shangdong Province of Northeastern China, a high incidence region for stomach cancer, You *et al*. (1988, 1989) reported that garlic and other vegetables reduced the risk for stomach cancer. An inhibition of progression of precancer gastric lesion by garlic preparation was also noted with no difference of side effects between placebo and treatment groups (You *et al*., 2001). A multicentric study in Italy also revealed that risk of stomach cancer declined with increased intake of garlic (Buiatti *et al*., 1989). Regular consumption of garlic was shown to be associated with decreased prevelance of adenomatous polyps in colon and rectum (Witte *et al*., 1996), thereby implicating the role of garlic in prevention of colorectal cancer. *Helicobacter pylori* infection is accepted as a high risk factor for gastric cancer and treatment of *Helicobacter pylori* infection is one approach for prevention of GIT cancers. You *et al.* (1998) reported that garlic consumption had a protective effect and an inverse association with *Helicobacter pylori* infection and suggested that this flavouring plant may prevent development and progression of advanced gastric precancer lesions. O'Gara *et al.* (2000) assessed the anti-*Helicobacter pylori* potential of a variety of garlic substances and noted widely differing anti-*Helicobacter pylori* effects and found alliicin to be more potent than DAD. A case control study conducted in England (Key *et al*., 1997) reported that garlic consumption could significantly reduce risk of prostate cancer. A French case control study involving patients with breast cancer revealed that increased consumption of fiber and *Allium* vegetables was associated with reduced risk (Challier *et al*., 1998). A meta analysis of epidemiologic literature on the association between garlic consumption and risk of head and neck, lung, breast, prostrate, stomach and colon cancer suggested a possible protective effect of both raw and cooked garlic consumption against stomach and colorectal cancers only (Fleischauer *et al*., 2000). The protective action of raw garlic and its consumption against carcinogen induced genetic damage may account for the risk reducing influence of garlic on human cancers. Habitual consumption of garlic was also reported to reduce gastric nitrite content and suppress urinary excretion of *N*-nitosoproline (Mei *et al*., 1982; Das, 2002).

The anticarcinogenic activity of garlic and/or its constituents has been reported and reviewed by several other investigators (e.g. Kimura and Yamamoto, 1964; Aboul-Enein, 1986; Nishino *et al*., 1990a,b; Liu *et al.*, 1992; Dorant *et al*., 1996; Geng *et al*., 1997; Hagerman *et al*., 1997a,b; Pinto *et al*., 1997; Chung, 1999; Gao *et al*., 1999; Siegers *et al*., 1999b; Arivazhagan *et al*., 2000; Lam and Riggs, 2000; Balaasenthil *et al*., 2001a,b; Fleischauer *et al*., 2001; Kharazi, 2004). In conclusion, it was reported that the white bulb of garlic, though not a panacea for cancer, is packed with cancer chemopreventive substances and should prove to be not just a flavouring agent, but also a natural cancer preventive formula (Das, 2002).

The study of the effect of garlic consumption on Th1/Th2 (two functionally distinct types of T-helper cells on the basis of their cytokine profiles) showed that garlic may directly and/or indirectly modify splenic T-cell function. It shows that oral garlic consumption may increase rat spleen lymphocyte IL-4 production and decrease gamma interferon (IFN-γ) production (Zamani *et al*., 2009). These findings correlate with the reports suggesting ajoene (a compound isolated from garlic) to exert a strong inhibitory effect on phytohemoagglutinin (PHA) induced proliferation of human lymphocytes (Romano *et al*., 1997).

There have been reports about the pharmacological effects of garlic through regulation and modification of immune system. Some of the garlic effects on the immune system include immunomodulatory (Lau *et al*, 1991; Kyo *et al*., 2001), inhancing cytotoxicity and proliferation of human lymphocytes (Morrioka *et al*., 1993) and suppression of inflammatory cytokines production (Hodge *et al*., 2002).

e- Other Activities

The antiprotozoal activity of *Allium sativum* and/or its constituents (e.g. alliicin) against *Entamoeba histolytica* (Mirelman *et al*., 1987; Reuter, 1994), *Giardia lamblia* (Ankri and Mirelman, 1999) and *Giardia intestinalis* (Harris *et al*., 2000) has been reported.

Borek (2006) reported that garlic extract prevents congnitive decline by protecting neurons from Aβ neurotoxicity and apoptosis. It also possess antiaging effect (Nishiyama *et al*., 1997), improvement of learning and memory impairment (Moriguchi *et al*., 1996; Nishiyama *et al*., 1997) and neutrophic activities (Moriguchi *et al*., 1997a), and these activities increase with the age of the extract. Jackson *et al*. (2002) reported the dose dependant inhibition of caspase-3 activity by aged garlic extract. Gupta *et al*. (2009) investigated the effects of aqueous garlic extract on Aβ fibrillogenesis *in vitro* [Aβ fibril is believed to be the main determinant in the pathogenesis of Alzheimer's disease (AD)]. The obtained results indicated that garlic may be of value for the prevention or delay of AD (Gupta *et al*., 2009). Garlic compounds are known to induce Aβ induced neuronal apoptosis, possibly by inhancing the endogenous antioxidant defenses (Peng *et al*., 2002c). Aged garlic extract may prevent physiological aging and may be beneficial for age-related conginitive disorders in humans (Moriguchi *et al*., 1997b). Chauhan and Sandoval (2007) found that aged garlic extract has a potential for preventing Alzheimer's disease progression.

Oral administration of aqueous extract of garlic to hypercholesterolemic patients for 2 months (dose 0.5 mL/kg/day) significantly reduced the cholesterol levels (Augusti, 1977). Sklan *et al.* (1992) reported that dietary garlic is more effective as a hypocholesterolemic agent than onion and has additional effects in reducing the activity of antioxidative enzymes. Methyl allyl trisulphide (isolated from garlic by Ariga, 1981) posess inhibitory activity on platelet aggregation. Also, the amino acid glycoside (-)-*N*-(1'-deoxy-1'-β-D-fructopyranosyl)-*S*-allyl-L-cysteine sulphoxide (isolated from garlic) revealed a significant inhibition of *in vitro* platelet aggregation induced by ADP and epinephrine (Mütsch-Eckner *et al*., 1993). Adenosine (isolated from the butanol extract of Dasuan, the tuber of *Allium sativum*) inhibited both the primary and secondary aggregation of human blood platelets induced by ADP (Okuyama *et al*., 1989). A polysaccharide, isolated from *Allium sativum*, has been found to possess anticoagulant activity (Kweon *et al*., 1996). The ability of garlic to lower serum cholesterol has been demonstrated in experimental animals and humans. In the past, it has been reported that steam-distilled garlic oil (Abo-Doma *et al*. 1991, Kamanna and Chandrasekhara 1984), the ether fraction of garlic (Bordia et al. 1975, Jain and Konar 1978), alliin (Itokawa *et al*. 1973) and its enzymatic transformation products, alliicin (Augusti and Mathew 1974) and dially disulfide (Adamu *et al*. 1982), might be responsible for the cholesterol-lowering effects of garlic in animal experiments. However, because of the high doses used in animal studies and the lack of data on the absorption/metabolites or pharmacokinetics, especially for alliicin, it is not known to what extent and by what mechanism these organosulphur compounds might contribute to the lowering of serum cholesterol levels (Matsuura, 2001).

Steroid saponins from aged garlic have interesting pharmacological properties, especially cardiovascular protective effects, which include the lowering of serum cholesterol in clinical studies and animal models (Efendy *et al*., 1997, Lau *et al*., 1987; Yeh *et al*., 1995; Steiner *et*

al., 1996). Also, Matsuura (2001) reported that saponins may account for cholesterol-lowering effect of garlic. The saponin fractions from garlic were found to lower plasma total and LDL cholesterol concentrations without changing HDL cholesterol levels in a hypercholesterolemic animal model (Matsuura, 2001). Garlic had a reducing effect on plasma and erythrocytes and their membrane lipids, and prevents the alimentary hyperlipidemia (Kocabatmaz *et al*., 1997). Garlic powder supplementation to the cholesterol-rich diet seemed more advantageous than aspirin because it had beneficial effects on both blood clotting and plasma cholesterol level (Keskin *et al*., 1998).

The efficacy of garlic concentrate in reducing blood pressure (as determined by standerdised pharmacological tests on cats) was early reported by Damaru (1940). Also, the administration of allyl sulphide (a constituent of garlic) reduced the blood pressure. Intraperitoneal injection of garlic concentrate also inhibited the normal adrenaline response (rise of blood pressure 30-40 mm.) in cats; this corroborates the direct blood pressure observations (Damaru, 1940). Oral administration of 12.5 ml of garlic juice (equivalent to 25 g of raw garlic) lowered fasting blood sugar in both normal as well as alloxan diabetic rabbits. The hypoglycemic activities of garlic juice were compared closely to that of tolbutamide. Garlic juice potentiated the plasma insulin like activity (PILA) of all the animals, the extent of PILA increase being same in both groups (Jain and Konar, 1977). *S*-Allyl cysteine sulphoxide (SACS), the precursor of alliicin and garlic oil has a significant antidiabetic effect in alloxan diabetic rats. Administration of SACS at a dose of 200 mg/kg body weight, decreased significantly the concentration of serum lipids, blood glucose and activities of serum enzymes like alkaline phosphatase, acid phosphatase and lactate dehydrogenase and liver glucose-6-phosphatase. It increased significantly liver and intestinal HMG CoA reductase activity and liver hexokinase activity (Sheela and Augusti, 1992).

It has been shown that some L-amino acids (such as L-arginine) in garlic exhibit vasodilator activity in the perfused rat mesentry through releasing and/or synthesizing endothelium-derived nitric oxide, Therefore, it is likely that the vasorelaxant properties of garlic may be related to its amino acid constituents (Baluchnejadmojarad and Roghani, 2003). It is believed that garlic may have a direct relaxant effect on smooth muscles, thus exerting an anti-hypertensive effect (Aqel *et al*., 1991).

Other activities of garlic and/or its constituents have been reported. The extract showed a slightly tonic effect on the heart (De Torrescasana, 1946). Allisatin (prepared from *Allium sativum*) has an anti-inflammatory activity. It reduced the foot volume, necrosis of the feet, and tenderness following formalin injection of albino rats (Prasad *et al*., 1966). Allerged contact dermatitis to garlic has been reported in some patients. Garlic-sensitive patients showed positive tests to diallyl sulphide, allyl propyl disulphide, allyl mercaptan and alliin (Papageorgiou *et al*., 1983). The ethanolic extract of *Allium sativum* has been shown to protect mice against acetaminophen-induced liver injury (Sumioka *et al*. 1998). Aged garlic extract has been found to protect the small intestine from the damage induced by the action of methotrexate on the crypt cells (Horie *et al*.,1999).

Alliicin, the active antimicrobial compound in *Allium sativum* demonstrates significant inhibition of leishmanial cell growth (Mcclure *et al*., 1996). The protective effect of garlic against propylene glycol-induced toxicity in the kidney of young and aged mice has been reported (Kaur *et al*., 1996). The garlic extract and a number of sulfides siginificantly inhibited thyroid iodine-131 uptake in rats (Aratcho *et al*., 1992). Methyl lineolate, a major compound from the chloroform fraction of the methanol extract of garlic possessed a high antimutagenic activity in *Salmonella typhimurium* (Kim *et al*., 1991). The potential of garlic oil as an effective grain protectant against the insects *Tribolium castaneum* (Herbst) and *Sitophilus zeamais* Motsch was also reported (Ho *et al*., 1996).

It has been shown that *Allium sativum* is a potential source of a molluscicide (Singh and Singh, 1993). Characterization of the molluscicidal component of garlic bulb indicates that alliicin is the active moiety which causes snail mortality (Singh and Singh, 1995). A significant increase in the toxicity of garlic in the pre-harvesting (2^{nd}-5^{th} month) period was due to an increase in the levels of alliicin, and post-harvesting (5^{th} month- 11^{th} month) is due to some changes in the chemical composition of garlic (Singh and Singh, 1996a). The mechanism by which the alliicin causes snail death is not known. Wills (1956) and Bogin and Abrams (1976) reported that alliicin inhibited nearly all the sulphhydryl enzymes, lactic dehydrogenase (LDH), alkaline phosphatase (AChE) and transaminase. Singh and Singh (1996b) studied the effect of synthesized pure alliicin on different enzymes of the snail *Lymnaea acuminata*. This snail is the intermediate host of *Fasciola hepatica*, which causes 95% fascioliasis of cattle and other livestock in the northern part of India. The study indicated that alliicin caused an uncompetetive inhibition of AChE and competitive inhibition of LDH and alkaline phosphatase (Singh and Singh, 1996b).