Review of Literature
REVIEW OF LITERATURE

The healthful properties of garlic are legion and have been identified and validated by extensive research and in innumerable publications. Therefore, an attempt has been made to present a brief review of literature which is in accordance with the present study on the effect of garlic on age and age related changes in rat.

Oxidative modification of DNA, proteins and lipids by reactive oxygen species (ROS) plays a role in age and age related disease, including cardiovascular, neurodegenerative and inflammatory disease and cancer. Extract of fresh garlic that are aged over a prolonged period to produce aged garlic extract (AGE) contain antioxidant phytochemicals that prevent oxidant damage. These include unique water soluble organosulphur compounds, lipid soluble organosuphur components and selenium. Long term extraction of garlic (up to 20 months) ages the extract creating antioxidant properties by modifying unstable molecules with antioxidant activity, such as allicin and increasing stable and highly bioavailable water soluble organo sulphur compounds such as S-allyl cysteine and S-allylmercaptocystine. AGE exerts antioxidant action by scavenging ROS, enhancing antioxidant enzymes and increasing glutathione in cell. AGE inhibits lipid per oxidation, oxidative modification of low density lipoprotein (LDL) and protect endothelial cells from the injury by oxidized molecules, which contribute to athrosclerosis. AGE may have a role in protecting against loss of brain function in ageing and possess other antiageing effect as suggested by the ability to increase cognitive function, memory in a senescence-accelerated mouse model. Substantial experimental evidence shows the ability of AGE to protect against oxidant induced disease, acute damage from aging, radiation and chemical exposure and long term toxic damage. Compelling evidence supports that the beneficial health effects attributed to aged garlic extract in reducing
the risk of cardiovascular disease stroke, cancer and ageing, including the oxidant-mediated brain cell damage that is implicated in Alzheimer's disease (Borec, 2001)

Chen et al (1999) found that diallyl sulfide (DAS), the flavour compound of garlic is active in inhibiting chemically induced cytotoxicity & carcinogenicity in animals. Male Sprague-Dawly rats treated with DAS at daily doses of 50 or 200 mg/kg for 8 days reduced hepatic catalase activity 55% and 95% respectively and reduced liver catalase protein level. There was no change in superoxide dismutase and glutathione peroxidase. Fresh garlic homogenate 2g or 4 g/kg for 7 days decreases liver catalase activity (35%). Author demonstrates that the treatment with DAS and garlic homogenate decrease the hepatic catalase level in rat.

**Antioxidant property:** Banerjee et al (2001) studied on various antioxidant enzymes and lipid peroxidation in liver and kidney by administering different doses of garlic (250, 500 &1000 mg/kg/day) for 30 days. Thiobarbituric acid reactive substances (TBARS) and glutathione peroxidase (Gpx) were reduced in lower dosage (250 mg) significantly. But there was no change in catalase and reduced glutathione (GSH) but superoxide dismutase (SOD) increased significantly. Catalase and SOD were reduced in both 500 mg & 1000 mg without altering TBARS. Higher dosage (1000 mg) also showed morphological changes in liver and kidney. They have expressed their concern for a need of safe dose of garlic.

Nicotine a major component of tobacco is partly responsible for the development of atherosclerosis. Helen et al (1999) studied the antioxidant effect of garlic oil and onion oil on nicotine induced lipid peroxidation in rat tissues. The lipid peroxidation products and scavenging enzymes were assessed in liver, heart and kidney. The rats were treated with 0.6 mg nicotine/kg body weight and simultaneously given 100mg garlic or onion oil /kg body weight for 21 days. Thiobarbituric acid reactive substances,
conjugated diene and hydroperoxide concentration were significantly increased in nicotine treated rats. Both the oils increased resistance to lipid peroxidation. The catalase, superoxide dismutase, glutathione peroxidase decreased in nicotine treated rats but increased in oil treated groups. The results indicate that oils of garlic & onion are effective antioxidants against the oxidative damage caused by nicotine.

Chen et al (2003) designed to investigate the combined modulatory effect of garlic oil (GO) & fish oil (FO) on the hepatic antioxidant and drug metabolising systems in rats. Rats were fed low –maize oil (MO) diet (50gMO/kg), high MO diet(235gMO/kg) or high FO diet (205 g FO+30g MO/kg) and all the animals received garlic oil (0-200mg /kg body weight ) three times /week for 6 weeks .It was found that GO increased glutathione –S- transferase (GST), glutathione reductase, superoxide dismutase (SOD) and ethoxyresorufin –O-deethylase (EROD) activities but decreased glutathione peroxidase , N-nitrosodimethylamine demethylase (NDMAD) activities. The results indicate co-administration of GO and FO modulates, the antioxidant and drug metabolizing capacity of animals.

Perez–Severiano (2004) observed S-allylcysteine, a garlic derived antioxidant, ameliorates quinolinic acid induced neurotoxicity and oxidative damage in rats. Rats were administered S –allylcysteine (150, 300, or 450mg/kg, i.p) 30 minutes before a single striatal infusion of 240 n mol quinolinic acid. The lower dose of S-allylcysteine resulted in preventing only the quinolinate- induced lipid peroxidation (p < 0.05). The higher dosage (300mg/kg) prevented the striatal decrease of copper/zinc–superoxide dismutase activity (p < 0.05) produced by quinolinic acid. This dose also reduced the quinolinic acid –induced neurotoxicity.

**Cholesterol lowering effect:** Dillon et al (2003) studied on the aged garlic extract (AGE) as an effective antioxidant as it scavenges superoxide...
ions & reduces lipid peroxide formation in cell free assays. Superoxide production was completely inhibited in the presence of 10% (v/v) aqueous preparation of AGE and reduced by 34% in the presence of a 10% (v/v) ether extract of AGE. In presence of 10% (v/v) diethyl ether extract of AGE significantly reduced Cu (2+) & 15-lipoxygenase mediated lipid peroxidation of isolated human LDL by 81% and 37% respectively. Thus in their in vitro studies which was challenged with a range of oxidants either in the presence or absence of AGE or its diethyl ether extract may have a role to play in preventing the development and progression of atherosclerotic disease.

Garlic depressed the hepatic activities of lipogenic & cholesterogenic enzymes such as malic enzyme, fatty acid synthase, glucose-6-phosphate dehydrogenase & HMG CoA reductase. Garlic also increased the excretion of cholesterol as manifested by enhanced excretion of acidic & neutral steroids after garlic feeding. LDL isolated from human subjects fed garlic were more resistant to oxidation. Suppression of LDL oxidation may be one of the possible powerful mechanism for the benefit of garlic in atherosclerosis. S-allyl cysteine (SAC) & diallyl-di-sulfide (DADS) in garlic are potent inhibitor of cholesterol synthesis (Sanjay et al, 2002).

Antihyperlipidemic effect of garlic formulation prepared from garlic and the individual components obtained from it, were studied by Sovova and Sova in 2004. They have done in vitro experiment on the culture of rat hepatocytes and found inhibitory effect on important enzymatic activities taking place in the biosynthesis of cholesterol & fatty acid. They showed antiatherogenic effect by reduction of lipid plaques in the arteries in hypercholesterolemic animals (rabbits) and decreased accumulation of cholesterol in vascular walls and other related and favorable changes.

Ali et al (1995) tested fresh garlic (approximately 3 g/day) on a group of male volunteers in the age group of 40-50 years for a period of 16 weeks.
After consumption of garlic there was an approximate 20% reduction of serum cholesterol and serum thromboxane (80%). It appears that small amount of fresh garlic consumed over a period of time may be beneficial in the prevention of thrombosis.

Phelps et al (1993) gave 600 mg /day of garlic powder to 10 healthy volunteers for two weeks. The serum lipid and lipoprotein levels were not lowered during this short period. But susceptibility to oxidation of apolipoproteins was decreased (34%). Retarding lipoprotein oxidation may contribute to the potential anti atherosclerotic effects of garlic.

Jain et al (1993) studied the effect of standardized garlic powder tablet (900mg/ day) on serum lipids, lipoproteins, glucose and blood pressure. The tablets significantly lowered the serum total cholesterol and LDL-cholesterol in 12 weeks. There were no significant changes in HDL cholesterol, TG, serum glucose and blood pressure.

Qureshi et al (1983) treated white Leghorn pullets with different preparations of garlic to find its effect on lipid metabolism. They fed a control diet based on soybean or corn & an experimental diet containing 3.8%garlic paste (solvent extract), residue of solvent fraction & commercial garlic oil for 4 weeks. In each case there was significant decrease in hepatic 3-hydroxy-3-methylglutaryl–CoA reductase (79-83%), cholesterol 7-alpha-hydroxylase (43-51%), fatty acid synthetase (17-29%). There was decrease in serum cholesterol (21-25%), LDL cholesterol (28-41%) and TG (10-26%) but HDL failed to respond to these treatments. Findings support that garlic can strongly lower the lipid level by suppressing the lipid metabolism.

Garlic supplementation to atherogenic diet on collagen biosynthesis in various tissues of rabbit was studied by Mirhadi et al (1990). Feeding cholesterol rich diet to male rabbits increases collagen biosynthesis and
accumulation in aorta, liver, kidney, heart and lungs. But when garlic supplemented atherogenic diet was fed, the above effects were suppressed. Cholesterol content of plasma, aorta and liver was suppressed when garlic was fed. They suggest that garlic reduced the accumulation of collagen through more mobilization of lipids or by decreased biosynthesis and maturation of collagen.

**Antiageing effect:** Breithaupt –Grogler et al (1997) made a cross sectional study on adult healthy subjects, age range of 50- 80 years, who were given standardized garlic powder for more than two years. It was found that chronic garlic powder intake has reduced age related increase in aortic stiffness. The finding strongly supported the hypothesis that garlic intake had a protective effect on elastic properties of aorta related to aging in human.

Rahman (2003) reviewed the preventive effect of garlic on age related disease like cardiovascular disease, platelet aggregation, thrombus formation, cancer and diseases associated with cerebral ageing, arthritis, and cataract formation .It can rejuvenate skin, improve blood circulation and energy level .It can either prevent or delay the onset of chronic disease associated with ageing.

Rashid and Khan (1985) suggested that the compound γ – glutamyl cysteine in garlic might lower blood pressure by modulating the endothelium derived relaxing and constricting factors.

**Protection from hepatotoxicity:** Kagawa et al (1986) studied the therapeutic effect of garlic extract on carbon tetrachloride (CCl₄) intoxicated liver. They administrated [CCl₄] in mice which enhanced lipid peroxidation, resulting in triglyceride (TG) accumulation in the liver .At the same time they introduced garlic extract in mice in the dose of 10,100 or 500mg/kg , 6 hour after carbon tetrachloride administration .The
increased conjugated diene level was diminished significantly to 82% by 100mg /kg extract and the thiobarbuteric acid reactivity was inhibited by all the doses of the extract. High dose of garlic extract lowered hepatic TG & lipid contents. Not only garlic extract was effective in diminution of lipid peroxide & on alteration of peroxidative status to more reductive condition like the effect of vitamin E, but also inhibited hepatic TG accumulation in injured liver.

The radio -protective effect of garlic was studied by Jaiswal et al (1996) in albino rats where whole body irradiated by 400 rads of irradiation by cobalt 60 source. S-allyl cysteine sulphoxide (SACS), a sulphur containing amino acid of garlic is the precursor of allicin & garlic oil markedly reduced the radiation, induced mortality and showed significant protection against the tissue damaging effects of irradiation in histopathological sections of liver and lung.

Wang et al (1998) produced hepatotoxicity with bromobenzene (BB) at a concentration 1mM in precisions-cut liver slices of rats. Pretreatment of animals with AGE for 7 days at a dose of 2 and 10 ml/kg /day dramatically reduced the toxicity of BB in a dose dependant manner . The GSH content of liver slices from rat treated with AGE at 2 or 10ml/kg/ day increased by 50 and 80% respectively . The decrease in GSH content was less in AGE+BB induced rats. AGE did not affect cytochrome P 450. Pretreatment with AGE protects against BB hepatotoxicity. The mechanism involved possibly was conjugation of organosulphur compounds present in AGE with toxic BB metabolites.

Khanum et al (1998) in their study fed fresh garlic or garlic oil – supplemented diet to rats for a period of 23 weeks with or without the treatment of a carcinogen azoxymethane (AMO). Their result showed that there was decrease in hepatic lipid peroxidation and catalase activity but only AOM treatment did not produce any change. Glutathion peroxidase
was increased by 40% and Glutathion–s transferase was unaffected. But AOM treatment reduced these enzymes. Gama-glutamyl transpeptidase activity was elevated but AOM treated rat fed with garlic or garlic oil reduced it to half. From these studies it can be concluded that garlic or garlic oil, reduces the toxic effect of AOM in rats.

Comparison of the effect of garlic oil on hepatotoxicity induced by acetaminophen in mice with N-acetylcysteine in albino male mice was done by Kalantari and Salehi in 2001. Eight groups of male albino mice were selected for this purpose. Animals were fasted over night. Garlic oil was administered intraperitionally in doses of 100mg/kg, 200mg/kg, and 500mg/kg. Immediately after a toxic dose of acetaminophen (500ng/kg orally) was administrated followed by another administration one hour later. Twenty-four hours after last administration blood was collected for serum enzyme activities and liver for histopathological observations. The group received with 200mg/kg of garlic showed good protective effect and the area of liver damage was also reduced significantly as compared with the positive control group. Garlic oil, as similar to N-acetylcysteine, can eliminate electrophilic intermediates and free radicals through conjugation and reduction reaction. The clearance of toxic metabolites of acetaminophen from the liver occurs much faster in mice with immediate garlic oil (200mg/kg) treatment.

Fukoa et al studied (2004) the effect of DAS, DADS, and DATS on phase II drug metabolizing enzymes and on the rat model of acute liver injury caused by $^{13}$CCl$_4$. A highly purified form of each sulfide was administrated i.p. to rats at a concentration of 10 or 100 micromol /kg body weight for 14 consecutive days. DATS 10 micromol /kg and DADS 100micromol/kg significantly increased the activities of glutathione S-transferase (GST) and quinone reductase (QR); Where as DAS did not produce such changes. In the $^{13}$C-Cl–induced acute liver injury model of rats, DATS (10 micromol/kg) significantly suppressed the increase in plasma lactate
dehydrogenase (LDH) and aspartate aminotransferase (AST) activities significantly. Hepatic phase II enzymes were induced strongly by the trisulfide and weakly by the disulfide. DATS significantly reduced the liver injury caused by CCl₄. DATS may be one of the important factors in garlic oil that protects the body against the injury caused by radical molecules.

Kodai et al (2007) evaluated the protective effect of S-allyl cysteine (SAC), one of the organosulfur compounds of AGE against CCl₄ induced acute liver injury in rats. SAC was administrated intraperitoneally (50-200mg/kg). It was found that SAC significantly suppressed the increase of plasma ALT and LDH levels. It also caused histological liver damage. CCl₄ increased the plasma MDA and hepatic 4-hydroxy-2-nonenal levels. SAC dose dependently reduced these increases. Their findings conclude that SAC decreased CCl₄ induced liver damage by attenuation of oxidative stress, and may be used in chronic liver disease.

**Antitoxic effect**: Role of garlic in restoring normal activity of organs and enzymes in, chemically induced toxicity or poisoning has been shown by Sheweita et al (2001). They found that garlic in repeated doses could restore the change in the activity of phase 1 drug metabolizing enzymes (alanine amino transferase, aspartate amino transferase) more fruitfully than single dose treatment prior to administration with CCl₄. In another study Sheweita et al (2001) also concluded that repeated doses of antioxidant in garlic could reduce toxic effect of CCl₄ on liver through cytochrome P450 system, there by proving its antitoxic & anti carcinogenic effect.

Orawan et al (2005) designed an experiment to see the possible protective effect of AGE against nephrotoxicity induced by Cyclosporin A (CsA). Male Wistar rats were treated orally with CsA (50 mg/kg/day), CsA+AGE (0.25, 0.5, 1, & 2g/kg/day started 3 days before the 1st dose of CsA) or the vehicle
of CsA for a period of 10 days. After 24h of last treatment CsA caused an increase in blood urea nitrogen (117%) & serum creatinine (100%) & decrease in creatinine clearance by 78 % compared to the vehicle treated rats. CsA treatment showed severe vacuolations and tubular necrosis, which were markedly improved by pretreatment of rats with AGE at the dose of 0.5-2g/kg. AGE can ameliorate nephrotoxicity caused by CsA

Murugavel et al (2007) studied the effect of diallyl tetrasulfide (DTS) from garlic on cadmium (Cd)-induced changes in lipid peroxidation and membrane bound enzymes in liver, kidney and testis of rats. Cd exposure (3mg/Kg body weight) for 3 weeks induced a significant elevation in the levels of lipid peroxidation markers (thiobarbituric acid substance and lipid hydroperoxide) with a significant decrease in the ATPase activity. Oral administration of DTS (40mg/Kg) with Cd significantly decreased the level of lipid peroxidation and restored the activities of ATPase. The result showed that DTS modulates the Cd –induced impairment of membrane bound enzymes in rats.

**Antimicrobial effect:** Elnima et al in 1983 showed the antimicrobial activity of garlic. It significantly inhibited the growth of Gram positive and Gram-negative organisms and fungi. A mouthwash containing 10% garlic in quarter ringer solution produced a drastic reduction in the number of oral bacteria.

An aqueous extract of garlic cloves was standardized for its thiosulfinate concentration and tested for its antimicrobial activity on Helicobacter pyloric. The susceptibility of Helicobacter pyloric to garlic extract of known thiosulfinate concentration, is a low cost intervention strategy with few side effects in population at high risk for stomach cancer (Gail et al, 1998).

An aqueous extract of freeze-dried garlic when incorporated in to growth media, inhibited many representative bacteria, yeast, fungi, virus. All
were susceptible to garlic, at a minimum concentration of 0.8 to 40 mg garlic/ml inhibited bacteria & yeasts growth. A low concentration of 2 mg garlic/ml inhibited 25% growth of fungal radial colony. Lactic acid bacteria were least sensitive (Elnima et al, 1993).

Bakri et al (2005) tested filter sterilized aqueous extract of garlic to inhibit the growth of a range of oral species and to inhibit the trypsin–like and total protease activity of Prophyromonas gingivalis. The garlic extract (57% w/v), containing 220 microg/ml inhibited the growth and killed most of the organism tested. The minimal inhibitory and minimum bactericidal concentration for Gram-negative strains were lower than those for Gram positive strains. Time kill curves for streptococcus mutans and P. gingivalis, showed that killing of P. gingivalis started almost immediately and there was a delay before S. mutans was killed. It also inhibits protease activity of P. gingivalis by 94.8%. This shows that garlic inhibits the growth of oral pathogens and certain proteases.

Eja et al (2007) tested the antimicrobial sensitivity tests of garlic in comparison with ciprofloxacin and ampicillin. The test were carried out on Escherichia coli, Shigella sp, Salmonella sp and proteus mirabilis. The Gram-negative diarrheagenic pathogens from the stool samples were highly sensitive to garlic, while ciprofloxacin was most effective against E.coli. It appears that garlic could interfere with DNA and RNA syntheses.

**Antidiabetic effect:** Research carried out by Augusti et al (1996) showed that treatment of alloxan diabetic rats with the antioxidant S-allylcysteine sulfoxide (SACS) reduced the diabetic condition almost to the extent, as did glibenclamide and insulin. SACS also controlled lipid peroxidation and stimulated invitro insulin secretion from β-cells isolated from normal rats. The beneficial effects of SACS could be due primarily to
its antioxidant and secondary to its secretagogue actions. These effects highlight the therapeutic value of garlic.

The antidiabetic effect of garlic ethanolic extract was investigated by Eidi et al (2006) in normal and streptozotocin-induced diabetic rats. The oral administration of garlic extract (0.1, 0.25 and 0.5 g/kg body weight) for 14 days on the level of serum glucose, total cholesterol, triglycerides, urea, uric acid, creatinine aspartate amino transferase (AST) and alanine amino transferase (ALT) in normal and streptozotocin induced diabetic rats were evaluated. Oral administration of garlic extract significantly decreased serum glucose, total cholesterol, triglyceride, urea, uric acid, creatinine, AST and ALT levels with increased serum insulin in diabetic rats but not in normal rats (p<0.05). They also made a comparison between garlic and glibenclamide (antidiabetic drug) and found that garlic extract was more effective than glibenclamide.

Anti stress effect: Zeybek et al (2007) investigated the effect of aqueous garlic extract on water avoidance stress (WAS) induced degeneration of the gastric and ileal mucosa and liver parenchyma. Wistar albino rats were exposed to WAS group for 5 days. After exposure 1ml/kg body weight aqueous garlic extract was injected i.p. The stomach, ileum and liver samples were collected for investigation. Malondialdehyde (MDA) and glutathione (GSH) levels of all tissues were also determined. In WAS group, stomach showed ulceration, dilations of gastric glands, degeneration of gastric glandular cells with prominent morphology, focal picnotic nuclei were observed in liver parenchyma. Aqueous garlic extract treatment reduced the degeneration of gastric and ileal mucosa and liver parenchyma. Increased MDA levels and decreased GSH levels in the WAS group were reversed to control values after AGE treatment.

Other effects: Boride et al in 1996 studied that aqueous extract of garlic & onion when given orally or intraperitoneally (50 mg/kg) to rats for 4
weeks it lowered thromboxane B2 levels in serum of rats. There was further reduction in thromboxane B2 levels at 500mg/kg of garlic and onion. Boiled extracts were not so effective (500mg/kg) in lowering thromboxane B2 level rather high dosage produces toxic effects in rats. Consumption of raw garlic in low doses had no side effects.

Ohaeri (2001) studied the effect of garlic oil on the levels of red cell, serum acid and alkaline phosphatase, serum amylase, alanine and aspartate transferase and bilirubin in streptozotocin–induced diabetic rats treated with garlic oil and compared with corresponding levels in diabetic control rats, normal rats and normal rats on garlic oil. Values of tissue amylase, total protein were also assessed from pancreas, liver, and kidney. Treatment of diabetic rats with garlic oil significantly decreased red cell phosphatase (p<.001), Serum acid and alkaline phosphatase (p<.001) when compared to the diabetic control rats. Serum amylase, aspartate transferase was significantly decreased in diabetic rats as compared to the diabetic control rats. However, administration of garlic oil to diabetic and normal rats showed significant increase in amylase levels of pancreas, liver and kidney.

The effect of garlic supplementation on protein metabolism was investigated by measuring testis testosterone and plasma corticosterone in rats fed with protein diets. Oi et al (2001) designed the experiment in two models. In experiment I–rats were fed experimental diet with different protein levels (40g, 25g or10g/100g casein) with or without garlic powder at the dose of 0.8g/100g or 8g/kg. In experiment 2, the effects of diallyldisulfide on the secretion of luteinizing hormone (LH) from pituitary gland of rats were measured as they regulate testosterone production. In the 1st experiment after feeding 28 days the testosterone content were significantly higher & plasma corticosterone concentration was significantly lower in rats fed 40 and 25% casein diet with garlic powder than those fed without garlic powder. Urinary 17-ketosteroid (an
index of testosterone), nitrogen balance, hepatic arginase activities were significantly higher in garlic treated group (fed 40% casein) than the control. In 2nd experiment plasma LH concentration increased in dose dependently. Thus it has been concluded that garlic alters hormonal level associated with protein anabolism by increasing testosterone and decreasing plasma corticosterone in rats fed a high protein diet.

Ichikawa et al (2003) isolated and identified six phenyl propanoids from garlic skin (peels) extract. In their study the 1, 1-diphenyl -2-picrothidrazyl from garlic skin extract was found to have radical scavenging activity. The active components from garlic skin were isolated by using high performance liquid chromatographic techniques were found to have antioxidant activities. Though garlic has been used as herbal medicine for a long time but there was no report on health benefits of the skin or peel of garlic.

Bespalov et al (2004) in a randomized double blind placebo-controlled trial studied the efficiency of "Karinat" containing 2.5 mg beta-carotene +1.5 mg alpha-tocopherol +30 mg ascorbic acid +150 mg garlic powder. Thirty three patients were given "Karinat" and 33 were given placebo. All were receiving 2 tablets /day for six months. It was found that Karinat reduced the severity of symptoms of mastalgia, dysmenorrhea & algomenorrhea & regression of palpable symptoms of breast fibromastosis. Karinat had positive action in 75.8% that was significantly greater by 45.5% as compared with placebo. It was useful for the treatment of patient with benign breast disease.

Lonsdale in 2004 reviewed that thiamine tetrahydrofurfuryl disulfide (TTFD) in garlic is a disulfide derivative of thiamine, produced as a result of enzymatic action on thiamine molecule in garlic bulbs when the bulb is cut or crushed. The compound TTFD was identified by Japanese researcher in 1951. The metabolic effect of TTFD on both human and
animal was much more powerful than thiamine. Japanese investigator emphasized that the disulfide was an extremely important part for its biological action and TTFD is the most modern of the disulfide derivatives as part of its beneficial effects are same as thiamine salts.

Demeule et al (2004) studied two organosulfur compounds (OSCs) i.e. DADS and SAC on p-glycoprotein (p-gp) and multidrug resistant protein 2(Mrp2) in renal brush border membrane which were transporter and involved in the defense of cell and multidrug resistance. They showed that DADS induces Mrp2 expression by 2 folds, which rises glutathione S-transferase (GST) and glutathione (GSH)-conjugates levels. Administration of OSC and cisplatin (an anticarcancer drug) significantly increased Mrp2 gene and protein expression by 30-fold. It was found that cisplatin potentiated the effect of OSC. OSC+cisplatin together decreased p-gp expression & mdr lb isoform mRNA levels. It was also observed that modulation of this effect was completely abolished by N-acetyl cysteine. There result showed that DADS and SAC in garlic rich diet might alter therapeutic treatments using p-gp or Mrp2 substrates.

Takasu et al (2006) evaluated the antioxidant effect of aged garlic extract (AGE) on sickle red blood cells as oxidative phenomena play a significant role in the disorder of sickle-cell anemia. AGE was administrated to five patients with sickle cell anemia at a dose of 5 ml daily. Whole blood samples were collected at base line and at 4 weeks, primarily for Heinz body analysis. In all cases Heinz bodies decreased over the 4 weeks period (59.8%+/−20.0% at base line to 29.8%+/−15.3% at follow up). This study suggest that AGE has a significant antioxidant activity on sickle red blood cells and may be further evaluated as a potent therapeutic agent to ameliorate complications of sickle cell anemia.

Chen et al (2007) examined that garlic oil supplement (Diallyl trisulfide rich) at 5 or 50 mg/kg body weight of rats significantly prolonged bleeding
time, thrombin time and enhanced anticoagulation factor activity. This is due to the anticoagulant action of DAT-rich garlic oil. However, high intake of garlic oil significantly increased plasma fibrinogen concentration and several hematological parameters such as erythrocyte count, hemoglobin and platelets. The adverse effect of garlic oil (high doses) might influence the homeostatic balance. Supplementation of garlic oil at 5mg/kg body weight has anticoagulation effect in the animals studied.

Morihara et al (2006) studied the anti-fatigue effect of aged garlic extract (AGE) on rats. Rats were subjected to endurance exercise 5 times/week for 4 weeks on a mechanical treadmill apparatus. AGE at a dose of 2.86g/kg was administered to rats 30 minutes before every exercise. Succinate dehydrogenase (SDH) in gastrocnemius and soleus muscles, superoxide dismutase (SOD), nitric oxide (NO) metabolites, lactic acid conc. in plasma were evaluated as biomarker of physical fatigue. Succinic dehydrogenase activity was increased 2-4 fold in exercised rats than the unexercised rats. AGE further up-regulated this activity by 40% and SOD activity was increased 5-fold where as AGE maintained it to that of unexercised rats. Levels of NO were not changed in any groups. Thus AGE may facilitate the turnover of aerobic glucose metabolism, attenuate oxidative stress, promote oxygen by vasodilatation and hence ameliorates the various impairments associated with physical fatigue.

Fuhrman et el (2000) studied on the antioxidant activity of garlic in synergism with other natural antioxidants. In this context they conducted a study to determine the effect of lycopene of tomato alone or in combination with other natural antioxidants present in garlic on LDL oxidation. It was concluded that flavanoids i.e. glabridin, phenolics rosmarinic and carnosic acid as well as garlic inhibited LDL oxidation in a dose dependent manner. This study strongly supported their hypothesis that lycopene synergistically inhibits LDL oxidation in combination with vitamin E, glabridin, rosmarinic acid, carnosic acid and garlic.
Betancor et al (2003) investigated the antioxidant activity of garlic by Trolox equivalent antioxidant activity (TEAC) assay. They showed that antioxidant activity was significant in the presence of total phenolic compound and copper.

Lang et al (2004) studied the immunomodulatory effect of allicin on intestinal epithelial cells. The spontaneous and TNF-alpha-stimulated secretion of IL-1beta, IL-8, IP-10 and MIG from HT-29 and Caco-2 cells were tested with or without pretreatment with allicin. Cytokine secretion was assessed using ELISA and expression of mRNA was determined by RNA protection assay. The result showed that allicin markedly inhibited the spontaneous and TNF-alpha-induced secretion of IL-1beta, IL-8, and IP-10 and MIG from the two different cells in a dose dependent manner and suppressed the expression of IL-8 & IL-1beta mRNA levels. Effect on cell viability was not noted. They concluded that allicin exerts an inhibitory immunomodulatory effect on intestinal epithelial cells and might have the potential to attenuate intestinal inflammation.

**Review and it’s relevance**: The extensive review of literature reveals the characteristic properties of garlic which can be corrected with its antiageing effects in animal and human being.

The strong antioxidant, cholesterol lowering, hepatoprotective and lipid peroxidation inhibiting effects of garlic may be preventive of senescent and degenerative changes of ageing and can promote healthful ageing.