



## NEUTRACEUTICAL POTENTIAL OF ORGANOSULFUR COMPOUNDS IN FRESH GARLIC AND GARLIC PREPARATIONS

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### ABSTRACT

Garlic (*Allium sativum* L.), one of the best-researched herbal remedies, holds a distinctive position in history, traditionally used to treat infection, colds, heart disease, diabetes, and other disorders. Clinically, it has been experimented or reducing blood pressure, cholesterol, and glucose level, as well as defense against arteriosclerosis and cancer. Other therapeutic properties of garlic and garlic preparations include antibacterial, antithrombotic, antioxidant, immunomodulatory, antidiabetic actions and modulation of drug metabolism. Presence of certain constituents such as organo-selenium compounds steroid saponins and sapogenins (e.g.  $\beta$ -chlorogenin) have been demonstrated in recent studies. Garlic is also reported to contain vitamin B<sub>6</sub> and B<sub>12</sub> flavonoids, lectins and N-fructosyl-aminoacids, which may contribute, along with organo-sulphur compounds, to the above mentioned biological effects of this herb. This review summarizes the research findings on garlic and its sulfur-containing compounds in preventing cardiovascular diseases, diabetes and cancer, along with antioxidant, antimicrobial and immunomodulatory activities. This review highlights potential biological role of garlic and views its promising role in disease prevention.

**KEYWORDS:** Garlic, Organosulfur compounds, Allicin, Neutraceutical potential.



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## INTRODUCTION

Garlic, scientifically known as "*Allium Sativum*", is a hardy, bulbous, rooted, perennial plant with narrow flat leaves and bears small white flowers and bulbils. The compound bulb consists of 6 to 34 bulblets called 'cloves' which are surrounded by a common, thin, white or pinkish papery sheet. Garlic has a strong flavour and taste. Garlic can be grown under a wide range of climatic conditions but prefers cool weather and grows at higher elevation (900 to 1200 meters) and grows best within the geographic areas having a mean monthly growing temperature ranging from 12°C to 24°C<sup>1</sup>. Its widespread use around the world as a dietary as well as therapeutic supplement, and belief that it helps in maintaining good health warding off illnesses and provides more distinct properties than other bulbs. Garlic has historically been used to treat aches and pains, leprosy, deafness, severe diarrhea, constipation, parasitic infections, asthma and to lower fever, fight infections and relieve stomachaches<sup>2</sup>. In ancient China, it has also been used to lower blood pressure, food poisoning, tumors<sup>3</sup>. These biological responses have been largely attributed to reduction of risk factors for cardiovascular diseases and cancer, stimulation of immune function, enhanced detoxification of foreign compounds, hypoglycaemic effect, anticoagulant effect, antimicrobial effect and antioxidant effects<sup>4, 5</sup>. This review given an overall view of the efficacy of garlic in various disease conditions in both human and animals.

### **CULTIVATION AND HISTORICAL PERSPECTIVE**

Garlic (*Allium Sativum*) is natively from the mountainous regions of central Asia, which afterwards reached to China and the Mediterranean regions before moving West to Central and Southern Europe, Northern Africa and Mexico<sup>6</sup>. Today garlic is cultivated world over, with much of the United States production centered in Gilroy, CA<sup>7</sup>. Universally, it is used as a flavoring agent, traditional medicine and a functional food to enhance physical and mental

health. Thus, it has acquired a special position in the folklore of many cultures as a curative agent. Garlic is denoted as one of the oldest cultivated plants in the Bible and in the literature of Ancient Israel (The Talmud), Egypt (Codex Ebers) and India (Vedas and Purans, Charak Samhita)<sup>6</sup>. In ancient China, garlic was one of the most used remedies since 2700 BC and it was recommended to those who suffered from depression<sup>8</sup>. They strongly believed that garlic prolongs longevity and is useful in treating most human diseases including infections, cancer and heart diseases<sup>9</sup>. Garlic was also found in Egyptian pyramids and in ancient Greek temples<sup>10</sup>. According to Bible, the Egyptians were fed garlic and other allium vegetables, to give them strength and increased their productivity<sup>11</sup>. The Israelis, Babylonians, Greeks (by Hippocrates), Romans and Europeans used garlic for healing purposes<sup>12</sup>. During the earliest Olympics in Greek, garlic was ingested to the athletes as a performance-enhancing agent, before they compete<sup>13</sup>. In ancient Indian medicine, garlic was a valuable remedy used as a tonic, roborans, to cure a lack of appetite, common weakness, cough, skin disease, rheumatism, haemorrhoids etc. In the Vedas (the Indian holy book) garlic was mentioned among medicinal plants<sup>8</sup>. In 1858, Louis Pasteur and Albert Schweitzer developed garlic's antibacterial application, and it was used as an antiseptic to prevent gangrene during both World Wars (I and II)<sup>14</sup>. American physicians believed in garlic as an antihypertensive agent until the late 1950's. The European Scientific Cooperative on Phytotherapy recommends garlic to prevent atherosclerosis, reduce blood lipids, improve circulation in patients with peripheral arterial vascular disease, and treat upper respiratory tract infections<sup>3</sup>.

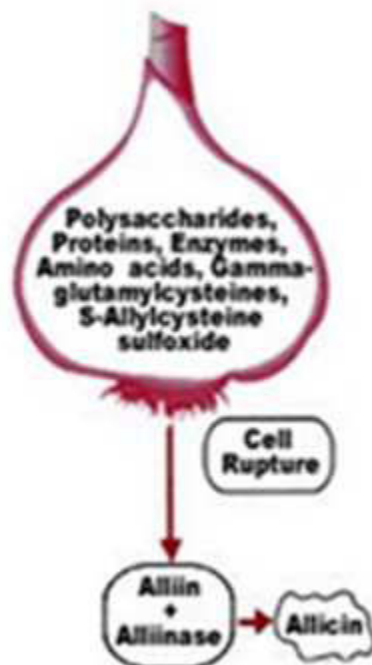
### **CULINARY USES OF GARLIC**

Garlic is the oldest cultivated plant and has been used as a spice, food and medicine. Garlic is used for flavouring various dishes practically all over the world. Not only the mature bulbs,

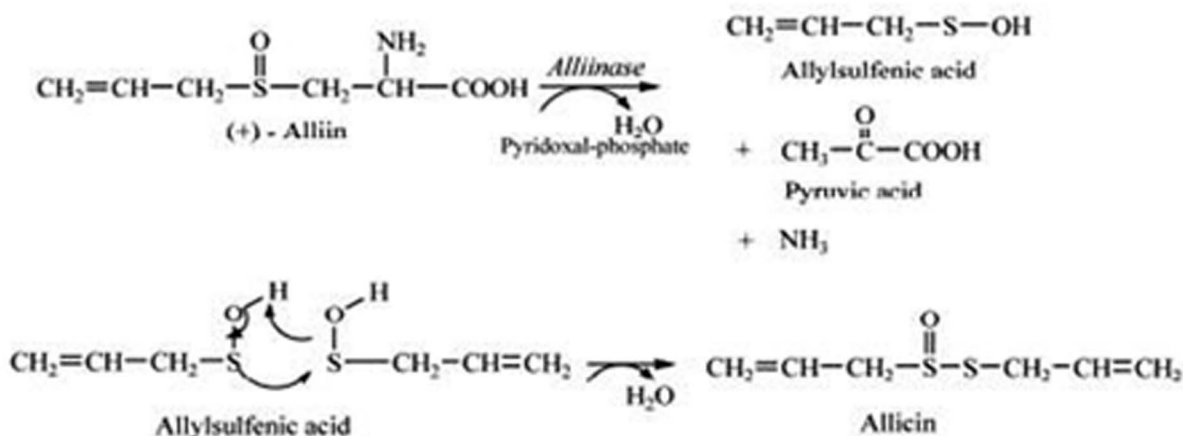
but also the leaves and scapes are used for various seasoning or edibles. In United States almost half of the produce is dehydrated for use in mayonnaise products, salad dressings and in several meat preparations. Raw garlic is used in the preparation of garlic powder, garlic salt, garlic vinegar, garlic cheese croutins, garlicked potato chips, garlic bread, garlicked bacon etc. Spray dried garlic products, liquid garlic preparations are other products have also been manufactured. In India and other Asian and Middle East countries; garlic is used in pickles, curry powders, curried vegetables, meat preparations etc. Oil of garlic is used as a flavouring agent in soups, canned foods, sauces etc.

Garlic (*Allium Sativum Linn.*) is a member of the Alliaceae family, in the same plant group as onions. Each garlic clove contains approximately 1.5-3.0 g of raw garlic, containing mostly fructose-rich carbohydrates, sulfur compounds, proteins and fiber (2% by weight)<sup>15</sup>. The principle agent for therapeutic activity of garlic are organic sulphur compounds, the most important among them is allicin (allylthiosulfinate) which is formed enzymatically from an odourless precursor, alliin in the bulb which may vary from 0.2 to 2.0% fresh weight. When garlic is chopped or crushed, allinase enzyme, present in garlic, is activated and acts on alliin (present in intact garlic) to produce allicin<sup>5</sup>. The formation of allicin (allyl 2-propene thiosulfinate) is complete in 0.2 to 0.5 min at room temperature<sup>9</sup>.

## CHEMISTRY



**Figure 1**  
**Generation of allicin in a garlic clove.**



### **Transformation of (+)-alliin in the garlic bulb under the influence of alliinase<sup>16</sup>**

It is responsible for the pungent odor of garlic and has antibiotic activity, but is very unstable and decomposes at room temperature within a few hours. Allicin, which was first chemically isolated in the 1940's, has antimicrobial effects against many viruses, bacteria, fungi and parasites<sup>3</sup>. Garlic cloves contain sulfur compounds (allicin, alliin and agoene), volatile oils, enzymes (alliinase, peroxidase and miracynase), carbohydrates (sucrose and glucose), minerals (selenium) and free amino acids such as cysteine, glutamine, isoleucine and methionine (glutamine is most abundant), which protect cells from free radical-mediated damage<sup>17</sup>. Furthermore, bioflavonoids and vitamins A, C, E, and B-complex (especially riboflavin) in garlic also protect from oxidation agents and free radicals. Thus, there are many potential sources of biological activity<sup>15</sup>.

### **GARLIC PREPARATIONS**

There are four major garlic preparations available: fresh garlic, garlic oil, garlic powder and aged garlic extract (AGE). Garlic oil is prepared by steam-distillation process; with a yield around 2.5-3 gm/kg chopped or crushed raw garlic. It contains sulfides especially diallyl and allyl methyl derivatives but none are water

soluble sulfides<sup>18</sup>. Water soluble compounds are completely eliminated by this process and allicin is totally eliminated from the oil. Commercially available garlic oil in capsules is generally diluted by 200-fold with vegetable oil to reduce the odor<sup>17</sup>. Garlic powder is simply dehydrated and pulverized garlic cloves. About 250 g of garlic powder is derived from 1 kg of raw garlic<sup>15</sup>. The yield of active sulfides (allicin) depends upon the activity of alliinase. It may be highlighted here that dehydration temperature should not exceed 60 °C, as alliinase is inactivated above 60 °C and allicin is not produced<sup>9</sup>. AGE is produced from chopped raw garlic stored without heating for more than 10 months in 15-20% ethanol<sup>19</sup>. The preparation of AGE is odor free because it is very low in allicin, and produces water-soluble sulfur containing compounds such as S-allylcysteine (SAC) and S-allylmercaptocysteine. This preparation has the highest concentration of antioxidant compounds, and is standardized by the SAC content<sup>15</sup>. Garlic oil, aged garlic and steam-distilled garlic do not contain significant amounts of alliin or allicin, instead in its place contain various products of allicin transformation; none appears to have as much physiologic activity as raw garlic or garlic powder<sup>10</sup>.

**Table1**  
**Garlic supplements on the market <sup>6</sup>.**

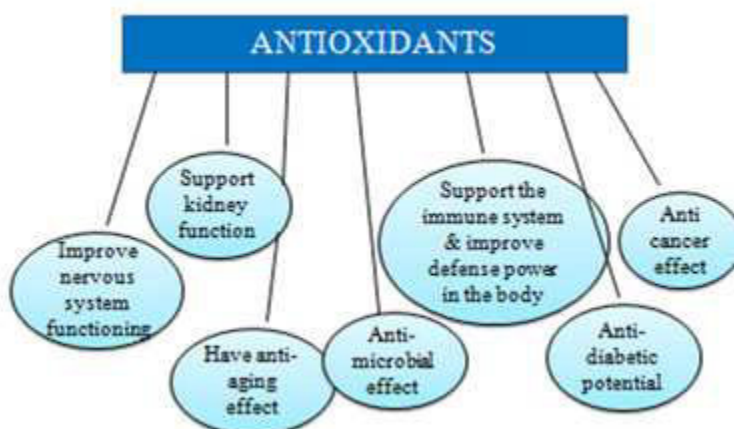
Garlic supplement	Main compounds and characteristics
Aged garlic extract	Commercially available as concentrated extract and in powdered form. Mainly water-soluble compounds (e.g. SAC, S- allylmercaptocysteine (SAMC) or saponons) and small amount of oil soluble sulfur compounds. Well standardized with SAC. Well-established safety.
Garlic powder	Commercially available in capsule and tablet forms. Alliin and a small amount of oil-soluble sulfur compounds. Standardized with allicin. Not well Standardized.
Garlic essential oil	Commercially available as oil capsules. Only 1% oil-soluble sulfur compounds [e.g. diallylsulphide (DAS), diallyldisulphide (DADS) or diallyltrisulphide (DATS)] in 99% vegetable oil. Standardized with allicin. Not well standardized.
Garlic oil macerate	Commercially available as soft gel capsules. Oil-soluble sulfur compounds (dithiins, ajoene and sulfides) and alliin. Standardized with allicin. Not well standardized.

## MEDICINAL USES OF GARLIC

### Antioxidant properties of garlic

Disorders of aging including cardiovascular, neurodegenerative, inflammatory diseases and cancer are caused due to the oxidative modification of deoxyribonucleic acid (DNA), proteins and lipids by reactive oxygen species

(ROS). *Allium sativum* (L.) is rich in antioxidants which help destroy free radical particles that can damage cell membranes and DNA, and may contribute to the aging process. Antioxidants neutralize free radicals and may reduce or even help prevent some of the damage they cause over time<sup>20</sup>.



Garlic has been shown to contain antioxidant phytochemicals that prevent oxidative damage. These include unique water-soluble organosulphur compounds, lipid-soluble organosulphur compounds and flavonoids<sup>21</sup>. *In vitro* antioxidant activity of aged (up to 20 months) 15% hydroethanolic extracts of different parts (bulbs, bulblets, flower bulblets, flowers, and leaves) of three *Allium* spontaneous species which are endemic for Italian flora: *Allium neapolitanum* Cyr., *Allium subhirsutum* L., *Allium*

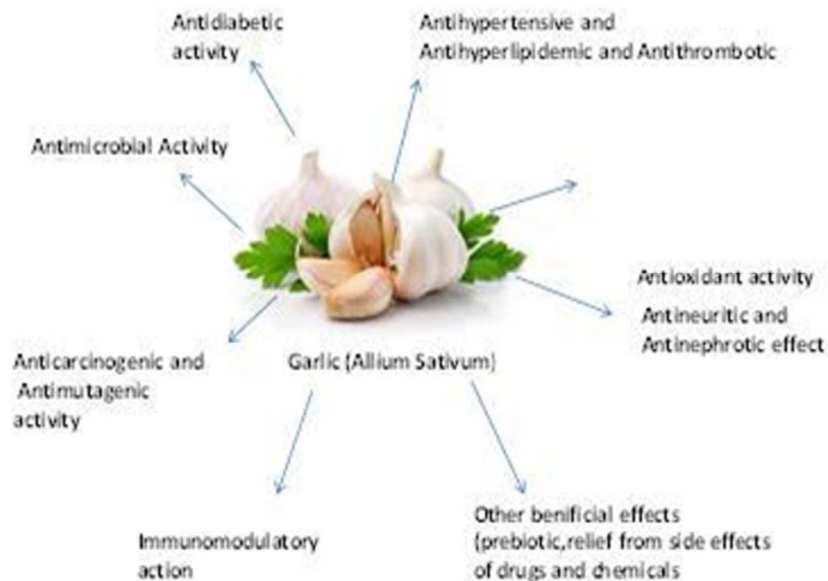
*roseum* L. garlic bulb. The aged extracts obtained from the leaves showed the best antioxidant activity, followed by flowers and then by bulbs in both used tests<sup>22</sup>. In yet another study antioxidant activity of the bulb extracts was evaluated in terms of inhibition of free radicals by 2, 2'-diphenyl-1-picrylhydrazyl. Aqueous and methanol extracts exhibited strong antioxidant activity<sup>23</sup>. Aged garlic extract and SAC have been shown to scavenge ROSs, protect endothelial cells from injury by oxLDL<sup>24</sup>. A number of human

intervention studies have evaluated the antioxidant potency of garlic in humans. The antioxidant functions of garlic have been ascertained in animal models of disease. In the fructose-induced metabolic syndrome model in rats, aqueous garlic extract attenuates oxidative stress and prevents vascular remodeling by suppressing NAD(P)H-oxidase<sup>25</sup>. It was observed that garlic oil helps to normalize impaired antioxidant status in rats with streptozotocin induced-diabetes<sup>26</sup>.

### **Antihypertensive potential**

A common definition of hypertension is a systolic blood pressure (SBP) of 140 mm Hg or higher or a diastolic blood pressure (DBP) of 90 mm Hg or higher or both, affecting an estimated 67 million individuals in America<sup>27</sup>. Prevention and proper management of hypertension decreases the incidence of related morbidity and mortality<sup>28</sup>. Blood pressure lowering effect of garlic has been linked to its hydrogen sulphide production<sup>29</sup> and allicin content –

released from alliin and the enzyme allinase which has angiotensin II inhibiting and vasodilating effects, as shown in animal and human cell studies<sup>30,31</sup>. High blood pressure is considered as a risk factor for cardiovascular diseases. Several studies were conducted to examine hypertensive effect of garlic and its products. According to Rainhart et al (2008)<sup>32</sup>, garlic has significant hypotensive action. Similar results were reported from a meta-analysis<sup>31</sup> of eleven placebo controlled clinical trials and the conclusion of this meta-analysis was that garlic powder supplementation exerts an antihypertensive effect compared to placebo, in particular in individuals with high blood pressure (SBP  $\geq$  140 mm Hg, DBP  $\geq$  90 mm Hg). On the other hand, a randomized, double-blind, placebo-controlled study was done with traditional Japanese garlic preparation and concluded that the garlic homogenate-based supplementation diet (GH diet) had a clinically relevant hypotensive effect in adults with mild hypertension but not with prehypertension<sup>33</sup>.



Studies on animal models to determine the effects of garlic on blood pressure are few but all of these reports indicate a blood pressure lowering ability of garlic. In spontaneously hypertensive rats (SHR), processed garlic (with a dose of 500 mg capsules BDS for 8 weeks) can significantly reduce the blood pressure<sup>34</sup>.

An experimental study was conducted to show the effects of two garlic sources AGE and raw garlic on systolic blood pressure (SBP) with spontaneously hypertensive (SHR) rats. At the end, both the AGE and raw garlic showed a lowering effect in increased SBP where as raw garlic indicated to cause harmful effects such as

anemia, the generation of papilloma in the fore stomach and a decline of body weight. Results suggested that AGE appeared safer than raw garlic in improvement of several circulatory diseases related to blood vessel<sup>35</sup>.

### ***Antiatherosclerosis and Hypolipidemic potential***

Atherosclerosis is a complex disease that is caused by damage to the arterial wall from inflammation and fibro-fatty deposits, the pathogenic substratum of many cardiovascular diseases. The disease process also involves several cell types, particularly smooth muscle cells, monocyte-derived macrophages, T-lymphocytes and platelets<sup>36</sup>. It is considered one of the causes of mortality and morbidity worldwide. However, in recent years, remarkable progress has been made in the prevention and treatment of atherosclerosis. Atherosclerotic diseases such as ischaemic heart disease, stroke, and peripheral arterial disease are associated with hyperlipidemia, age, hypertension, cigarette smoking and diabetes<sup>37</sup>. The medicinal importance of garlic is best known for its lipid lowering and antiatherogenic effects<sup>5</sup>. A clinical study was conducted on two groups of experimentally induced Hyperlipidemic rats to show hypolipidemic effect of garlic. In both groups experimental hyperlipidemia was induced by feeding cholesterol (500mg/kg body wt) in addition to usual diet for four weeks. After that cholesterol feeding was stopped and group 2 was supplemented with garlic extract (2 ml/kg body wt/day) for four weeks, whereas group 1 was fed with usual diet. At the end, significant reduction ( $P < 0.001$ ) in serum cholesterol, serum triglycerides, low density lipoprotein (LDL-C) and very low density lipoprotein (VLDL-C) was noticed in group 2. Whereas high density lipoprotein (HDL-C) level was significantly increased<sup>38</sup>. In yet another study Streptozotocin (STZ)-induced diabetic rats fed a diet supplemented with raw garlic (500mg/kg) exhibited significant reductions of serum glucose, cholesterol and plasma triglyceride levels<sup>39</sup>. Similarly a study on albino rats, observed that Garlic consumption although can

decrease the level of serum cholesterol (with a dose of 3 mg and 10 mg garlic/ 10 mg feed) but it increases the body weight. Hence, it was concluded that garlic consumption alone can decrease serum cholesterol level, but cannot be used as the main therapeutic agent for hyperlipidaemia<sup>40</sup>.

A double blind placebo controlled randomized study on garlic powder tablet (Allicor- coated tablet contain 150 mg garlic powder) showed that consuming 1 tablet BD for 12 months decreased risk of cardiovascular disease by 1.5 fold in men and 1.3 fold in women. The main effect that played a role in cardiovascular risk reduction was the decrease in LDL-C by 32.9 mg/dl in men and by 27.3 mg/dl in women<sup>41</sup>. Human subjects having cholesterol level between 200-400 mg/dl were treated with Garsin (garlic extract from Goldarou Company, Iran) for four weeks. It was observed that their total serum cholesterol and LDL-C levels decreased by 9% ( $P = 0.004$ ) and 14% (0.001) respectively with a simultaneous decrease in HDL-C and triglyceride though not to a significant level ( $P = 0.284$  and 0.672 respectively)<sup>42</sup>. Similarly, in a meta-analysis and systematic review (with 29 studies) the impact of garlic on total cholesterol, TAG levels, LDL-cholesterol, and HDL-cholesterol was determined. Analysis of the data revealed significant reduction in total cholesterol by 0.19 mmol/l and TAG level by 0.11mmol/ l while LDL and HDL cholesterol levels were not significantly affected, although very modest qualitative reductions in LDL and elevations in HDL were noted 32. However, no significant beneficial effects of garlic were demonstrated on serum cholesterol in a meta-analysis conducted with 13 trials.

### ***Antidiabetic potential***

Diabetes is a metabolic disorder that gradually affects the function of various systems in the body. It's a group of diseases characterized by high blood glucose levels resulting from defects in insulin secretion, insulin action, or both. Poorly controlled blood sugar is responsible for the development of various diabetic complications in both type 1 and type 2

diabetes. According to a WHO report, garlic can be used in treatment of hyperglycemia<sup>30</sup>. It is reported that garlic oil can correct hyperglycemia in diabetic patients. Garlic has been found to be effective in lowering serum glucose levels in STZ-induced as well as alloxan-induced diabetic rats and mice. Many studies have shown blood glucose lowering effect of garlic in diabetic mice, rats and rabbits<sup>44-46</sup>. It is reported that both garlic oil and diallyltrisulfide improved glycemic control in STZ-induced diabetic rats<sup>44</sup>. In alloxan-induced diabetic male rabbits, intake of aqueous garlic extract resulted in better utilization of glucose during glucose tolerance tests performed, with allicin at a dose of 1% solution of garlic/kg body weight. It significantly lowered serum glucose level (38.88%) and serum cholesterol level (57%)<sup>45</sup>, perhaps by stimulating  $\beta$  cells<sup>46</sup>. Similarly garlic administration to obese mice resulted in weight loss and reduction of blood sugar<sup>47</sup>. In humans, antidiabetic potential of garlic is not well studied. But many large-scale clinical studies with diabetic patients are warranted to confirm the usefulness of garlic in the treatment and prevention of diabetes. A 24 week, single-blind and placebo controlled study<sup>48</sup>, was conducted in 210 type 2 diabetic patients with FBG above 126 mg/dl. At the end of 24 week, the findings showed a significant reduction ( $P < 0.005$ ) in FBG as well as in HbA1c. However, a review of 12 trials<sup>49</sup> examining the effect of garlic on serum glucose levels found that only one trial in nondiabetic persons to report a statistically significant reduction in glucose. It is not clear whether garlic preparations would add benefit to the management of diabetes mellitus at this time. An open labeled prospective comparative study conducted on T2DM patients (n=60) with obesity where the patients were divided in 2 groups of 30 subjects, group 1 was given metformin 500 mg BD/TDS and group 2 was given metformin 500 mg BD/TDS along with garlic capsule 250 mg BD. At the end of 3 months it was observed that both reduced FBG and HbA1c significantly but % reduction in FBG was more with garlic although change in HbA1c was not significant<sup>50</sup>.

### **Anticancer potential**

A number of studies have demonstrated the anticancer activity of garlic by using different garlic preparations and a number of organosulfur compounds derived from garlic. The anticancer activity has been attributed to organosulfur compounds<sup>30</sup>. Allyl sulfides (sulfur compound) are characteristic flavor components of garlic. These compounds inhibit both initiation and promotion stages of tumorigenesis in experimental carcinogenesis model for various types of cancer. It has been suggested that diallyltrisulfide (a phytochemical derived from garlic) is responsible for the anticancer effect of garlic<sup>51</sup>. A study reported that pancreatic cancer risk was 54 % lower in individuals who consumed larger amounts of garlic compared with those who ate lower amounts<sup>52</sup>. Similarly, the higher intake of onion and garlic were associated with a reduced risk of intestinal cancer<sup>53</sup> and garlic and compounds having garlic derivatives were assured for breast cancer control<sup>54</sup>. People have more and more concerned about allitridum as studies have revealed that taking more raw garlic was linked with a lower risk for cancers of the alimentary system. In a study, each subject of the intervention group orally took 200 mg synthetic allitridum every day and 100 microg selenium every other day for one month of each year during November 1989 to December 1991. At the same time, subjects in control group were given 2 placebo capsules containing corn oil with the same appearance to that in the intervention group. The study confirmed that large doses of allitridum and micro dose of selenium may efficiently avert gastric cancer, especially in men. In the group that received allitridum and selenium, the risk for all tumors combined was reduced by 33 % and the risk for stomach cancer was reduced by 52 % in comparison with the group that received only the placebo<sup>55</sup>. A case-referent study indicated that allium vegetables (including garlic, onion, Welsh onion and Chinese chives) consumption has a strong preventive action against not only esophageal cancer, but also stomach cancer<sup>56</sup>. In contrast, findings from another randomized double-blind trial involved subjects



with precancerous stomach lesions found that garlic supplementation (800 mg garlic extract + 4 mg steam-distilled garlic oil daily) did not improve the prevalence of precancerous gastric lesions or reduce the incidence of gastric cancer<sup>57</sup>.

### **Antiplatelet potential**

Platelet aggregation superimposed on an atherosclerosis vessel is an antecedent event causing total blockage of blood flow leading to myocardial infarction and thromboembolic diseases. Platelets adhere to the exposed collagen, laminin and von Willebrand factor in the injured vessel wall. This entire course of action is called platelet activation. Activation can also be produced by adenosine diphosphate (ADP) and thrombin. The activated platelets change shape, put out pseudopodia, discharge their granules, and stick to other platelets, initiating the process of platelet aggregation. Aggregation is also promoted by platelet activating factor (PAF), a cytokine secreted by neutrophil and monocytes as well as platelets<sup>5</sup>. Thus, increased platelet aggregation is a risk factor for certain cardiovascular diseases<sup>6</sup>. The anti platelet potential of garlic and its derivatives is much more established than its any other biological effects. Garlic preparations have demonstrated antiplatelet effects by obstructing cyclooxygenase activity and thromboxane A<sub>2</sub> formation<sup>58</sup>. Garlic suppresses intracellular calcium mobilization, increases intracellular levels of cyclic adenosine mono phosphate (cAMP) and cyclic guanosine monophosphate (cGMP), activates nitric oxide synthase and thus increases nitric oxide derived from platelets, and interacts with glycoprotein (GP) IIb/IIIa receptors, inhibiting platelet binding to fibrinogen. The activity in garlic that leads to antiplatelet activity survives heating by oven, and boiling or heating at 200°C for 3 min or less, but not longer<sup>59</sup>.

Blood anticoagulant substance was isolated from garlic and its physical and chemical properties were studied. A half mg of garlic extract completely restrained one ml of blood from coagulating. The inhibiting effect of

garlic extract on blood clotting was almost the same as that of potassium oxalate<sup>60</sup>. A dose dependent inhibition of platelet aggregation (induced by ADP, epinephrine and collagen) was first demonstrated in garlic oil (0.5 mg/day)<sup>61</sup>. Platelet aggregation control by garlic is observed in both *vitro* and *vivo*. A recently conducted animal study with rat model has demonstrated overall antithrombotic effects of garlic by modulation of fibrinolytic activity through increased plasminogen activation and by inhibiting thrombin formation<sup>62</sup>. According to a meta-analysis, consumption of garlic preparations led to inhibition of platelet aggregation in human<sup>58</sup>. It's also established that the effect of cooking on antiplatelet activity of garlic and its content in thiosulfates. And the results suggested that allicin and thiosulfates are responsible for the antiaggregatory activity *in vitro*<sup>59</sup>. In the process of moderate cooking, partial loss of antithrombotic effect in crushed cooked garlic may be compensated by increasing the amount consumed.

A randomized placebo-controlled study was conducted to find out the acute effect of garlic oil on platelet aggregation in 14 healthy subjects. Platelet aggregation was induced by adrenaline, collagen and adenosine diphosphate (ADP). And 4 hours after consuming a large dose of garlic oil (derived from 9.9 gm garlic), there was a slightly but significant ( $P < 0.05$ ; 12 %) reduction in adrenaline induced aggregation although platelet aggregation induced by collagen or ADP was not reduced<sup>63</sup>. But when a garlic preparation was used for 2 weeks to test the effect on collagen-stimulated platelet function, no effect was found<sup>64</sup>. Similarly, platelet function was not impaired by a dietary dose of (4.2 gm) raw garlic in 23 healthy volunteers<sup>65</sup>. Thus, the potential effect on platelet aggregation may be the best documented effect of garlic in humans, but it has not yet been shown to have a clinically significant effect, either in causing bleeding, preventing thrombotic sequelae, or leading to alteration of doses of anticoagulant medication<sup>15</sup>.

**Other Therapeutic Properties**

AGE in sickle cell anemia: Sickle cell anemia is one of the most prevalent hereditary disorders with prominent morbidity and mortality. With this disorder oxidative, phenomena play a significant role in its pathophysiology. One of the garlic (*Allium sativum* L.) formulations, aged garlic extract (AGE), has been reported to exert an anti-oxidant effect *in vitro*. In a small cohort of sickle cell anemia patients, an association of AGE therapy with decrease in Heinz bodies in their ribose nucleic acid(RBC) was demonstrated. The results are suggestive of potential effect of AGE as an anti-oxidant in sickle RBC<sup>66</sup>. Antimicrobial function: Garlic inhibits *Aerobacter*, *Aeromonas*, *Bacillus*, *Citrella*, *Citrobacter*, *Clostridium*, *Enterobacter*, *Escherichia*, *Klebsiella*, *Lactobacillus*, *Leuconostoc*, *Micrococcus*, *Mycobacterium*, *Proteus*, *Providencia*, *Pseudomonas*, *salmonella*, *Serratia*, *Shigella*, *Staphylococcus*, *Streptococcus* and *Vibrio*. Importantly, Garlic demonstrates a broad antibiotic spectrum against gram-positive and gram-negative bacteria<sup>67</sup>. Complete lack of resistance of bacteria to garlic has been found<sup>68</sup>. Antibacterial activity of garlic against non-MDR (multi drug resistance) and MDR isolates of *M. tuberculosis* was evaluated. The study demonstrated that the garlic extract has showed its effectiveness against clinical isolates of MDR *M. tuberculosis*. It is worthwhile to utilize garlic as natural supplement with other standard antituberculosis therapy (ATT)<sup>69</sup>. Immunomodulatory activity: Garlic has been suggested to have potential to maintain immunomodulatory activity<sup>70</sup>. Garlic appears to be effective for restoration of immune suppression by different agents such as chemotherapy, ultra-violet radiation and physical and psychological stress<sup>71</sup>. The pharmacological effect of AGE to inhibit the tumor cell growth through immune stimulation has also been described<sup>72</sup>.

**Nephroprotective Function:** The effects of SAC and AGE on blood pressure, renal damage, oxidative and nitrosative stress were investigated in nephrectomised rats treated with SAC (200 mg/kg ip) and AGE (1.2 mL/kg ip)

every other day for 30 days. SAC and AGE reduced hypertension, renal damage, the abundance of inducible NOS, besides increasing superoxide dismutase (SOD) activity. These observations suggest that the antihypertensive as well as renoprotective effects of SAC and AGE bear association with their antioxidant properties. Therefore; they may be used to improve hypertension and delay the progression of renal damage<sup>73</sup>. Neuroprotective function: High cholesterol, high Hcy (homocysteine), hypertension and inflammation, are all risk factors for cardiovascular disease, also increase the risk of dementia, including its most common form, Alzheimer's disease (AD). High cholesterol is also associated with elevated beta-amyloid (Abeta), the hallmark of AD. Inhibition of 3-hydroxy-3-methylglutaryl-CoA reductase by AGE reduces cholesterol synthesis. These effects retard arterial plaque formation. AGE decreases Hcy, lowers blood pressure and increases microcirculation, which is important not only in diabetes management but also reduces dementia risks. AGE also may help prevent cognitive decline by protecting neurons from Abeta neurotoxicity and apoptosis. This prevents ischaemia- or reperfusion-related neuronal death, thus improves learning and memory retention. Evidence supports the beneficial health effects attributed to AGE in helping prevent cardiovascular, cerebrovascular diseases, lowering the risk of dementia and AD. However, additional studies are warranted in humans<sup>74</sup>.

**Garlic dosage, bioavailability and Safety:** Garlic has been used as food and medicine since ancient times. Consumed for hundreds of years, garlic is regarded as a safe food. However, in addition to the possible interaction with drugs cited above, several health risks have been reported to be associated with the excess consumption of garlic, or with contact with garlic in the workplace. In particular, gastrointestinal tract injury and allergic reactions caused by garlic attract concern. Dosages generally recommended in the literature for adults are 4 g (one to two cloves) of raw garlic per day, one 300-mg dried garlic powder tablet (standardised to 1.3% alliin or 0.6% allicin yield)

two to three times per day, or 7.2 g of AGE per day<sup>12</sup>. Biological effects attributed to AGE may be due to compounds, such as S-allylcysteine, S-allylmercaptocysteine, N<sup>α</sup>-fructosyl arginine and others, formed during the extraction process. Although not all of the active ingredients are known, ample research suggests that several bioavailable components likely contribute to the observed beneficial effects of garlic<sup>17</sup>.

## CONCLUSION

A single clove of garlic has therapeutic potential. The active component in garlic is allicin responsible for antibiotic effect of garlic. Garlic's antidiabetic, hypotensive and perhaps anticancer effects are well-accepted world over

because many studies support these effects. Garlic also has anticoagulant, antioxidant, and fibrinolytic effects. The new age garlic, under the scanner of scientific provings superimposed on the garlic of old leaves voids to be filled: The time tested antihelmentic, anti inflammatory, immunomodulatory and wound healing properties of garlic shall lead researchers worldwide into the provings to do justice to manifold pharmacological properties. In summary, evidence from several research reports and clinical trials points toward garlic having a role to play in either preventing or modifying risk factors for various Non communicable Diseases (NCD'S). However, more research is still required for garlic to be established as a complementary therapy for diseases prevention and treatment.

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