Garlic as an Anticancer Agent….. A Brief Review

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Abstract

Cancer is the major public health issue in the global health. Cancer is caused by the abnormal cell growth and cell proliferation in the body. Cancer cell attack and demolish normal cells. Carcinogens damage the DNA and cause the activation of oncogene and turminate the function of tumor suppressor gene (TSG) or lead the inactivation of TSG, making of hyperactive protein or high amount of oncoproteins, encourage cell signalling of cell cycle causing either activation of abnormal uncontrolled cell division or inhibition of apoptosis and thus form the tumor and also start metastasis to malignancy. There are many anti cancer treatments like radiation therapy and anticancer chemical drugs but all of these lead to side effects as resulting in destruction of normal cells and these may also lead to toxicity. Usually fresh vegetables, fruits and natural stuff of fresh plant components are abundant in a lot of powerful compounds with effective therapeutic drugs as ancient traditional medicines. In 1960, United States National Cancer Institute (NCI) began an widespread plant collection programme, which discovered many types of plants having medicinal value against many types of cancers . In this review an effort has been made to evaluate the anticancer potency of *Allium sativum* (Garlic).

Keywords:

cancer, Allium sativum ; anticancer drugs, inhibitors; natural products, medicinal plants.

Review

Background

Cancer can influence people regardless of their social class, race or age group, even foetuses and causing deaths. Environmental factors are the major cause of cancer (Hueper, 1956), which include physical carcinogenic factors like exposure to ultraviolet radiation, chemical carcinogens including cancer causing chemical compounds (Harris, 1991), cigarette smoke, intake of imbalanced diet, fast food and hormonal, heredity, metabolic, job related factors and biotic factors particularly micro organisms such as bacteria, viruses etc. leading to induction of mutations which further cause carcinogenisis (Meurman and Uittamo, 2008).

Garlic (*Allium sativum*) is an essential vegetable that has been widely utilized as seasoning, flavoring, culinary and in herbal remedies (Rivlin, 2001). Garlic has been exhibited to have dynamic biological actions

including antithrombotic, antidiabetic, anticarcinogenic, antitumorigenetic, antiatherosclerotic and a variety of other biological functions (Augusti, 1996). Scientific investigations have depicted that it contains water (65%), carbohydrates (30%), organosulfur compounds (2.3%), protein (mainly allinase) (2%), amino acids (1.2% mainly Arginine) and fiber (1.5%) along with other bioactive components (5 %) mainly sulfur containing compounds (Milner, 2004). The garlic has biochemically a large amount of sulphur containing compounds such as alliin, allicin and diallyl disulphide (DADS). And also contains Vitamin A, C and B1, flavonoids, phosphorous, selenium, sulphur, potassium, magnesium, sodium, calcium, manganese, germanium, trace iodine and iron. Its main constituents are classified as; sulfur containing compounds and non sulfur containing compounds. Among these organosulphur compounds particularly cysteine sulfoxides and thiosulfinates have greater importance (Tapiero *et al.,* 2004). Allicin (diallylthiosulfinate) and S-allay cysteine are the main thiosulfinates out of which 60-80% is allicin (Lawson *et al.,* 2001). Allicin is the main potentially active component of garlic as Allin is converted to allicin with the help of the enzyme allinase which is activated when garlic is crushed or chopped (Fenelli *et al.,* 1998). These compounds provide garlic flavor and odor as well as most of its therapeutic properties and also have the hypocholesterolemic effect in human and animals (Chowdhury *et al.,* 2002).Garlic and its various preparations have potential to lower total plasma cholesterol, reduction in blood pressure and alleviation of blood glucose level (Sterling and Eagling, 2001).

Significance of Garlic especially as anti-cancer drug:

Garlic is loaded with various bioactive components which have a range of unique functions such as antibacterial (Daka, 2011), anticoagulant, antibiotic (Bungu et al., 2008), antihistamine, antifungal, antiparasitic (Yamada & Azuma, 1977), antiviral properties and antiprotozoan, antidiabetic (Eidi et al., 2006), stimulant, diuretics, , cause sweating, antispasmodic, reduces blood sugar, decrease blood pressure and reduces blood cholesterol levels. The derived compounds of garlic are immunostimulatory stimulate cellular immunity and appear to be cheap, safe and broad-spectrum (Davis, 2005). Garlic enhances the body's natural defences against the foreign invaders and strengthens the immune system and considerably acts against infectious diseases. Garlic or its components trigger phagocytes, T-cells, β-Cells and indirectly activates β-cell to increase the antibodies production by activating the β-Cells activity. Diallyl trisulfide of garlic enhances the activity of macrophages (natural killer cells).

Allicin has strong odor and possesses antibiotic properties (Bungu, 2008). The garlic and onion contain a valuable therapeutic compound which is allyl. Garlic or its components destroy or attack microorganisms directly such as fungi, mold, bacteria, viruses and parasites. Garlic has the antimicrobial effect against some of the microorganisms. (which are: Aspergillus fumigates, Herpes simplex virus type, Escherichia coli, Herpes simplex virus type 2, Human cytomegalovirus (HCMV), Histoplasma capsulatum, Human immunodeficiency virus (HIV), Influenza B, Vaccinia virus, Human rhinovirus type 2, Mycobacterium tuberculosis, Saccharomyces cerevisiae, Pseudomonas aeruginosa, Salmonella typhimurium) (Goncagul & Ayaz, 2010). Carcinogenesis process is successfully stopped by garlic and its organic allyl sulfur constituent (Milner, 2001). Garlic possesses 20 types of sulfide compounds like methyl allyl trisulfide, allicin and diallyl trisulfide which have antibacterial, anticancer, antithrombotic activities respectively (Ariga and Seki, 2006).

In spite of many remarkable functions of, garlic, hinders the development of cancer that is particularly the very significant and desirable. Garlic and its different forms as aged garlic, extract of fresh garlic, garlic oil and a wide range of organosulphur compounds prevent some cancers. Smilarly garlic has various synergistic natural properties that make it possible to fight against cancer and ultimately cure it. The chemoprotective property of garlic has been recognized as garlic has power to control the function of several enzymes that are involved in the activation or detoxifying of carcinogens such as cytochrome P450s and glutathione *S*-transferases and also stops the development of DNA adduct in various cancer targeted tissues (Hassan 2004). Garlic has several significant agents that possess antitumor and anticarcinogenic characteristics.

The cure of human cancer is possible by the chemoprevention which is very realistic and biologically significant approach (Wu et al., 2005).The cancer patients use a wide range of herbal medicines or approaches (e.g. garlic, Essiac, mistletoe, astragalus and Lingzhi,) are for treating the cancer and/or reducing the chemotherapeutic drugs toxicities Many bioactive food constituents particularly attack multiple signal transduction pathways and cancer cells to hinder the development of cancer cells in both in vivo and in vitro (Münchberg *et al.,* 2007). Anticancer properties are mainly due to anti oxidative activities, which have tendency to trigger the activity phase 2 drug-metabolizing enzymes, antioxidative enzymes and capturing free radicals. Recent researches indicate that dietary cancer specifically chemo preventive compounds cause creation of ROS (reactive oxygen species) to activate signal transduction culminating in cell cycle arrest or apoptosis (programmed cell death) (Antosiewicz *et al.,* 2008).

There are two vital naturally occurring sulfur-containing compounds (OSCs) which are particularly GC (garlic compounds) and ITCs (isothiocyanates) as both are efficient and potent chemo protective compounds

encourage apoptosis in experimental animals and multiple cell lines. Multiple signal-transduction pathways and especially production of ROS (reactive oxygen species) and in regulation of Mitogenactivated protein kinases s (MAPKs) play vital roles in stimulation of apoptosis by GCs and ITCs. Both not only hit the apoptosis signalling molecules but also the metabolism of carcinogens (Wu *et al.,* 2005).

The anticancer characteristics of garlic are enhanced when it is processed in different forms such as fresh garlic extracts, garlic oil, aged garlic and many of particular OSCs. Recent researches have revealed that the naturally occurring OSC analogues can prevent proliferation of cancer cells in culture and as well as *in vivo*.

There are certain numerous mechanisms are concerned in anti carcinogenic property of garlic and its organosulfur compounds (OSCs) that involve inhibition of cell proliferation by stopping cell cycle progression and/or inhibition of DNA adduct formation, enhancing apoptosis, up regulation of antioxidant defences, modulation of carcinogen metabolism, and DNA repair systems. The dietary constituents such as garlic potent with its bioactive OSCs inhibit the cancer progression and acts as active chemo defensive and chemotherapeutic agents. In cancer the multiple signalling pathways become dysfunctional and oncogenic mutations build up which lead to development of carcinogenesis (Nagini, 2008). In an animal study greater inhibition of breast cancer cells was seen in rats with progressive carcinogenesis when treated with organo selenium compounds or selenium-enriched garlic or organo sulfur analogues and its extracts. The most effective derivatives of garlic are oilsoluble compounds such as diallyl disulfide (DADS). DADS intensifies the effect of eicosapentaenoic acid, (a breast cancer suppressor), and antagonize the effect of a breast cancer enhancer which is linoleic acid (Tsubura, 2011). Organo sulphur compounds of garlic hamper activation of carcinogens, increase detoxifying processes at phase 2 level, capture and arrest cell cycle at its G2/M phase, encourage mitochondrial apoptotic pathway and enhance histones acetylation, influence intercellular gap-junctional communication and take part in the formation of multidrug resistance , participation in post-translational modification and signal transduction (Iciek *et al.,* 2009). The proliferation process of cancer cells *in vitro* is suppressed through the generation of apoptosis by using natural OSCs (organosulfur compounds) which have chemoprotective effects (Melino *et al.,* 2011)**.** Garlic and its linked allyl sulfur compounds hinder the tumor proliferation/apoptosis and play key role in blocking tumors in the breast, lungs, liver and colon.

Garlic and its potent components control breast cancer and their mode of action include the inhibition of DNA adduct formation, the activation of metabolizing enzymes that are involved in detoxifying carcinogens, the suppression of the formation of reactive oxygen species, cell-cycle arrest regulation and the stimulation of

apoptosis (Tsubura *et al.,* 2011). The constituents of garlic have alk(en)yl sulfides with altering numbers of sulfur atom (i.e., mono-, di-, and trisulfide). Some researchers showed that the diallyl trisulfide hampered the tumor cell growth significantly but not by other components of galic named as diallyl disulfide and diallyl monosulfide. By introducing diallyl trisulfide treatment cell cycle at G2/M phase was arrested and there was increase in the sub-G1 DNA portion of cell, and the number of cells having caspase-3 activity. Human colon cancer cells including HCT-15 and DLD-1 were examined after giving the treatment with diallyl trisulfide and it was seen that there was significant distruption in microtubule network formation capacity of the cells (Seki *et al.,* 2008). Upon crushed garlic heating the ajoene is produced that is one of the important compounds yield a combination of E- and Z-isomers (E- and Z-4,5,9-trithiadodeca- 1,6,11-triene 9-oxide) and have a significant range of biologically natural functions such as having cytotoxic or anticancer action via an apoptotic mechanisms like generation of the mitochondrial-dependent caspase cascade. I*n vitro* tumor cell growth is inhibited by ajoene and ajoene analogues, Z-isomer (Kaschula *et al.,* 2010).

Garlic was also seen as significant agent in the activation of immune regulatory cells especially in the activation of number and mode of action of T- and natural killer cells. A large number of epidemiological, medical and laboratory studies were conducted to check the chemoprotective task of garlic in the prevention of cancer (Galeone *et al.* 2006; Setiawan *et al.* 2005) specifically in curing cancers in digestive tract, especially cancers of stomach and esophagus (Gao *et al.* 1999, Berspalov *et al.* 2004).

In a clinical study named as Iowa Women's Health Study, about 41,387 women of middle age were selected and their lifestyle, dietary and general health were observed strictly. It was concluded that women who were taking garlic in their diet had the less chance to develop the cancer of colon (Steinmetz *et al.* 1994).

Scientific Studies have also confirmed that garlic powder and its related allyl sulfur compounds are efficient in the developmental phases of cancer progression either initiation or promotion phase (Liu *et al*. 1992).

Conclusion:

Several medicinal plants have shown in possessing the significant cancer protective property. Garlic has the beneficial chemical constituents which have been consumed from ancient times to treat cancer. From this review we can demonstrate that the garlic has potent compounds such as Allicin, Alliin, and Ajoene, which play key role in preventing cancers and they may be designated as anticancer agents. Noticeably further studies and researches are desired to identify the various other medicinal uses of garlic and its potent constituents.

Abbreviation:

DADS: diallyl disulphide; OSCs: sulfur-containing compounds; GC: garlic compounds; ITCs: isothiocyanates; ROS: reactive oxygen species; HCMV: Human cytomegalovirus

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Authors' contributions

SS participated in the experimental coordination including draft to manuscript. AM searched the articles according to the keywords. MH helped out in reviewing and arranging the article and finalized the manuscript. All authors read and approved the final manuscript.

Conflict of Interest:

There is no conflict of interests regarding the publication of this article.

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