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A Review of Anticancer Effects of Garlic from Organosulfur Compounds

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Abstract: **Garlic (Allium Sativum.l.), is a widely consumed, ingredient in foods with its health benefits. It is known for its unique taste and odor along with immune-boosting functions in the body. Organosulfur compounds in garlic act as chemotherapeutic agents to prevent carcinogens. It also prevents antibacterial, anti-inflammatory and anti-fungal activity. These organosulphur compounds incite the activity of enzyme and formation of adducts in several tissues. This review discusses the mechanism of formation of cancer cells by mitosis (early) followed by apoptosis (cell death). The findings taken together will promise therapeutic potential in chemotherapy and chemoprevention. However, an increase in the consumption of garlic can cause gastrointestinal cancer. Studies are still on-going through the absorption and preparative methods of garlic.**

Index Terms: **Apoptosis, cancer cells, garlic, mitotic arrest, organosulfur compounds (OSCs).**

I. INTRODUCTION

Garlic is one of the most widely cultivated and consumed natural remedy worldwide and has been grown for more than 5000 years. It belongs to the family Lilaceae and has a botanical name "Allium Sativum". The word 'Allium' from the Celtic word signifies hot or burning and Sativum means planted or cultivated. About 70% of garlic is primarily focused in the fields of cardiovascular, antimicrobial and tumor-related diseases (Ariga and Seki, 2006). Garlic is known to have 33 sulphur compound and 17 amino acids .Epidemiological studies suggest that the consumption of garlic on daily basis gives rise to stomach, esophagus, colon and prostate cancer. The route of administration of garlic is followed by oral, intraperitoneal and intratumoral. Experiments performed on animals show a reduced risk of cancer by formulating garlic extracts. Also in vitro and vivo studies inhibit the growth using various cancer cells. Several reviews have been published on garlic as a therapeutic potential in many diseases (Bianchini and Vainio, 2001). The sulfur chemistry of garlic is well understood. The main sulfur compound in garlic is Alliin. Alliin accumulates naturally and is found to be the odorless precursor of OSCs. Garlic and its constituent's diallyl sulfide and diallyl sulfone inhibit the activity of cytochrome of P-450 using pseudo first order kinetics (Trio et al. 2014). The paper further suggests a potential for garlic derived compounds in chemoprevention or chemotherapy.

II. CHEMICAL PROPERTIES AND CONSTITUENTS OF GARLIC

Garlic contains a large number of compounds with different chemical properties. The most chemically reactive species is sulfur-containing compounds (Eric et al.2009). Depending on the plant cultivation or bulb storage the OSCs (Organosulfur compounds) varies in composition and some are under investigation. Allium species in garlic varies in composition influences the properties of the garlic. A consistent number of OSCs are formed by mechanical crushing in contact with some specific enzymes. Not all OSCs are present in the bulb but are normally separated into vacuoles and then come in contact with some chemical species (eg.Alliin) in cytoplasm. Several chemical conversions and formation of a number of OSCs reflects with high chemical reactivity and instability, which accounts for large number of species extracted from garlic (Jacob, 2006).

The selective active OSCs from allium species are DAS (Diallyl sulfide), DADS (diallyl disulphide), DATS (diallyl trisulfides), DATTS (diallyl tetrasulfides), AMS (allyl mercaptan), MATS (methylallyltrisulfide) and DMTS

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(dimethyltrisulfide). The experiments show an interrelation between sulfur-sulfur linear side chain and its anti-cancer properties. Polysulfides containing unsaturated diallyl trisulfides are compared to polysulfides containing same number of sulfur atoms in saturated alkyl groups, but the result are inconsistent. An experiment (ref) performed in laboratory indicates biological activity with DATS played by the side chain. Also presence of alkenyl group promotes thiol-disulphides on cellular targets gives a different redox state (Munchberg et al. 2007). The hardest technique used for extraction of garlic oils is steam distillation.

III. MECHANISM SHOWING ANTI-CANCER PROPERTY OR GARLIC FROM SULFUR COMPOUNDS

From the above discussion, anti-cancer property of garlic derived OSCs is based on the pre apoptosis and anti-proliferative properties. Diallyl sulfides derived from allicin with one to four sulfur atoms are the most focused and abundant sulfides obtained by crushed garlic. According to some research (ref), diallyl monosulfides (DAS) are not biologically relevant and diallyl disulfides (DADS) alters proliferation in cancer cells but do not affect other systems. Diallyl trisulfides (DATS), the recent investigated one and tetrasulfides (DATTS), the most active one affects cancer cell models. The pattern of alteration consists of an early mitotic arrest and accumulation of cells in G2 phase followed by apoptosis (Cerella et al.2009). When cells are treated with DATS or DATTS in pre-anaphase step of mitosis accumulation of cyclin B1 and phosphorylation of histone H3 occur. Degradation of cell cycle intermediates is normally required for the transition of pro-anaphase to mitosis and then in to the cell cycle. Many studies have attributed cell cycle to mitotic catastrophe (MC), recognized as chromatin condensation in pre anaphase, accumulation and so on. MC can be initiated by DNA damage or microtubule (MTs) network alterations to be a crucial target of garlic OSCs (Castedo et al. 2004). One of the effects of OSCs on the MT network is to thiol groups belonging to cysteine residues of the MT component. Cysteine modulations is known to affect tubulin conformations and residues of protein undergo three different types of reactions; 1) presence of oxidants or thiol reagents to react with second thiol group belonging to same or another molecule to form disulphide bond. 2) Thiol may react and bind with transition metal ion. 3) Due to their nucleophilic property thiol groups react to electrophiles. Other features of garlic derived OSCs are they have high lipophilicity, hydrophobic interactions with membranes and proteins and also able to react with metal ions and metalloproteins. Metalloproteins help in transportation and helps in metabolism of the cytochrome metalloenzyme family (Thomson and Ali, 2003).

A tubulin conformation of highly reactive cysteine in turn affects MT network leads to MT disarrangements and mitotic arrest of the cycle takes place. OSCs due to sulfur atoms, act as a small pool of thiol and thiol-disulfide bond exchange reactions with intracellular thiol groups present on tubulin leads to covalent binding to tubulin. This promotes apoptosis through the mitochondrial pathway, characterized by an early activation of Bak (Bcl2 homologous antagonist killer) prior to Bax (Bcl2 associated X protein). The above flowchart shows the mechanism of anti-cancer properties of OSCs (Omar and Al-Wabel, 2010).

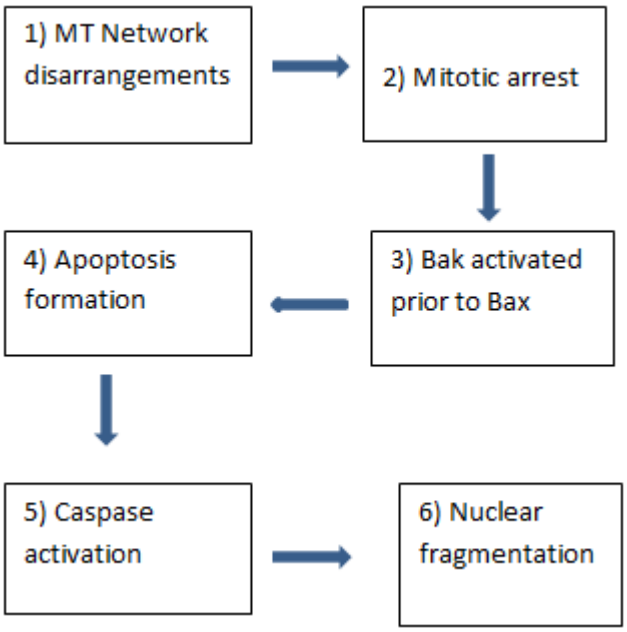

Fig. 1. Mechanism implicated in the anti-cancer effects of garlic-derived OSCs.

Apoptosis is form of cell death, serves as a process by body which eradicates damaged cells. The two main apoptotic pathways are triggered by the agents used in anti-cancer therapies (Pena-Blanco and Garcia-Saez, 2017). The intrinsic pathway is carried by DNA damaging cells, oxidative stress and the extrinsic pathway is carried after binding of specific ligands to the corresponding receptors. But the apoptosis in garlic derived OSCs is carried by mitochondrial pathway and releases cytochrome c from the outer membrane. Bcl-2-associated X (Bax) and Bcl-2 homologous (Bak) are two pre-apoptotic proteins. Bak is activated with cytochrome c release and cell arrest while Bax is activated when the cell undergoes apoptosis and Caspase activation occurs. The events suggest that the mitotic arrest by activating Bak prior to Bax leads to activation and modulation of apoptosis (Upreti et al. 2008).

CONCLUSION

An overall study implies that garlic and its sulphur compounds are effective in cancer treatments. Also garlic-derived OSCs

represent chemo preventive or chemotherapeutic agents as a source. Although the mechanisms are not fully elucidated, but role of OSCs induced mitotic arrest followed by apoptosis is implicated. Future research should be mainly in the fields of large-scale productions with many medical applications .Production of OSCs to develop polysulfides with large number of sulfur atoms can be assessed for their anti-cancer activities. The dosage of garlic: how much and how long is to consume to boost immunity is still yet to be researched.

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