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"The Chemopreventive Power of Garlic and Onion": A Review of Their Anticancer Mechanisms

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Abstract

The paper reviews the anticancer properties of these two Allium plants, focusing on their bioactive compounds and mechanisms of action. Adrenocortical carcinoma (ACC), a highly aggressive cancer with low survival rates, underscores the importance of preventive strategies. Garlic and onion, rich in active phytoconstituents such as amino acids, flavonoids, organosulfur compounds, and vitamins, are recognized for their antioxidant and anticancer properties. The mechanisms by which garlic and onion exert their chemopreventive effects include promoting the expression of detoxification enzymes like GST and CYP2B1, which metabolize carcinogens. Additionally, organosulfur compounds such as Diallyl Sulfide (DAS) and Diallyl Disulfide (DADS) enhance GST activity and reduce harmful enzyme levels, contributing to cancer prevention. The high organoselenium content in onions further aids in activating detoxification enzymes that eliminate carcinogens. By examining cancer dynamics, including uncontrolled cell proliferation and metastasis, the paper highlights the potential of garlic and onion in developing effective chemopreventive strategies. These findings support the use of garlic and onion as natural agents in cancer prevention through their bioactive components and detoxification-enhancing mechanisms.

Keywords: Allium plants, Bioactive compounds, Antioxidant, Chemopreventive, Detoxification

Introduction

Cancer is a group of illnesses that disrupt normal cell cycle dynamics, resulting in uncontrolled proliferation. Cancerous cells can recruit non-cancerous cells to form a "tumor microenvironment," which results in the production of new blood vessels and the spread of metastasis throughout the body. Adrenocortical carcinoma (ACC) is a cancer that develops in the cortex of the adrenal glands, which generate steroid hormones. It also includes a number of less common malignancies. ACC is a highly aggressive cancer with low survival rates in advanced stages, even after surgery. Mitotane (o,p0-dichlorodiphenyldichloroethane) is the only licensed drug with good specificity for treating adrenocortical carcinoma. It can be used alone or in conjunction with other anti-cancer therapy. Mitotane is derived from the insecticide dichlorodiphenyltrichloroethane (DDT), and its adrenolytic capabilities have been known since 1959 (Corso *et al*.,2021). However, challenges in administering mitotane, such as its insolubility in water and maintaining therapeutic range in the bloodstream, must be addressed in ACC treatment (Woiski *et al*., 2017).To address these constraints, research into new therapy options is necessary. Phytochemicals have been employed as a first-line or supplementary cancer treatment (Patra *et al*., 2021; Zhu *et al*., 2019). According to research, onions and garlic may help prevent a variety of cancers, including colorectal, stomach, liver, renal, lung, bladder, breast, ovarian, brain, and oesophageal cancer. According to laboratory evidence, garlic has components that are effective at destroying cancer cells. Garlic consumption has been associated to a lower risk of cancer, according to international agencies such the National Cancer Institute (NCI), the American Institute of Cancer Research (AICR), and the World Health Organization (WHO) (Surh., 2003). A 2006 European study published in the American Journal of Clinical Nutrition discovered that moderate onion consumption can help prevent colorectal, laryngeal, and esophageal cancer. Onion organosulfur compounds have been found to exhibit strong anticarcinogenic capabilities in cell research, animals, and human trials (Chu *et al*., 2002; Fukushima *et al*., 1997; Hatono *et al*., 1996; Munday and Munday., 2001). This could be related to their involvement in activating detoxification enzymes, which remove cancer-causing substances. Onions have significant levels of organoselenium compounds, which may help prevent cancer. Selenium is usually coupled to sulfur-containing amino acid derivatives.

Onions contain quercetin and its derivatives, which are highly valued for their anticarcinogenic properties (Formica and Regelson., 1995).

Allium L. is the largest genus in the Amaryllidaceous family, with approximately 1063 petaloid monocotyledon species found worldwide, in habitats ranging from northern temperate to alpine.Allium species are prevalent throughout the Northern Hemisphere.The majority of Allium species live in the dry subtropical-boreal zone, while others grow wild in the subarctic belt. This family is frequently cited in phytochemical and pharmacological literature, particularly when it comes to plants or their alkaloids (Takos & Rook., 2013). The bioactive compounds of the Amaryllidaceae family have a wide range of properties, including anticarcinogenic, antioxidant, anti-inflammatory, antimicrobial, antifungal, antiviral, antiplasmodial, antispasmodic, antiplatelet, antiasthmatic, antithrombotic, antitumor, antihyperlipidemic, antihyperglycemic, antiarthritic, antimutagenic, and immunomodulatory properties.Allium cepa, A. hirtifolium, A. sativum, A. schoenoprasum, and A. tuberosum are all Allium species (Sood & Samii., 2005). Allium plants have long been utilized in medicine and are known for their healing powers (Poonthananiwatkul., 2015). These plants include a wide range of active phytoconstituents, such as amino acids and phenolic compounds, flavonoids like anthocyanins, fatty acids, 63 organosulfur molecules, saponins, organic acids, steroids, and vitamins. These obversions demonstrate the diversity of Allium species and contribute to a better understanding of the wide range of antioxidant and anticancer capabilities present in many Allium plants, stressing their usefulness in potential therapeutic interventions as active agents. Allium as a potent source of anticancer agent and antioxidants

Plants are well-known as a source of pharmaceuticals, and phytochemicals are essential for discovering anticancer agents. Allium has strong antioxidants, sulfur, and a high concentration of phenolic compounds, making it a popular culinary component (Beretta., 2017). It has been used for many years to treat diabetes, arthritis, colds, coughs, headaches, bleeding, asthma, atherosclerosis, and inflammatory diseases (Suleria., 2015). It also contains antibacterial (Sharifi-Rad., 2016), antifungal, antiviral, antiprotozoal, antiproliferative, antimotility (Abdelrahman., 2017), and cytotoxic properties that are often used in cancer

treatment (Kazemi., 2017). Allium is the world's second most significant and produced horticulture vegetable crop, grown in over 175 countries and covering around six million hectares of land. Approximately two-thirds (66%) of global Allium production originates from Asia, with China and India leading the way (Wang., 2005).It is an excellent resource for researchers investigating anticancer properties. Wild Allium species are used as vegetables, spices, sauces, medicine, and ornamentals, and they play an essential role in hill agriculture in the Indian Himalayas (Negi.,2023). The majority of clinically approved drugs contain medicinal plants, which are significant sources of phytoactive compounds with therapeutic potential and have long been used to treat a variety of cancers. Plant-based medications include vincristine, camptothecin, vinblastine, topotecan, taxol, irinotecan, and podophyllotoxin. Bioactive chemicals have the ability to improve the anticancer properties (Mahato.,2024). Kuete et al.,2013 investigated 280 Korean medicinal plants from 73 families and 198 genera and discovered a strong relationship between cancer cell line responses and the usage of therapeutic plants and natural ingredients for tumor treatment. Drug development can be aided by choosing and improving absorption, distribution, metabolism, and excretion qualities while minimizing toxicity and side effects .Traditional medicine is still used for medicinal purposes around the world (WHO.,2019).

Photochemistry of Garlic (Allium Sativum)

Allium species are well-known for their abundance of secondary metabolites with intriguing biological features (**Yousafe *et al*., 2004**). Allium crops, such as garlic and onion, are economically important components of daily diets, serving as both vegetables and therapeutic chemicals. Garlic bulbs contain about 65% water, 28% carbohydrates, 2.3% OSCs, 2% protein, 1.2% free amino acids, 1.5% fiber, and trace elements (**Nagini S., 2008; Zhang *et al*., 2020; Butt *et al*., 2009; Agarwal KC., 1996**). Garlic contains a variety of bioactive compounds, including saponins, sapogenins, steroid saponins, phenolic compounds, polysaccharide compounds, alkaloids, essential amino acids, flavonoids, glycosides, adenosine, allixin, steroidal glycosides, lectins, anthocyanins, essential oil, prostaglandins, fructan, pectin, vitamins B1, B2, B6, C, and E, biotin, nicotinic acid, fatty acids, glycolipids, and phospholipids (**Bozin *et al*.,2008;Agarwal KC.,1996;Matsuura *et al*.,1988;Amagase H.,2001; Amagase**

H.,2006; Diretto *et al*.,2017; Szychowski *et al*.,2018; Wang *et al*.,2018; Shang.,2019; Yee MM.,2019).

The genus Allium is a rich source of compounds with diverse bioactivities, both in vivo and in vitro, due to its diverse metabolites. This genus has alkaloids, including three pyridine-N-oxide alkaloids with disulfide functional groups identified in A. stipitatum: 2-(methyldithio) pyridine-N-oxide, 2-(methylthiomethyl)dithio] pyridine-N-oxide, and 2,2′-dithio-bis-pyridine-N-oxide. Furthermore, the Allium genus frequently contains the thiosulfinate natural product allicin (**Donnell *et al*., 2009**). Flavonoids and their derivatives have been isolated from many Allium species, such as A. cepa, A. sativum, and A. schoenoprasum. These flavonoids exhibit antioxidant, anticancer, anti-inflammatory, and antimutagenic effects. **(Borlinghaus *et al*.,2014)**. Allium species contain a variety of flavonoids, including flavone, flavonol, and flavanone.A phytochemical analysis of garlic revealed the presence of bioactive sulfur-containing and non-sulfur-containing chemical components (**Zhang *et al*., 2020; Bozin *et al*., 2008**). Garlic has over 33 types of OSCs. These compounds contribute to the distinctive flavor, taste, and health benefits (**Nagini S., 2008; Zhang *et al*., 2020; Butt *et al*., 2009**).Sulfur compounds extracted from Allium species include di-allyl sulfide, sulfinate, allyl propyl sulfide, and S-methyl-L-cysteine sulfoxide. Allicin (diallyl thiosulfinate), a defensive chemical identified in A. sativum, has numerous biological activities, including cancer, diabetes, and cardiovascular disease prevention (**Borlinghaus *et al*., 2014**). Many Allium species, notably A. sativum, contain cysteine sulfoxides (alliin). A. tuberosum produces 27 volatile sulfur-rich compounds, including sulfides, disulfides, trisulfides, and tetrasulfides with ethyl, butyl, and pentyl groups (**Borlinghaus *et al*., 2014; Krest, Glodek, & Keusgen., 2000**). Thioethyl and thiopentyl compounds have also been found in A. schoenoprasum. These sulfur-containing compounds have potent antioxidant and anticancer effects.Garlic contains non-sulfur bioactive chemicals such as saponins, sapogenins, steroidal saponins, phenolic compounds, and polysaccharide compounds.Alkaloids, flavonoids, glycosides, adenosine, allixin, steroidal glycosides, lectins, anthocyanins, essential oil, prostaglandins, fructan, pectin, vitamins B1, B2, B6, C, and E, biotin, nicotinic acid, fatty acids, glycolipids, and phospholipids. Garlic contains both volatile and non-volatile bioactive chemicals, as demonstrated in **Fig 2**.Thiosulfinates and other OSCs are volatile chemicals, while saponins,

sapogenins, flavonoids, phenolics, and others are non-volatile (**Lanzotti, 2005**). Polysaccharides make up several compounds in garlic, consisting of ~85% fructose, ~14% glucose and ~1%galactose **(Wang*et al*.,2018; Xue-song H.,2005)**. Then there are amino acids in garlic. In total, 20 amino acids were found in garlic. They include alanine, glycine, valine, leucine,

Isoleucine, threonine, serine, proline, asparagine, aspartic acid, glutamic acid, phenylalanine,

glutamine, lysine, histidine, tyrosine, tryptophan, arginine, methionine and cystine **(Agarwal KC.,1996; Lee &Harnly.,2005).** Garlic is an excellent source of many nutrients and minerals, including selenium, to which human beings would crave for optimal health. It has the amount of energy contained in 100 g of raw garlic has been estimated to be 146 kcal. It also contains: protein 6.4 g, total lipid 0.5 g, Carbohydrates 33.1 g, Fibre 2.1 g Sugars 1.0 g, Calcium 181 mg, Iron 1.70 mg magnesia 25mg, phosphorus 153mg, potassium 401mg, selenium 14.2mcg, vitamin C 31.2mg and folate 3 mcg **(Nicastro, Ross&Milner.,2015)**. Some of the novel anticancer compounds of garlic are shown in **Fig.1**

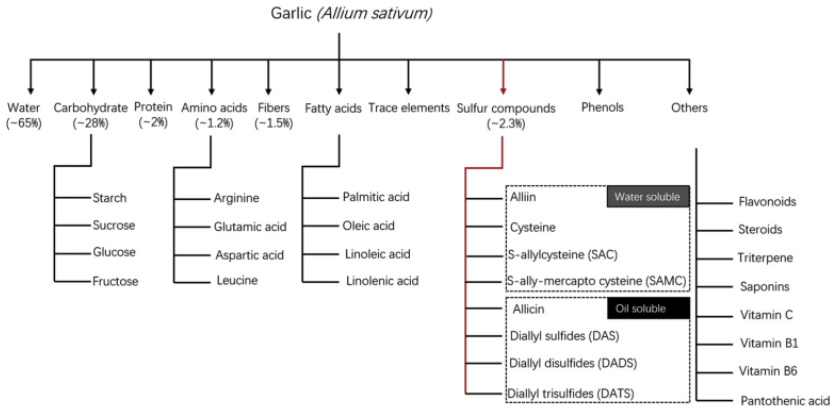

Fig.1 Major classification of the bioactive constituents in garlic.

Generally, garlic bulb contains approximately 65 % water, 28 % carbohydrates (mainly fructans), 2 % protein (mainly alliin), 1.2 % free amino acids (mainly arginine), 1.5 % fiber, and 2.3 % organosulfur compounds.

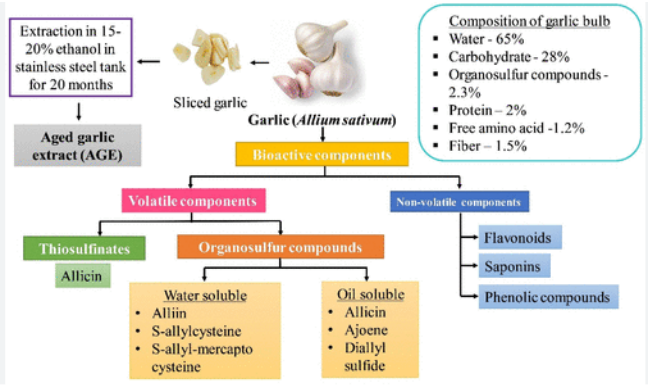

Fig.2 Pharmacological Activity of Garlic

Garlic & its metabolized compounds

Garlic bulbs contain two primary sulfur compounds: S-allyl-L-cysteine sulfoxide (alliin) and γ-glutamyl-S-allyl-L-cysteine (GSAC) (Butte *et al*., 2009; Amagase H., 2006). In plant cells, γ-glutamyl transpeptidase and oxidase convert GSAC into S-allyl-L-cysteine sulfoxide, which initiates the synthesis of various OSCs (Kothari *et al*., 2019). Garlic cloves contain 8 g/kg of alliin, which is the main organic compound present in both raw and powdered garlic (Zhang *et al*.,2020).Chewing, slicing, or crushing garlic releases a vacuolar enzyme called alliinase. The enzyme catalyzes reactions with alliin, resulting in reactive intermediates such as allyl sulfenic acid, pyruvic acid, and ammonia. Then the allyl sulfenic acids react spontaneously with each other (self-condensation) to form allicin or diallylthiosulphate which is an unstable alkenyl alkene thiosulfinate. Allicin is the primary OSC in garlic, and it is responsible for its distinctive pungent odor. In vitro, allicin decomposes to produce various OSCs such as diallyl sulfide (DAS), diallyl disulfide (DADS), diallyl trisulfide (DATS), diallyl tetrasulfide (DATTS), dipropyl disulfide (DPDS), allyl methyl sulfide (AMS), allyl methyl disulfide (AMDS), allyl methyl trisulfide (AMTS), E-ajoene, Z-ajoene, and 2-vinyl-4H-1,3-dithi.This breakdown occurs within hours at room temperature and within minutes during cooking conditions. (Butt *et al*.,2009;Schäfer &Kaschula .,2014;Amagase H.,2006;Kothari *et al*.,2019;Blania&Spangenberg.,1991). The allyl sulfide molecules are further decomposed into allyl mercaptan (AM)

and allyl persulfide (AS2H) (Trio *et al*., 2014).By contrast, GSAC is degraded into aqueous-soluble forms such as S-allylcysteine (SAC) and S-allylmercaptocysteine (SAMC) via the direct catabolic pathway (Amagase *et al*., 2001; Kothari *et al*., 2019). Furthermore, allicin reacts in vivo with glutathione (GSH) and L-cysteine to generate S-allylmercaptoglutathione (SAMG) and SAMC, respectively (Diretto *et al*., 2017). Fig.3 shows the absorption, metabolism, and distribution of garlic organosulfur compounds in the gastrointestinal (GI) tract. Human red blood cells reduce organic polysulfides produced by garlic to hydrogen sulfide (H2S). Polysulfides like DADS and DATS undergo nucleophilic substitution at the α-carbon of the allyl substituent, resulting in S-allyl-glutathione and allyl perthiol. Allyl Furthermore, it experiences nucleophilic displacement of the S-atom. This yields allyl glutathione disulfide and H2S. Allyl glutathione disulfide becomes nucleophilic glutathionee disulfide (GSSG) with additional H2S (Trio *et al*., 2014; Benavides *et al*., 2007). After consuming a large amount of garlic, allicin and its metabolites are not identified in blood or urine, indicating that these chemicals are swiftly degraded (Lawson *et al*., 1992; Freeman & Kodera., 1995).Intake of raw and cooked garlic provides bioactive OSCs that can be absorbed moderately, and raw garlic is more digestible than cooked garlic (Palazzolo *et al*., 2018).

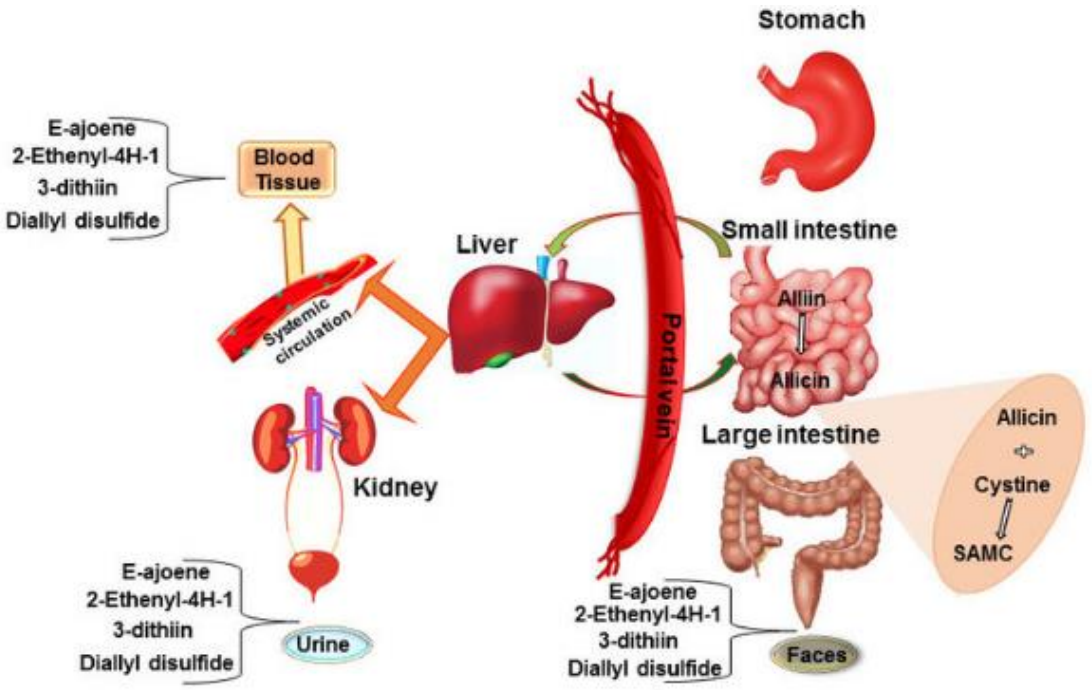

Fig.3 Schematic illustration of absorption, metabolism, and distribution of various garlic organosulfur compounds in the gastrointestinal (GI) tract. Ansary J, Forbes-Hernández TY, Gil E, Cianciosi D, Zhang J, Elexpuru-Zabaleta M, Simal-Gandara J, Giampieri F, Battino M. Potential Health Benefit of Garlic Based on Human Intervention Studies: A Brief Overview. Antioxidants (Basel). 2020 Jul 15;9(7):619. doi: 10.3390/antiox9070619. PMID: 32679751; PMCID: PMC7402177.

Bioavailability of garlic

When participants ate 25 g of chopped raw garlic, no allicin, transformation chemicals, or Allyl Mercaptan were identified in their blood, urine, or feces (Lawson, Ransom, & Hughes, 1992). After consuming fresh garlic, S-allylcysteine can be identified in the plasma, liver, and kidney. S-allylcysteine is known to be the best existing compliance marker for oil garlic because it is highly stable in the blood (Steiner & Li., 2001) due to how quickly active sulfur travels through the bloodstream. Even at high garlic concentrations, oxygen and sulfur volatile components such as allicin, sulfides, ajoene, vinyldithiins, and other oil-soluble organosulfur compounds cannot be detected in the blood or urine (Steiner & Li., 2001). S-allylcysteine, a water-soluble, odorless molecule, has been shown in clinical trials to have antioxidant and cholesterol-lowering properties. The evidence obtained from clinical investigation of adverse events and

therapeutic effect of SAC suggests that SAC is an active constituent of garlic that exerts biological effects (Berginc, Milisav, & Kristl.,2010).The NCI revealed that S-allylcysteine was thirty times less toxic in that study than allicin or diallyldisulfide (Amagase *et al*., 2001). Available data have revealed that S-allylcysteine is a potent agent against the further progress of human non-small cell lung carcinoma in both in vitro and in vivo models of disease.

The bioavailability of allicin in enteric tablets ranged from 36 to 104%, but fell to 22-57% when combined with a high protein diet. Nonenteric tablets demonstrated substantial bioavailability (80-111%), regardless of meal type, but garlic powder capsules had bioavailability ranging from 26-109%. Allicin is swiftly removed from the body after an IV infusion, showing that it is transformed into secondary compounds (**Freeman, 1995**).Extraction boosts the strength and bioavailability of crude nutrients like garlic while reducing harshness and toxicity. An aged garlic extract (AGE) can be utilized for twenty months. Over time, the garlic plant's 'odor' and some of its powerful and unpleasant chemicals are transformed to stable inorganic sulphur compounds. Many toxicological studies have been conducted to demonstrate the safety of aged garlic (**Miraghajani *et al*., 2018**). Aged garlic extract (AGE) is composed of water-soluble organosulphur compounds, primarily SAC and SAMC. Water-soluble organosulfur compounds emphasize the kinetic element, which differs from oil-soluble garlic organosulfur compounds (**Nagae *et al*., 1994**).SAC has a bioavailability of 98.2% in rats, 103.0% in mice, and 87.2% in dogs. The SAR of garlic was similarly quickly absorbed from the GI tract. The half-life of SAC following oral administration in humans was more than 10 hours, with a clearance period of more than 30 hours calculated (**Kodera *et al*., 2013**).

Garlic can make foods substantially richer through a variety of processing methods. In addition to fresh garlic, the market provides four types of garlic products: aged garlic extract (AGE), dehydrated garlic powder, garlic oil, and garlic oil macerate (**Tanaka *et al*., 2006**). AGE is a processed product obtained from aged garlic, which is sliced and extracted with water or alcohol. It is predominantly composed of water-soluble allyl amino acid derivatives (e.g., SAC, SAMC, and N-fructosyl arginine), with a small amount of oil-soluble molecules (**Chu *et al*., 2007**). (**Fig. 4**). Aged garlic extract (AGE) has been proven to have immune-enhancing, hepatoprotective, antioxidant, and anticancer properties while being

safe.SAC and SAMC may be the principal active components in AGE, as allicin, vinyldithiins, ajoene, and diallyl disulfide (DADS) were not detected in blood or urine after therapy. SAMC (S-allylmercaptocysteine; chemical formula: CH2=CH-CH2-SS-CH2-CHNH2-COOH) is a nonvolatile sulfur-containing compound found in AGE. **Fig.5** depicts a rapid and spontaneous interaction of L-cysteine with allicin in aqueous solution (PH 6) that yields 93% (**Lee, 2008**).

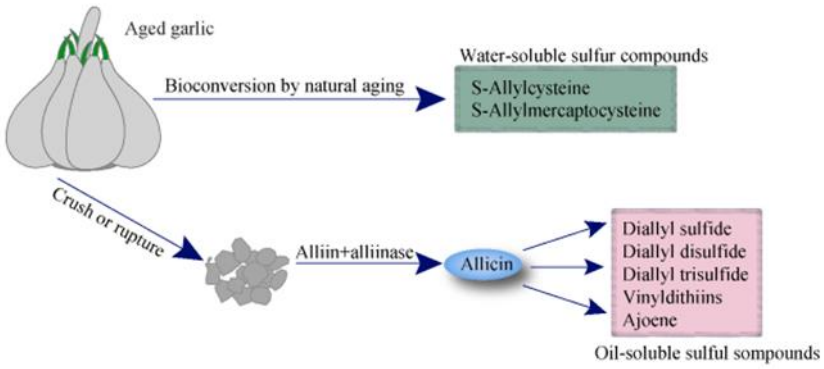

Fig.4: Major components derived from aged garlic

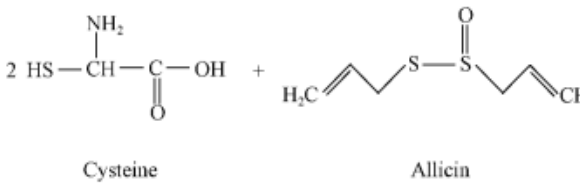

Fig.5 :Chemical synthesis reactions of SAMC during garlic aging process

Role of Garlic in Cancer Prevention

Garlic has been shown in multiple in vitro studies to successfully kill cancer cells. Garlic's anticancer activities include mutagenesis suppression, free radical scavenging, enzyme activity regulation, protein folding in the endoplasmic reticulum inhibition, cancer cell proliferation, apoptosis resistance, and immune surveillance (**Fig. 6**). **Fig.6** indicates that blocking phytochemicals at the initiation stage prevents carcinogens from becoming bioactivated by inhibiting oxidation, mutation, and detoxication. During the promotion stage, decreasing phytochemicals inhibits clonal cell proliferation by affecting protein folding and DNA repair processes. During the progression stage, phytochemicals prevent tumor development and metastasis by modifying cell properties such as antiproliferation, apoptosis, and immunocompetence. Garlic has been shown to increase carcinogen-detoxifying enzymes such glutathione S-transferases and cytochrome P450s (CYPs).Adding garlic powder to the diet significantly increased GST activity in rat liver (**Berges**

***et al.*, 2004**).Garlic compounds with an allyl group increase GST activity in mouse livers, outperforming those with a propyl group (**Sparnins *et al.*, 1988**).DAS oxidant derivatives have been shown to reduce CYP2E1 enzymatic activity (**Yang *et al.*, 2001**), lowering the toxic products of common carcinogens such as carbon tetrachloride, acetoaminophen, and N-nitrosodimethylamine. DADS and DATS have no effect on CYP2E1 or CYP1A1/2 activity in their original form (**Wanwimolruk & Prachayasittikul, 2014**). However, they can inhibit arylamine N-acetyltransferase (NAT) from producing carcinogens from foreign chemicals **(Chen *et al.*,1998)**. Garlic's ajoene has been shown to accumulate misfolded protein aggregates in cancer cells, stimulating the unfolded protein response **(Kaschula *et al.*,2016;Siyo *et al.*,2017)**.

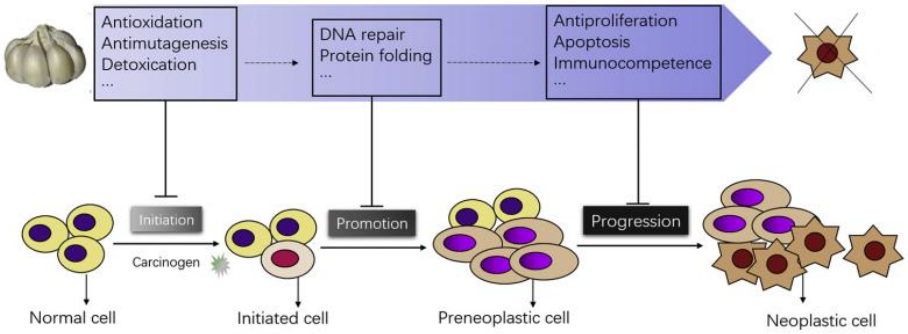

Fig.6 Anti-carcinogenic effect of garlic bioactive compounds in different stages of cancer progression.

Garlic possible mechanism in cancer

Several molecules have been isolated from garlic, and two major families of chemicals with strong anticancer activities have been identified. Thomson and Ali (2003) identified two forms of allyl sulfur compounds: lipid-soluble (DADS and DATS) and water-soluble (γ-glutamyl S-allylcysteine, SAC and SAMC).Several mechanisms have been hypothesized to explain the cancer-preventing properties of garlic and comparable organosulfur compounds found in other Allium plants. These include mutagenesis inhibition, enzyme activity regulation, DNA adduct inhibition, free radical scavenging, and impacts on cell proliferation and tumor growth. AGE, as the name implies, is formed by aging garlic. Sliced raw garlic preserved in 15-20% ethanol for 20 months is known as AGE. The AGE garlic acts on several fronts to inhibit prostate

cancer growth, including inhibiting polyamines required for cell division, increasing testosterone breakdown, which is required for prostate cancer growth, and lowering prostate specific antigen (PSA) levels, a prostate cancer marker (Pinto *et al*., 1997; Pinto *et al*., 2000). Other investigations have found that S-allyl mercaptocysteine inhibits the growth of breast cancer cells, erythroleukemia (Sigounas *et al*., 1997), and colon cancer cells (Xiao *et al*., 2003). S-allyl mercaptocysteine reduced colon cancer cell growth by 71% by destroying cellular microtubules that make up the cytoskeleton and mitotic spindle in cells, hence disrupting cell division. Furthermore, S-allyl mercaptocysteine triggered cell suicide (apoptosis) in colon cancer cells by activating apoptosis signalling pathway enzymes, including caspase, which eventually killed the cells (Xiao *et al*.,2003). Although evidence supports these pathways for organosulfur compounds, they remain theoretical, and further study is needed to establish causality between such characteristics and cancer-preventive activities in experimental animals.

Mutagenesis inhibition: Garlic extracts, both aqueous and methanolic, reduced aflatoxin B1's carcinogenic activity in Salmonella typhimurium **(Soni et al. 1997).**

Enzyme activities modulation: Organosulfur compounds can influence the activity of glutathione S-transferases (GST), which detoxify carcinogens, and cytochromes P450 (CYP), which activate chemical carcinogens in experimental animals. Sparnin *et al*. (1986) discovered that allylmethyltrisulfide (AMTS) boosted GST activity in mouse forestomach, small intestinal mucosa, liver, and lung. Other allyl derivatives have also increased. These tissues show GST activity (Sparnins *et al*., 1988).Derivatives with a propyl group showed less or no action than those with an allyl group. Induction of GST prevented benzo[a]pyrene-induced carcinogenesis in the stomach but not in the lung, demonstrating that the cancer-preventive effects of organosulfur compounds are not primarily attributable to increased carcinogen clearance. Sumiyoshi and Wargovich (1990) provided some confirmation.Thioallyl compounds were found to have a greater effect on hepatic and colonic GST in mice than thiopropyl derivatives. In contrast, DAS did not boost GST activity in mouse liver (Wargovich, 1987) or in rat hepatocyte cultures (Hayes

et al., 1987).Adding garlic powder to rats' diets increased the activity of mammary and hepatic GST. Increased GST activity did not result in maximum carcinogenesis suppression, which does not fully account for garlic's protective effects. Powder that inhibits carcinogenesis. So, the impact on enzymes Activating chemical carcinogens is insufficient to explain cancer-preventive activity. For example, receiving an oral dose of DAS prevented oesophageal carcinogenesis caused by N-nitrosomethylbenzylamine in rats and significantly reduced However, the nitrosamine is transformed microsomally in the liver, not in the oesophagus (Wargovich *et al*., 1988). DAS is a competitive inhibitor of N-demethylase activity (Brady *et al*.,1988). It reduced CYP2E1 activity in a time and dose-dependent manner while boosting it. CYP2B1, as well as pentoxy- and ethoxyresorfindealkylases, were found in liver microsomes. A increase in CYP2B1 mRNA was also observed. Treatment with the DAS. The metabolites diallyl sulfoxide (DASO) and diallylsulfone (DASO2) have similar effects on rat hepatic monooxygenases. Activities (Brady *et al*., 1991; Pan *et al*., 1993). Recks and Crankshaw (1996) discovered that DAS, DADS, and AMS decreased p-nitrophenol hydroxylase activity and CYP2E1 protein concentration in rat liver. Supplementing rats' meals with DAS/DADS boosted the activity of monooxygenases and transferases in the intestine and liver, as well as the protein levels of epoxide hydrolase and CYP2B1/2. Also increased. DADS also reduced CYP2E1 levels in the liver. DAS and DADS have similar effects on the liver. However, only epoxide hydrolase activity and CYP2B1/2 protein levels were increased in the stomach.A study on the impact of garlic oil, DAS, and DADS on the actions of many metabolic enzymes in the liver of rats given a high-fat diet (Sheen et al., 1999) found that all treatments boosted GST activity. Garlic oil promoted the expression of the placental form of GST and CYP2B1, and reduced CYP2E1 expression. DAS and DADS both affected these enzymes, however DAS mostly raised CYP2B1, whereas DADS primarily enhanced GST activity. Similar effects were reported on CYP2E1 expression. In rats, glutathione is coupled with DAS and its oxidation products DASO and DASO2, as reported by Jin and Baillie (1997). A study looked into the effects of potential GST polymorphisms on the deactivation of these Allium vegetable-derived chemicals, while this may provide some explanations. The slow and rapid actylator phenotypes have been linked to an increased risk of Cancers of the bladder and colon. DAS & DADS

lowered its activities. DAS and DADS reduced the activity of this enzyme in Helicobacter pylori strains from peptic ulcer patients (Chung et al., 1998) and a human colon carcinoma cell line (Chen et al.). 1998) and in human bladder carcinoma cells (Chung, 1999) in a dose-dependent way.

Inhibitions of DNA adduct formation: Chemical-induced carcinogenesis is assumed to start with DNA adducts. Garlic powder inhibited the production of 7,12-dimethylbenz[a]anthracene (DMBA)-DNA adducts in rat mammary glands, with a significant association between total and individual adduct levels and mammary tumor incidence. Garlic powder, garlic water extract, deodorized garlic powder, garlic powder with a high sulfur content, and SAC all proved effective against breast DMBA DNA binding (Amagase & Milner, 1993). DAS and DADS decreased DNA adducts produced when human bladder cancer cells were incubated with 2-aminofluorene (Chung, 1999). In contrast, a water extract of raw garlic and SAC were not DAS and significantly reduced benzo[a]pyrene-DNA adduct formation in simulated human peripheral blood cells. In vitro (Hageman et al., 1997)Humans can generate N-Nitroso compounds from dietary precursors, which can bind to DNA and potentially cause cancer. Shenoy and Choughuley (1992) discovered that onion and garlic liquids inhibit the nitrosation reactions in vitro are dosage dependent. In rat liver, the levels of 7-methyldeo-xyguanosine (7-MedG) and O6 -ethyldeoxyguanosine (O6) -MedG were reduced when garlic powder was mixed with a meal containing inaminopyrine and sodium nitrite (Lin *et al*., 1994). Garlic powder also reduced DNA methylation in rats' livers treated with N-nitrosodimethylamine and in mammary tissue treated with N-methylnitrosourea. Garlic, SAC, and DADs. N-methylnitrosourea inhibited the production of 7-MedG and O6 -MedG in mammary DNA, which related to the chemicals' potential to suppress breast cancer (Schaffer *et al*., 1996).

Free-radical scavenging: Free radicals have been linked to various age-related illnesses, including cancer (Ames *et al*., 1993). Reduced glutathione (GSH) is a cofactor for GST and acts as a reductant for glutathione peroxidase (GPX), an enzyme involved in natural defense against free radicals, in addition to Superoxide dismutase and catalase. Garlic and onion oils increased the activity of GPX while inhibiting the reduced ratio of 12-O-tetradecanoylphorbol-13-acetate reduces to oxidized glutathione in epidermal cells (Perchellet *et al*., 1986). In animal tissues,

GPX activity was similarly elevated. Sheen *et al*. (1999) studied DAS, DADS, and garlic oil. The DAS and DADS also improved the activity of glutathione reductase and garlic oil enhanced the activity of superoxide dismutase (Sheen *et al*. 1999). Chen *et al*. (1999) found that DAS and garlic homogenates lowered catalase levels in rats and mice's livers. S-Allylmercaptosysteine (SAMC) and SAC levels increased. Human prostate cancer cells synthesize GSH (Pinto *et al*., 1997). Imai *et al*. (1994) reported Aged garlic extract, SAC, and SAMC shown radical scavenging activity. DAS, DADS. and AMS shown selective actions on many markers in experiments for their capacity to react with carbon tetrachloride derived free radicals (Fanelli *et al*.,1998). DADS also prevented carbon tetrachloride-induced lipid peroxidation. Allium veggies' antioxidant capabilities could thus be attributed to the Contributions of various sulfur components at different stages of the process.

Effects on cell proliferation, apoptosis and tumor growth: Organosulfur compounds have been shown to inhibit tumor cell proliferation in many cell cultures, including canine mammary tumor cells (Sundaram and Milner, 1993), as well as human colon, lung, and skin cancer cells. Organosulfur compounds and the potential mechanism of garlic in cancer 55 lines (Sundaram and Milner, 1996; Sakamoto *et al*., 1997), human neuroblastoma cells (Welch *et al.,* 1992), human and mouse melanoma cells (Takeyama et al., 1993), and human Prostate cancer cells (Pinto et al., 1997). Research on the effects of organosulfur compounds on non-neoplastic cell lines has yielded conflicting results, with some studies indicating inhibition (Lee et al., 1994; Seki et al., 2000). Garlic and onion oils produced a significant suppressing the growth of human promyelocytic leukemia cells (Seki et al. 2000). Garlic powder and an Alliin-enriched

In a dose-dependent manner, garlic extract reduced the development of a human lymphatic leukemia cell line. Growth of human hepatoma and colorectal cancer Cells may only be applied in a mixture. This finding indicates Garlic's antiproliferative action is caused via breakdown. The alliinase enzyme system catalyzes the production of alliin. found in garlic powder (Siegers et al., 1999). Polyamines, particularly spermine, serve crucial roles in cell division and differentiation. SAMC, but not SAC, has been demonstrated to modify polyamine concentrations in human prostate cancer cells, boosting spermidine while lowering others. of putrescine and spermine (Pinto et al., 1997). Ornithine decarboxylase is a rate-limiting enzyme involved in the manufacture Polyamines are similarly decreased by DAS (Perchellet et al., 1986; Baer Wargovich., 1989), however there is evidence of a rise. in the livers of rats untreated with initiators (Takada et al., 1994). Apoptosis (or programmed cell death) is a Cellular suicide is

a strictly controlled and evolutionarily conserved process that is necessary for optimal embryonic development and tissue homeostasis maintenance. Death underpins various clinical disorders, including cancer and, therefore, apoptosis is a valid target in cancer therapy and prevention (Kaufmann and Gores., 2000). Organosulfur compounds appear to have an antiproliferative impact by inducing apoptosis. Sundaram and Milner (1996) and Sakamoto et al., (1997) found that exposure to DADS and DATS resulted in cell death, as evidenced by morphological alterations and/or DNA fragmentation. A significant association was discovered between the DADS-induced DNA fragmentation and increased intracellular free calcium levels Concentration may activate calcium-dependent endonucleases, resulting in apoptosis. A research (Hong et al., 2000) demonstrated DAS, DADS, and garlic extract all increase the number of nonsmall-cell lung cancer cells in an apoptotic state. This increases Following the activation of p53 protein by DADS, or the rise of Bax expression and a decrease in Bcl-2 expression. using DAS and garlic extract. Ajoene induces apoptosis in humans. Leukemia cellsbut not in peripheral mononuclear blood cellslear blood cells from healthy donors (Dirsch et al., 1998).

Inhibition of cell cycle progression: DADS decreased the percentage of human colon cancer cells in the G1 and S phases while increasing the percentage in the G2/M phase (Knowles and Milner, 1998). These effects were dependent on DADS dose and incubation time. The capacity of DADS to inhibit cell proliferation was linked to induction. G2/M phase arrest and inhibition of p34cdc2 kinase activity, which regulates cell migration from the G2 to M phases of the cell cycle. DADS inhibited p34cdc2 kinase activity by modifying the components involved, rather than directly interacting with the protein itself (Knowles & Milner, 2000). DADS also strongly suppressed the growth of H-ras oncogene altered tumors implanted in nude mice, inhibiting the association of p21H-ras interacts with the cell membrane (Singh *et al*., 1996).

Onion(Allium Cepa)

The onion (A. cepa) is said to have originated in Persia and Baluchistan (modern Iran and Pakistan). It is also possible that onions are native to the Palestine-India region. Onions have been cultivated for over a thousand years and are not known to grow wild. Their range is broad, including China, Europe, Japan, North and South Africa, and the Americas. Allium has been used for thousands of years to improve the flavor of foods and traditional treatments (**Hanelt., 2018**).

After all, spicing has been one of the most popular aroma languages in Eastern areas of the world throughout history, and it's time to replace taste enhancers with

therapeutic spices that were misinterpreted as spices! According to **Srinivasan (2005)**, the spice sector generates approximately $2 billion in sales. Spices like these help reduce the risk of atherosclerosis, cardiovascular disease, cancer, and diabetes (**Ali *et al.*, 2000; Ashraf *et al.*, 2005; *Banerjee et al.*, 2003; Cazzola *et al.*, 2011; Lai and Roy., 2004**). Throughout history, the genus Allium has been regarded as a panacea, with applications ranging from prevention to medicine (**Kendler,1987**). The Egyptian Codex Ebers, a 35-century-old manuscript describes this treatment for heart and other diseases including tumors, worms, bites **(Fenwick and Hanley., 1985)**. **Hippocrates and Pliny** the Elder recognized Allium's medicinal properties, while **Charak**, the father of Ayurvedic medicine, discussed the potential benefits of eating garlic and onion on blood circulation as well as their protective role for heart health (**Chutani and Bordia., 1981**). According to **CorzoMartinez *et al.* (2007)**, garlic and onion consumption provides protection against cancer growth, and their use as therapeutic agents appears to be extremely safe. Onions contain quercetin, a flavonoid that prevents oxidative damage to cells and other body organs (**National Onion Association, 2011**). Quercetin is the most prevalent flavonoid in the human diet, mostly found in onions (**Duthie and Dobson, 1998**).

CLASSIFICATION & CHEMISTRY OF ONION

Onions originated in the Afghanistan/Iran/USSR region and are now farmed in over 175 countries worldwide. Onions (Allium cepa) belong to the Liliaceae family (although some writers include them as Alliaceae). Onions are a perennial crop that can be both red and white. They are green, orange, or yellow-colored bulbs that are ingested pickled and tender as raw or ripe (**FAO, 2011**), and can also be utilized in powder form. These plants produce little white or purple flowers. Pickled onions are an important ingredient of the dish because of their pungent flavor and nutritional content.

Onions have approximately 90% water ,high dietary fiber and sugar content. In terms of vitamins and minerals, onions include little sodium but a high concentration of folic acid, B6, calcium, phosphorus, magnesium, and potassium. Onions, on the other hand, have a low lipid content, and only arginine and glutamic acid stand out among the amino acids.

Bioactive Compounds of Allium Cepa (Onion)

Flavonoids, Quercetin and quercetin glucosides

Onions: One of the highest food sources of flavonoids, onions account for a significant share of overall flavonoid intake. Flavonoids are classified into two types: anthocyanins, which give some cultivars their pigmentation (red-purple skins), and flavonols, such as quercetin and its glycosides, which give yellow and brown skins.

According to **Caridi *et al*.,(2007)**, the main flavonols present in onions are quercetin 3, 4'-diglucoside (QDG) and quercetin 4'-glucoside (QMG). Quercetin (3,30,40,5,7-pentahydroxyflavone) is an important phenolic component in vegetable-based diets (**Srivastava *et al*., 2016**). Quercetin has been identified as an anticancer drug, owing to its ability to induce apoptosis, prevent metastasis, and suppress proliferation. Its effects have been observed in a variety of cancer subtypes, including breast, lung, and prostate (**Chang *et al*., 2017; Ward *et al*., 2018; Wu *et al*., 2018**). Onions contain a variety of flavonoid derivatives, including quercetin glycosides, which have been linked to health benefits.

Organosulfur compounds (OSCs)

Yamazaki *et al*., (2011) identified 11 sulfur-containing taste precursors in onions, these include S-alk(en)yl.-L-cysteine derivatives include methiin, alliin, isoalliin, cycloalliin, deoxyalliin, and N-(gamma-glutamyl).-S-methylL-cysteine, N-(gamma-glutamyl).-S-(2-propenyl)L-cysteine, N-(gamma-glatamyl).-S-(E-1-propenyl)-L-cysteine (Glu-PEC), N-(gamma-glutamyl)-S-(2-propenyl).-L-cysteine Sulfoxide, N-(gamma-glutamyl)-S-(E-1-propenyl)Glu-PECSO and S-(2-carboxypropyl) glutathione.

Fructans and fructooligosaccharides (FOS)

According to **Benkeblia (2005)** and **Kahane et al., (2001)**, non-structural carbohydrates account for 65-80% of bulb dry matter. The non-structural carbohydrates found in onions are primarily glucose, fructose, sucrose, and low molecular-weight fructans, with no starch or raffinose. Fructans, also known as fructooligosaccharides (FOS), are polyfructosylsucroses with different molecular sizes that represent the primary carbohydrate resource of onions.

Onions typically have a fructan degree of polymerization (DP) of 3 to 15. Short chain fructans with less than 5 degrees of polymerization show promise as natural, low-calorie sweeteners. **Kahane *et al*.,**

(2001) propose that onion bulbs high in DP fructans can replace lipids while providing health benefits. Onions have a higher soluble to insoluble dietary fiber (SDF:IDF) ratio than other vegetables, which may affect metabolism and physiological activities. According to **Jaime *et al*.,(2002)**, SDF enhances nutritional absorption by increasing stomach viscosity, whereas IDF shortens intestinal transit time and increases food mass.

Onion & its Metabolised compounds

When onion tissue is diced, crushed, or chewed, the enzyme allinase converts the ACSOs (S-Alk(en)yl-L-cysteine sulfoxides, organosulfur compounds that are precursors to onion flavor and medicinal components) into isopropionic acid and alk(en)yl cysteine sulfenic acids. Iminopropionic acid degrades into ammonia and pyruvic acid on its own. Sulfenic acids decompose spontaneously. Methyl and propyl sulfenic acids largely produce thiosulfinates, whereas prop-1-enyl sulfenic acid produces both thiosulfinate and thiopropanal S-oxide, the onion lachrymatory component (**Block *et al*.,1993**).

Sulfur compounds generate onion pungency, which causes burning feelings in the back of the mouth and throat. To determine onion pungency, analyze pyruvic acid, which is produced in a stoichiometric ratio with thiosulfinates. Pyruvic acid has been shown to have a considerable influence on taste perception. The ratio of pungency to sugar content determines an onion's perceived sweetness. High pungency can mask high sugar levels, causing onions to look less sweet. Onions with little pungency and sugar content may be seen as bland. According to **Vagen and Slimestad (2008)**, a sweet onion should be high in sugar and low in pungency.

Role of Onion (Allium Cepa) in Cancer Prevention

Onion eating has been related to a lower risk of many malignancies, including colon and rectal cancer (**Steinmetz, 1994; Millen, 2007**), lung cancer, brain cancer, prostate cancer, bladder cancer, liver cancer, breast cancer, ovarian cancer, endometrial cancer, and skin cancer. **Fig 5** shows how onions modify carcinogenic metabolism by stimulating phase II enzymes such as NAD(P)H-dependent quinine reductase, GST, and UDP-glucuronosyltransferase. This increases the polarity of carcinogens, facilitating their

removal from the body. It also inhibits procarcinogens and bioactive enzymes while protecting against oxidative damage.Onion was tested for its effect on chemically induced preneoplastic lesions in rats' livers. Onion has been shown to inhibit the first stage of hepatocellular carcinogenesis by suppressing oxidative stress, modulating peroxidase (glutathione) activity, and inhibiting cellular division, proliferation, and apoptosis (**Perchellet, 1990; Brisdelli, 2007**); inhibiting gene transcription (**Bora, 2009; Miodini, 1999**); and protecting against UV-induced immunosuppression (**Bora, 2009**). Research has showed that the water- and lipid-soluble sulfur compounds found in onions have anticancer effects. DAS groups, such as DPS (dipropylsulphide), DPDS (dipropyldisulphide), DAS (diallyldisulphide), SMC (S-methylcysteine), and SAC (S-allyl cysteine), have inhibitory effects on the oesophagus, colon, lung, and liver in both early and late stages. Onion contains luteolin, a flavonoid with anticancer, antitumor, antioxidant, and anti-inflammatory effects in cancer test animals. It successfully prevents the development of chemically induced skin cancers in rats. Luteolin can help prevent cancer caused by UVB exposure. Methiin, a sulfur compound, slows cell proliferation and promotes apoptosis in human cell cultures, including leukemic cells. Onions contain organo-sulphur chemicals, such as tetra sulfides, which reduce sensitive cell proliferation and human breast cancer by targeting cell division 25 phosphatase, a key cell cycle enzyme. Onion's anticancer activity is primarily due to its organo-selenium components, rather than its organo-sulphur components. Onions exhibit higher anticancer activity compared to typical vegetables. Substituting Se for S increases its anticancer activity. Diallylselenide is 300 times more effective than DAS in reducing mammal cancers. Onions contain ɣ-glutamyl-Se-methyl selenocysteine, which has anticarcinogenic activity and is the most effective chemopreventive. Raw onions contain multiple forms of selenium, including selenite/selenite, selenocysteine, and selenomethionine.Quercetin has been shown to enhance the bioavailability of anticancer medications, including Tamoxifen, a non-steroidal antiestrogen used for breast cancer therapy and prevention. It reduces metabolism and promotes intestinal absorption (**Shin, 2006; Wu, 2005**). Research indicates that the combination of quercetinsulforaphane, an anticancer agent found in broccoli, and 1-isothiocyanato4-(methylsulfinyl)-butane, a member of the isothiocyanate family, has a greater impact on melanoma migration

and proliferation (B16F10) than either compound alone.

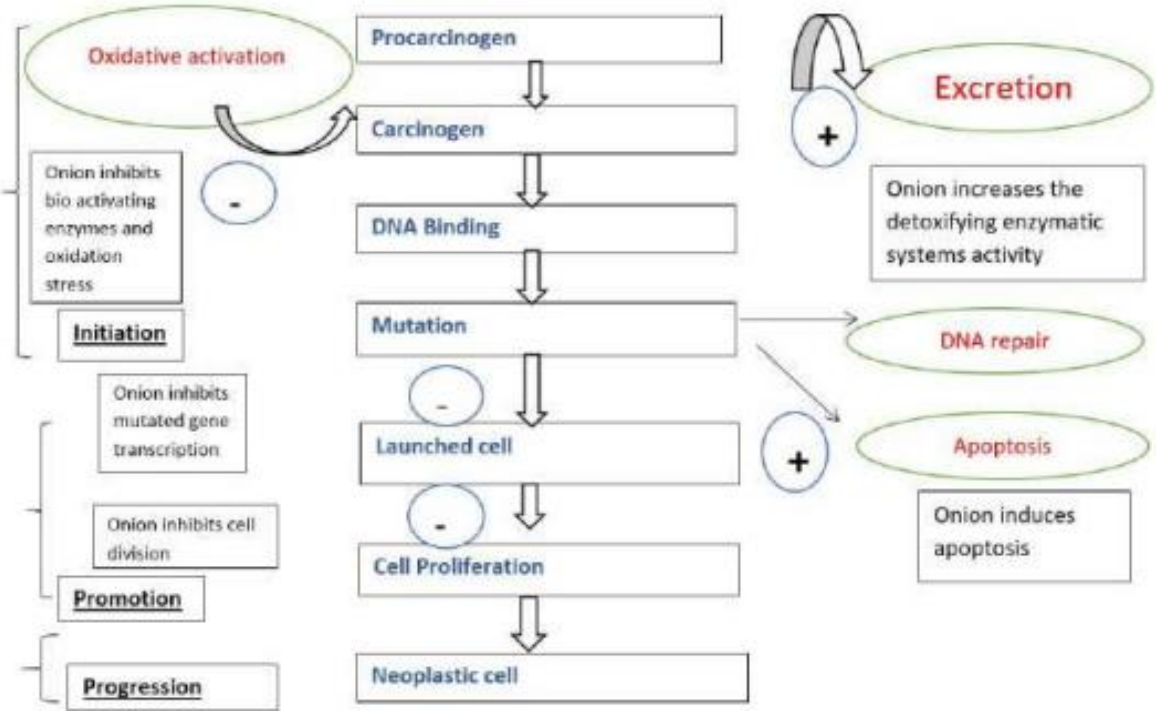

Fig.7 Onions alter carcinogenic metabolism by inducing enzymes such as NAD(P)H-dependent quinine reductase, GST, and UDP-glucuronosyltransferase, which are phase II enzymes.

Anticancer mechanism of *Allium cepa*:

1. Bioactive Compounds in *Allium cepa:*

- **Organosulfur compounds**: These include S-allyl cysteine, diallyl disulfide, and allicin.
- **Flavonoids**: Quercetin is the major flavonoid found in high concentrations in onion skin and flesh.
- **Phenolic acids**: Caffeic acid and ferulic acid are among the key phenolic acids found in onions.

These compounds work synergistically to target cancer cells through multiple mechanisms, including modulation of cellular signaling pathways, induction of apoptosis, and suppression of cancer metastasis.

2. Antioxidant and Reactive Oxygen Species (ROS) Modulation

The flavonoids and sulfur-containing compounds in onions have strong antioxidant properties, scavenging free radicals and reducing oxidative stress. Oxidative stress is a known contributor to DNA damage, mutations, and cancer initiation. By reducing oxidative stress, onion compounds can prevent the formation and progression of cancer cells.

ROS-Induced Apoptosis: Certain onion compounds can also increase ROS production within cancer cells beyond a tolerable level, triggering mitochondrial dysfunction and leading to apoptosis (programmed cell death) in cancer cells. This selective ROS modulation is key to targeting malignant cells without affecting normal cells.

3. Modulation of Cell Signaling Pathways

a) NF-κB Pathway (Nuclear Factor-kappa B) Inhibition

Onion bioactives, particularly quercetin, inhibit the NF-κBsignaling pathway, which is responsible for regulating inflammation, cell proliferation, and survival in many cancers.NF-κB is often constitutively active in cancer cells, promoting tumor growth and survival. Quercetin suppresses NF-κB activity, leading to reduced inflammatory cytokine production, decreased cancer cell proliferation, and enhanced susceptibility to apoptosis.

b) MAPK/ERK Pathway (Mitogen-Activated Protein Kinase)

Onion compounds modulate the MAPK/ERK pathway, which plays a critical role in controlling cell growth and differentiation. Onions can downregulate the MAPK/ERK pathway, thereby inhibiting the proliferation of cancer cells. This effect is particularly important in preventing the spread (metastasis) of cancer.

4. Induction of Apoptosis and Cell Cycle Arrest

a) Mitochondria-Mediated Apoptosis

Onion-derived quercetin and organosulfur compounds trigger the intrinsic apoptosis pathway by disrupting mitochondrial membrane potential, leading to the release of cytochrome C and activation of caspases (caspase-3 and caspase-9).These caspases are crucial in executing apoptosis, and their activation leads to the controlled death of cancer cells. Onions promote apoptosis selectively in cancer cells, minimizing the impact on healthy cells.

b) p53 Activation

Quercetin upregulates the tumor suppressor protein p53, which is responsible for DNA repair, cell cycle arrest, and apoptosis induction. Mutations in the p53 gene are common in many cancers, leading to uncontrolled cell division. Onion bioactives can restore p53 functionality, enhancing its ability to trigger apoptosis in cancer cells.

c) Cell Cycle Arrest

Onion extracts can induce cell cycle arrest, particularly at the G2/M phase, through upregulation of p21 and p27, which are cyclin-dependent kinase inhibitors. Arresting the cell cycle prevents cancer cells from proliferating, thereby halting tumor growth and allowing other therapeutic mechanisms to take effect.

5. Anti-Angiogenesis Activity

Quercetin and other phenolic compounds inhibit angiogenesis, the process by which new blood vessels form to supply nutrients to growing tumors. This is achieved by downregulating pro-angiogenic factors such as vascular endothelial growth factor (VEGF) and matrix metalloproteinases (MMPs). Without sufficient blood supply, tumors are starved of oxygen and nutrients, which limits their growth and ability to metastasize (spread to other parts of the body).

6. Inhibition of Cancer Metastasis

a) Inhibition of Epithelial-Mesenchymal Transition (EMT)

Onion-derived flavonoids, particularly quercetin, suppress EMT, a process by which epithelial cells acquire mesenchymal traits, enhancing their migratory and invasive capabilities.By inhibiting EMT, onion compounds prevent cancer cells from detaching from the primary tumor and invading surrounding tissues, reducing the risk of metastasis.

b) Suppression of Matrix Metalloproteinases (MMPs)

Onion bioactives reduce the expression and activity of MMPs, enzymes that degrade the extracellular matrix, facilitating tumor invasion and metastasis. Inhibiting MMP activity hinders cancer cells' ability to invade adjacent tissues and form secondary tumors in distant organs.

7. Modulation of Immune Response

Onions can enhance the immune system's ability to detect and destroy cancer cells. Flavonoids like quercetin enhance the activity of natural killer (NK) cells and macrophages, which play critical roles in targeting and eliminating cancerous cells. A robust immune response is essential in

preventing tumor formation and progression. By boosting the immune system, onions may help in both cancer prevention and adjunctive cancer therapy.

8. Synergistic Effects with Conventional Therapies

- **Chemotherapy Sensitization**: Onion compounds can sensitize cancer cells to conventional chemotherapy agents, making them more effective at lower doses and reducing the toxic side effects.
- **Radiation Therapy**: Quercetin and organosulfur compounds may also enhance the efficacy of radiation therapy by promoting DNA damage in cancer cells while protecting normal cells from radiation-induced oxidative stress.

Allium cepa (onion) exhibits potent anticancer properties through a variety of mechanisms, including modulation of oxidative stress, inhibition of key signaling pathways (such as NF-κB and MAPK), induction of apoptosis, suppression of angiogenesis and metastasis, and enhancement of immune response. The bioactive compounds—especially quercetin, organosulfur compounds, and phenolic acids—play a significant role in these effects. Given these mechanisms, onions hold potential as a preventive dietary component against cancer and as a complementary therapy to enhance the efficacy of conventional cancer treatments.

Conclusion

In conclusion, garlic and onion hold significant chemopreventive potential due to their rich bioactive compounds, including organosulfur and organoselenium. These compounds have demonstrated efficacy in reducing cancer risk by targeting various cancer mechanisms, such as enhancing the activity of detoxification enzymes like glutathione S-transferases, which play a key role in neutralizing carcinogens. Additionally, the organosulfur compounds in garlic and onion have been found to exert protective effects against cancer by modulating phase I and phase II enzyme systems involved in the metabolism of carcinogens.Furthermore, the presence of high organoselenium content in onions further contributes to their anticancer properties, as selenium is known for its role in DNA repair and protection against oxidative stress. The diverse phytoconstituents, such as flavonoids and phenolic acids, found in garlic and onion, play key roles in modulating cell cycle dynamics and reducing cancer cell proliferation by targeting various signaling pathways involved in tumor growth and

progression.While promising, further research is needed to fully understand the mechanisms and effectiveness of these Allium plants in cancer prevention and therapy, including exploring their interaction with specific cancer types and their potential synergistic effects with conventional cancer treatments.

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