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## The Toxic Effect Ways of Allicin on Different Cell Lines

### Abstract

In this review, the biological structure of garlic, its active ingredients, especially allicin and its way of antimicrobial effects on cells evaluated and also the toxic possibility of allicin on diverse cells was investigated. Various academic papers have been found in reliable literature. It is stated that garlic includes lots of phytoconstituents with activities against cells. The toxic action of allicin on different cell lines such as bacteria kinds such as Gram-positive (*Staphylococcus aureus*, *Bacillus subtilis*, *Streptococcus pneumoniae*) and Gram-negative bacteria (*Klebsiella pneumoniae*, *Helicobacter pylori*, *Escherichia coli*, *Pseudomonas aeruginosa*) for all that fungi like *Candida albicans* and parasites, virus, glioma and human neuroblastoma cell lines and also oral tongue squamous cell carcinoma, cancer cell lines which are characterized as malignant (leukemia, colon, gastric, and breast cell lines) cancer. It has been revealed that, on those cells, allicin has also been demonstrated toxicity mechanisms on cells like canceling deed of nitric oxide synthase, the peroxidation of lipids, nuclear factor, kappa B, arranging cell period, modulating the activity of redox precision proteins and influence cellular signaling.

**Keywords:** Allicin, cells, cytotoxicity, garlic, toxicity mechanisms

### Introduction

In prohibiting and treating diverse beneficial diseases, native herb yields are acquiring popularity. It has been seen that garlic is the furthest broadly investigated native yield. Its potential health benefits and treatment properties take its source from the bioactive ingredients of garlic. The significant functional act of garlic is its anticancer, antimicrobial, antioxidant, antidiabetic, antifibrinolytic, immune enhancing, antiplatelet collected effect and its possible act in prohibiting cardiovascular illnesses. Declared well-being advances of components of garlic in healing diverse irregularities have been researched in animals and humans.<sup>[1]</sup> Garlic (*Allium Sativum* L.) shows wide series of nutritional and medicinal features. Lemma *et al.*<sup>[2]</sup> investigated oil extracts of garlic's effects of biological and physicochemical. It has been stated that, oil essences of garlic bulb releases indicated important biological effects which can be utilized as resources for nutraceutical and pharmaceutical components. *Allium*, several species (spp) containing garlic, demonstrates a wide

spectrum of pharmacological effects. Sulfur including components of garlic such as alliin, allicin and ajoene, aminoacids (methionine, glutamine, cysteine and isoleucine), enzymes, minerals (zinc, germanium and selenium), solvable sugars, flavonoids (allistains I and II, quercetin and cyanidin) and vitamins (A, E, C, B, B2),  $\beta$ -carotene have therapeutic qualities. Counter to infections and free radicals waited and cooked garlic essences and oils have been demonstrated as preferable preservation to fresh garlic. The bioactive ingredients of garlic are primarily for recovering features.<sup>[1]</sup> First, in the 1940s, it was reported that the antimicrobial activities demonstrated by garlic were due to its active component allicin. Allicin is an evaporating ingredient removed from uncooked garlic. Thenceforth, it has been researched broadly counter to wide series of microorganisms. It has indicated an ability like aiming thiol, including proteins and enzymes in microorganism. Furthermore, it has been shown that allicin has an ability such as arranging lots of genes necessary for microorganisms intensity. Furthermore, allicin demonstrates lots of bioactive qualities, which cover diverse areas of investigations containing

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anti-inflammatory, antimicrobial, anticancer, and immunomodulatory activities.<sup>[3]</sup>

### The biological and chemical components of garlic

The construction of garlic is seen as fairly complicated. In all untouched garlic, the S-alk(en)yl-l-cysteine sulfoxides and  $\gamma$ -glutamyl-S-alk(en)yl-l-cysteines are revealed as main sulfur components that contain alliin. It is an advanced own preventive contraption toward microorganisms and other insults. The  $\gamma$ -glutamyl peptides are interceders that are biosynthetic for communicating cysteine sulfoxides. All garlic ordinarily includes ~1% alliin, in common with (+)-S-methyl-l-cysteine sulfoxide (methiin) and (+)-S-(trans-1-propenyl)-l-cysteine sulfoxide. S-(2-Carboxypropyl) glutathione,  $\gamma$ -glutamyl-S-allyl-l-cysteine,  $\gamma$ -glutamyl-S-(trans-1-propenyl)-l-cysteine, and  $\gamma$ -glutamyl-S-allyl-mercapto-l-cysteine are stated as available in garlic cloves. It has been seen that when garlic bulbs were preserved at cold temperatures, alliin was gathered inherently. On average, whole garlic includes until 0.9%  $\gamma$ -glutamylcysteines and till 1.8% alliin. Moreover, primary sulphur complexes and untouched garlic bulbs include few quantity of S-allyl cysteine but they do not contain allicin. In Figure 1, it is demonstrated that by catabolism of  $\gamma$ -glutamyl cysteine, S-allyl cysteine is composed. It has been informed to conduce to the well-being profits of some garlic arrangements.

Afterward, treating like mashing, cutting, masticating, or dehydration processes, allinase enzyme arises. Allinase enzyme quickly comminutes alliin which is a cytosolic cysteine sulfoxide to create alkyl alkane-thiosulfonates. These have toxic effects on cells and also has a scented as allicin. Allicin and other thiosulfonates immediately dissociate with another complexes such as diallyl trisulfide, ajoene, diallyl sulfide, dithiins, and diallyl disulfide.<sup>[4]</sup> These complexes of garlic that are bioactive ingredients and organosulfur ingredients in garlic, demonstrate health features of it. Moreover to those compounds, garlic is also symbolized according to phenolic complexes. They also show amazing features that are pharmacological. Great polyphenolic ingredient, a count of native antioxidants, and numerous dissimilar bioactive complexes can straightly and implicitly improve the production of antioxidant enzymes

that guard regular cells. Genetic unsteadiness is provided by reactive oxygen species (ROS) that contain oxygen radicals and some nonradical involutions of molecular oxygen. These molecules can diffuse into the nucleus and assault Deoxyribonucleic acid (DNA). The excess output of ROS breaks functional homeostasis. This event causes to apoptosis, so it activates the mitochondrial pathway. Elevated getting foods that are plenty in natural antioxidants or foods that give rise to the enhanced output of enzymes that shows antioxidant property. It considerably decreases the thread of a few kinds of cancer, containing breast, bladder, prostate, and colon cancers. It is also approved that garlic substances and complexes which are acquired from garlic intercept oxidative alteration of DNA, lipids, and proteins according to clean ROS and improve the production of cellular antioxidant enzymes and increase glutathione grades within regular cells. The mechanism of enhancing ROS metabolizing enzymes is linked on insignificant inducement of ROS output in cells. Besides these, depending on their manufacturing processes, trading garlic preparations vary in their sulfur-containing compounds. Depending on their producing operation ways, treated garlic includes a diversity of sulfur-including complexes rather than complexes that are discovered inherently in full garlic. In addition, scented oil-soluble complexes, less scented water-soluble organosulfur complexes were showed to be effective in diverse fields biologically. S-allyl cysteine provides declining in bioactivity as carcinogenic and also it provides collapsing in oxidative harm. The nonevaporating sulfur-including complexes that S-allyl cysteine and S-allyl mercaptocysteine has been available in lots of garlic providences, even though the ingredient alters significantly. It has been shown that garlic preparations demonstrate hypolipidemic, antiplatelet, and procirculatory effects. Throughout with other garlic preparations, aged garlic extract (AGE) has been indicated to have hepatoprotective, immune, improving, anticancer, and chemoprotective actions. In addition, AGE shows antioxidative effects, while unrefined garlic induces oxidation. Therefore, whole garlic providences cannot be accepted same in their combination, and more significantly, they may sediment.<sup>[5]</sup>

### Allicin

Garlic has a defensive molecule called as Allicin. It has a broad effect area in biology. When tissue is harmed, it has an enzyme called allinase catalyzes a reaction. By this reaction, alliin that is nonproteinogenic amino acid, has been produced. Allicin is from reactive sulfur kinds called as thiosulfonates. It carries a redox reaction with thiol groups in glutathione and proteins which are required for the effect of biological properties. Allicin is physiologically effective in cells that are microbial, mammalian, and plant. It is revealed that allicin restricts the reproduction of bacteria and fungi and also slay those cells completely dependent to dosage-related act with the inclusion of

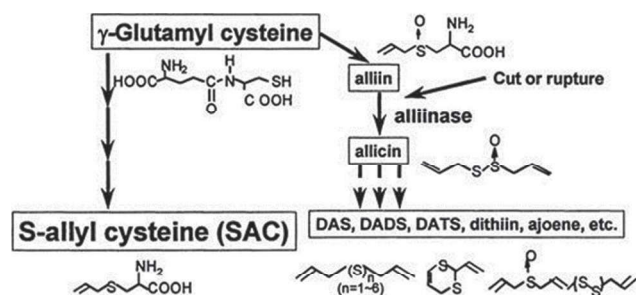


Figure 1: Garlic chemical modification

antibiotic counteractive kinds such as Methicillin-resistant *Staphylococcus aureus*. In addition, it causes cell mortality moreover diminishes cancer cell reproduction. Allicin embarrasses ovum sprouting and also diminishes root growth in herbs. The plurality of allicin's actions is relied on to be intervened over redox-linked contraptions.<sup>[6]</sup>

In general, allicin does not exist in garlic and allinase which is an enzyme that is required to activate to generate the allicin by the help of water. The mechanism is shown in Figure 2. Solvent extraction, ultrasound-assisted extraction, pressurized liquid extraction, and supercritical carbon dioxide are the mutual techniques to take out allicin. The enzymatic process, subtraction process, using organic solvent, and long extraction time are accepted as the drawbacks of these techniques. Subcritical water extraction is presented to improve the traditional treatment with the elevated refinement of yield, water exposures, an imitation of the qualities of organic dissolvent, and the enzymatic and exclusion treatment pass on in one system.<sup>[7]</sup>

### Cytotoxicity Effect Ways of Allicin

Allicin provides the mechanism of toxicity of garlic. An organosulfur complex, Allicin is set to behave like wide-spectrum antibiotics that contain effects which are bactericidal on both Gram-positive and Gram-negative bacteria. Hence, extreme input cause to death of regular bodily floral by reasoning the increment of strange microbes. Another and substantial toxicity mechanism of allicin shows similarity to that of organophosphate ingredients that is discovered in a specific plant. Allicin has an impact on the autonomic nervous system through its inhibiting activities on cholinesterase; thence, it makes the action as an indirect-acting muscarinic agonist. Symptoms such as sweating, miosis, salivation, vomiting, cognitive disturbances, coma, bronchial constriction, diarrhea and convulsion start with the presence of extra toxicity of cholinergic reseptor agonist. In investigations, allicin's parasympathetic effects cause diarrhea and fast evacuation are declared. The gastrointestinal system has been stimulated by this parasympathetic effect of allicin and that leads an increment in gastrointestinal contractility and movements. Therefore, this may cause to

hydration and further hypovolemic shock. By using allicin additions, bronchoconstriction may be very dormant, due to extra acetylcholine, which can not be destroyed withal cholinesterase, the central nervous system is effected.<sup>[8]</sup>

### Anticancer effects of garlic

In another research, the toxicity of garlic on three flagitious cancer cell lines (breast, gastric, and colon) as well a nonmalignant cell line were investigated by using (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) test. According to these test results, gastric and breast cells were delicate to garlic extract. Despite a lot of other reports, this study demonstrated that these impacts are neoplasm precise and dosage related. Significant molecules and their mechanisms are required to be explained by any more analysis on animal models and humans.<sup>[9]</sup> In the opposite, lots of investigations revealed that cancer cells show an enhanced grade of ROS that is the impact of elevated metabolic and peroxisome action, mitochondrial dysfunction, improved cellular receptor signaling, elevated action of oxidases, lipoxygenases, thymidine phosphorylase, and cyclooxygenase and oncogene action. This quality makes them, particularly to an additional rise in the number of ROS. Because of that, a little premonition of ROS generation that is good for regular cells, but it may be mortal against cancer cells. Ossama *et al.*<sup>[10]</sup> appraised allicin's cytotoxic potential on dissimilar cancer cells, especially such as lung, hepatic, prostatic, and breast cells. Predisposed allicin-loaded gelatin nanoparticles have been arranged where the ideal formulation was surface-inosculated to glycyrrhetic acid. To our knowledge, glycyrrhetic acid gelatin which is used for ligand carrier pair was not discovered before, and the advanced array provides an accomplished liver cancer therapy.

Mösbauer *et al.*<sup>[11]</sup> showed by their study, cell line Vero E6 as well Calu-3, which are human lung cell lines were reproduced in the primate kidney, allicin at bioconvenient dosages reduces infectious viral particles and viral RNA of SARS-CoV-2. The infection of SARS-CoV-2 cause to proteome changes and the impact of allicin on these host tracks has been defined. Meanwhile, the gene which

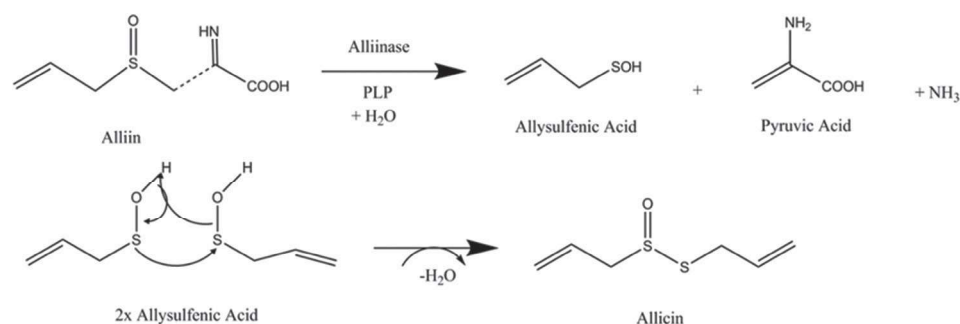


Figure 2: Biosynthesis of allicin



is stimulated with interferon has been significantly upregulated in Calu-3 cells that are transmitted by SARS-CoV-2. Thence, the impact of allicin which are antiviral and immunomodulatory were applied *in vitro* cell cultures that is assisted at the proteome grade. In another study, Rauf *et al.*<sup>[12]</sup> stated that garlic includes lots of phytoconstituents with effects on cancer and also they revealed the ingredients such as diallyl sulfide, diallyl disulfide, diallyl trisulfide, allicin, and allyl mercaptan. In according to this investigation, samples taken from the countless source of garlic as well the effect of its nanoformulations and phytochemicals on liver, breast, oral, colorectal, pancreatic and prostate cancers have been researched. The molecules in garlic which are bioactive have been discovered to diminish the diverse phases of cancer. Furthermore, ingredients of garlic also cancel the effectiveness of nitric oxide synthase and lipid peroxidation mechanism and also epidermal growth receptor, protein kinase C, and nuclear factor kappa.

### Effected cells by allicin

In an investigation, Allicin (diallylthiosulphinat) has been demonstrated to reveal antimicrobial features counter to a wide range of microbes containing pattern strains and clinical isolates of bacteria called *S. aureus*. Further, it has been concluded in that research, Allicin aims Fem enzymes to sense the reason of spaces on cell walls and simplifies fragmentation of peptidoglycans and access of hydrolases access into them. The capability of allicin to influence cell wall performs it as an ideal assembling therapy cum alcohol, including bactericides, so it is presumed to have a synergistic effect on cures together with decreasing the risk of extending resistance of antibiotics.<sup>[13]</sup> Allicin which is diallyl thiosulfinate derived from garlic, is used as a wide spectrum of antimicrobials to threat bacterial infections. Allicin can also break up diallyl disulfides and diallyl polysulfanes to seven sequential sulfur atoms with heat. Allicin and diallyl polysulfanes demonstrate a wide range spectrum of antimicrobial effect to multi-resistant bacteria, including *Bacillus subtilis*, *Escherichia coli*, *Klebsiella pneumoniae*, *S. aureus*, *Helicobacter pylori*, *Streptococcus pneumoniae* and *Pseudomonas aeruginosa* with fungi such as *Candida albicans* and parasites. Allicin can be implemented above the pulmonary way as a steam because of its volatile nature that also ensures it is appealing on antimicrobial therapy for respiratory pathogens to fight pneumonia infection. Allicin can pass through the cellular phospholipid membrane with ease as an evaporating complex. This property conduces to its antimicrobial way of act.<sup>[14]</sup>

In another study, Nakamoto *et al.*<sup>[15]</sup> summarized the impacts of hydrophobic complexes of garlic on bacteria. Diverse hydrophobic antimicrobial complexes were isolated by extracting from garlic. The structures of them are shown in Figure 3. Among these complexes, allicin has been

thought to get a main part of the biological act of garlic. However, allicin molecule is unstable and slants to be transformed into lots of complexes like diallyl polysulfides and ajoenes. These compounds were indicated to demonstrate antimicrobial activity. Therefore briefly, allicin is a typical sulfur-including complex discovered in unprocessed garlic generated from alliin and shows antimicrobial activity con to Gram-negative and Gram-positive bacteria. Borlinghaus *et al.* demonstrated that allicin exhibits dose-dependent antimicrobial activity. Allicin can stimulate apoptosis or necrosis at higher doses while biocompatible ingredients can arrange the activity of redox precision proteins and influence the signaling of cells. Allicin obviously reacts as an oxidant, especially in diet. Allicin has a mutual effect with the mechanism that is oxidative stress sensing on a few sample systems. Allicin has an amazing impact underlined by giving harm on the cellular envelope as throughput on upregulated transcripts or proteins. Allicin can form openings in the cell wall and so the plasma membrane might have been extracted. In the experiments, the impact of allicin by the property of its catching thiol reagent is indicated obviously. Furthermore, it was seen that dissimilar cell lines have been demonstrated to reply in specific mechanisms mutually. For example, *Escherichia coli* represents that allicin exhalation have not only been used for bacteriostatic impacts to avoid expansion it is also have been used to kill bacteria cells. Besides these, frequently in cultured cell investigations, plenty of times it was declared that allicin shows antitumorigenic and proapoptotic and antitumorigenic qualities counter to lots of cancer types. As also it is stated, in human cells, allicin has been showed multiple cellular destinations such as enzymes which are glycolytic and cytoskeletal proteins which are nominees due to cancer cures. Lots of research have demonstrated that significant signaling mechanisms on neoplasm cells can be connected cum allicin therapy. The great issue of targeting allicin to tumor tissues immediately needs to cope and also it is stated that cautiously checked future investigations on animal models and clinical experiments including humans are required.<sup>[16]</sup> Luo *et al.*<sup>[17]</sup> revealed that, allicin was discovered to be powerful in cancer therapies. It is an

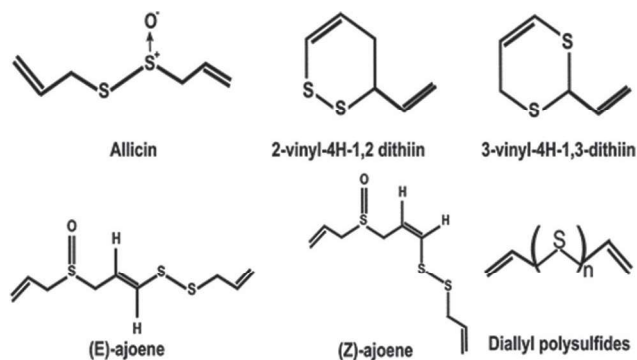


Figure 3: Hydrophobic compounds in garlic

assertive material with a wide range of biological qualities such as obstruction on the growth of fungus, virus and bacteria tested hypertension, diabetes, and chemosuppression on lots of cancers. Trials also have been demonstrated that by embarrassing the development of cancer cells, allicin can be chemopreventive to gastric cancer. Allicin shows this effect as apprehending cell cycle at mitochondria and G2/M phase intervened apoptosis which contains caspase-linked and unlinked mechanisms and endoplasmic reticulum stress. These pathways likely include arranging enzymatic action, obstructing DNA creation, cleaning independent radicals and influencing cell multiplication and also even the development of tumor. In another research, it is stated that *Mycobacterium tuberculosis* is obstructed by allicin with the mechanism of embarrassing receptors on the top and removes bacteria according to the use allicin's antimycobacterial lethal mechanisms. Researchers stated that allicin does not just destroy the bacteria withal it demonstrates an action as an immunomodulator stimulating host preventive immune reply that defends the host by reducing the side effects.<sup>[18]</sup> Furthermore, Rehman<sup>[19]</sup> indicated that garlic demonstrates a wide antibiotic act counter to Gram-positive and Gram-negative bacteria which have become durable to antibiotics and powerful against many mutual pathogenic bacteria. The antimicrobial activity of garlic is the only account of thiosulfates compound. It detoxifies the body cleansing the kidney and increase the urine flow. It was demonstrated that a few garlic components changes the activation of cancer as well they cause to inhibit the growth of tumor cells. It has been finalized from this study that allicin comes in sight to fulfill the criteria as antifungal agent. In another study, it is stated that allicin has beneficial effects on the human neuroblastoma cell line that is induced neurotoxicity with amyloid  $\beta$  in terms of cell viability, oxidative stress, and apoptosis.<sup>[20]</sup> Diverse garlic species have been demonstrated antibacterial activity on a wide spectrum area against to Gram-positive and Gram-negative bacteria such as *Klebsiella*, *Streptococcus*, *Clostridium*, *Salmonella*, *E. coli*, *Staphylococcus* and *Bacillus*. In fact, it has been seen that *Mycobacterium tuberculosis* which is acid-fast bacteria are delicate to garlic. The extracts of garlic showed powerful antifungal action, liable from the prevention of fungal development. These investigators demonstrated the eventual antibacterial and antifungal activities of garlic openly. Therefore, it would be good to utilize of uniform providences of garlic. It has been revealed that mouthwash including garlic is not cytotoxic on human gingival fibroblasts. Moreover, it was required to state the actions of garlic on oral illness.<sup>[21]</sup> In another study, it was suggested that allicin can kill cancer cells by cell cycle retention and apoptosis, and allicin kill cancer cells. Besides, according to real-time polymerase chain reaction analysis and western blot analysis protein and gene expressions were examined. Allicin encourages apoptotic cell death by the activation of caspase proteins with intrinsic pathways.<sup>[22]</sup> Jian *et al.*<sup>[23]</sup>

tried to discover a curing way of allicin in ratty bladder tumor. They concluded in their experiment that Allicin has an evident restrictive impact on bladder tumor. Perchance that impact could be linked to cytotoxicity and activation of immune reply straightly and also it is stated that for cursory bladder cancer allicin could verify to be an efficient intravesical cure agent. Ilic *et al.*<sup>[24]</sup> also studied on allicin's cytotoxic and antimicrobial activities and its conversion substances. They stated that Allicin has been demonstrated powerful action counter to proven Gram-positive and Gram-negative bacteria by minimum restrive concentration. Further, the conversion yields of allicin showed powerful antifungal and antibacterial action. However, this action was less than the action of allicin. Studies appraising allicin mostly reported cytotoxicity and apoptosis as contrary results which are intermediated by dissimilar resolution incidents such as modified genes and expression of protein or cell cycle alterations. It is revealed in three dissimilar cell lines, ajoene was more poisonous than allicin. Distinct investigators made researchments on this complex, ajoene. They watched cytotoxicity on dissimilar cell lines demonstrating varied tenderness and apoptosis.<sup>[25]</sup> Miron *et al.*<sup>[26]</sup> revealed that according to dosage adjustment, allicin was demonstrated to be poisonous in diverse mammalian cells. These investigators provided the use of this cytotoxicity property to improve a new attempt to the therapy for cancer based upon conducted production of allicin. Guo *et al.*<sup>[27]</sup> also pointed out that in traditional medicine, allicin is a great component of mashed garlic. Allicin has plural pharmacologic acts that lend to a broad spectrum of anticancer activities. To give an instance, according to the consuming intracellular grade, allicin embarrasses cell production in colon cancer cells. In addition, it has been demonstrated that the allicin molecule causes apoptosis of gastric cancer cells by a signaling mechanism called protein kinase stimulated with p38 mitogen. Furthermore, it was seen that it improves apoptosis on human renal cancer cells. It was discovered that cell multiplication and advanced cell apoptosis in oral tongue squamous cell carcinoma were blocked by allicin. In another study, it is stated that allicin has various biological effects and it has been implied that anti-inflammatory factor. It is known that in intestinal inflammation epithelial cells have a significant act.<sup>[28]</sup> Jung *et al.*<sup>[29]</sup> revealed that it was known in comparison with its antimicrobial and anti-inflammatory effects, allicin has been accelerated wound healing. Investigators aimed to evaluate that if allicin coated tracheal tube can obstruct tracheal stenosis by virtue of improving wound healing after tracheal damage. It was demonstrated that covering the tracheal tube with allicin has anti-inflammatory and antibacterial effects on harmed tracheal mucosa. Based on these studies, tracheal tube covered with allicin can be used to support physiological wound healing to prevent laryngotracheal stenosis. Catanzaro *et al.*<sup>[30]</sup> stated that the development of dissimilar kinds of tumor has been pushed

down by allicin. Especially, it was goaled that lots of signaling cells combined with cancer growth. Furthermore, further exploratory ways were summarized to define this encouraging native crop. In a study, it was stated that Tamoxifen (TAM) is broadly used on therapy for breast cancer which is related to hormones. Nevertheless, it may cause to hepatic damage. It is suggested that in cancer therapy, allicin takes a beneficial significant role like an adjuvant to TAM according to relieve liver harm. In another study, it has been demonstrated that in a dosage-linked way *in vitro*, allicin revealed an action as being poisonous to diverse mammalian cells. This cytotoxicity property of allicin was used to improve the new way for cancer therapy area conducted production.<sup>[31]</sup> Li *et al.*<sup>[32]</sup> studied on the cytotoxicity effect of allicin which was viewed on glioma cells in a dosage-linked way. The capability of the colony formation and the growth of glioma cells prevented by allicin in a time and dosage-linked way. Hence, allicin has demonstrated cytotoxicity act on glioma cells by dosage-linked way. The reproduction and apoptosis of glioma cells *in vitro* were stimulated by allicin. Therefore, in curing glioma, allicin has been indicated as a new antitumor factor. In other study, the effects of allicin on leukemic cell lines have been studied. It was seen that allicin has shown growth on these cells. According to glutathione discharge and alterations in the intracellular redox condition, the antiproliferation function of allicin mechanistic basis includes the act of mitochondrial apoptotic way.<sup>[33]</sup> Sultan *et al.*<sup>[34]</sup> stated that allicin is cytotoxic to monocytic leukemia cells (THP-1 cells) and stimulates calcium-linked hemolysis and eryptosis in human red blood cells. Investigations demonstrated that Allicin advances calcium grades in cells, reasons to oxidative stress and also induces CK1 $\alpha$ , caspase, p38, mitogen-activated protein kinase. In chemotherapy, utilization of allicin needs attentive thought, and it is stated that the inhibitors of symptosis were defined and the utilization of these agents was accordingly restricted its harmful effects on red blood cells. Jung *et al.* stated that tracheal tubes coated with allicin demonstrated antibacterial and anti-inflammatory actions for harmed mucosa that belongs to tracheal cells.<sup>[29]</sup> In another study, sulfur ingredients of the herb may diminish the growth of dissimilar protozoan parasites containing *Leptomonas colosoma*, *Giardia lamblia*, *Tetratrichomonas gallinarum*, *Crithidia fasciculata*, *Leishmania majör*, *Cryptosporidium baileyi*, *Trypanosoma* spp., *Histomonas meleagridis*, and *Plasmodium berghei*. *In vitro*, the reproduction of *L. Infantum* and *Leishmania donovani* were obstructed. It was seen that Allicin demonstrated antileishmanial effect thus *in vitro* and *in vivo* circumstances, this effect was evaluated.<sup>[35]</sup> Chen *et al.*<sup>[36]</sup> also researched the actions of allicin on *S. aureus* stimulated mastisits in rats. It is showed, according to the advancing LXR $\alpha$  effect and decreasing lipid mass nascency, allicin carried out anti-inflammatory actions counter to *S. aureus* mastitis. In

another investigation, according to determine the apoptotic and oxidative ways in human embryonic kidney cells, it was goaled to state the toxic property of allicin. It enhances reactive nitrogen and oxygen species and gives to reason to oxidative stress. Transcription of superoxide dismutase 2 and upregulation of Nrf2 were investigated on allicin's antioxidant properties. However, according to allicin's oxidant capability, this impact was covered at the IC50 value. Consequently, the fate of the cell is formed over apoptotic pathway by courtesy of killer caspases and the precursor activation. Moreover, this researchment showed that allicin-induced proapoptotic proteins which are detached from p53 in kidney cells called HEK293. Segmentation of Poly [ADP-ribose] polymerase 1 (PARP-1) and decreased production of p53 which are responsible from the disintegration of DNA in those kidney cells, pointing out that allicin has toxic effect on cells at high amount concentrations. To sum up, through this study, it was demonstrated that by the transaction of allicin the expression of p53 was downregulated meantime PARP-1 was upregulated.<sup>[37]</sup> Sheppard *et al.*<sup>[38]</sup> evaluated the chemical reactivity of allicin to look its antimicrobial effect counter to the board of pathogenic bacteria. It is restricted to apply allicin-like medications assembled with drugs which are used as antibiotics that are used for Gram-positive bacterial infections that show decreased sensibility to vancomycin. In another study, allicin's toxicity on cells and virucidal effect has been linked to the virus cell membrane and envelope. It has been demonstrated that allicin inhibits getting or grasping viruses into cells. In addition to that, diverse combination of merchant garlic yields, containing mellow garlic which was dissolved in alcohol and oil of garlic that is fermented, powder formed tablets and capsules which were stated to reveal virucidal effects of yields counter to herpes simplex virus 1 and human parainfluenza virus type 3. The effects of virucidal of merchant yields have been linked to their provision procedure. Allicin and other thiosulfinates in great amounts had been shown as the best virus cell toxicity effects.<sup>[39]</sup> Khakbaz *et al.*<sup>[40]</sup> demonstrated that the propagation of gastric cancer cells that show resistance to chemotherapy may be obstructed with mutual therapy process of 5-fluorouracil and allicin according to compress cells that express CD44. For this reason, those researches severaly encourage the utilization of allicin-established mutual chemotherapy medical treatment in lower dosages has importance in gastric cancer clients. In another research, the antimicrobial effect of allicin has been decoded and the enzyme DNA gyrase has been approved. The antibacterial effect of allicin has also demonstrated encouraging antifungal effects counter to diverse yeasts that are pathogenic. Counter to diverse herb pathogenic fungi, the broad set of effects of allicin that are antifungal were approved. In prior investigations, according to suggest a diverse effect pathways, allicin's antifungal effect has been clarified. Nevertheless, allicin's mechanism and effect pathways related to its sanitary utilities are not



still fully known. The potential effects of allicin that are antifungal counter to a diversity of pathogenic fungi were exposed by that investigation. Allicin demonstrated encouraging effects which are antifungal against pathogens that are counter to herbs. Apparently, more researchments were required to discover the cytotoxic and antimicrobial effect of allicin.<sup>[41]</sup> Wu *et al.*<sup>[42]</sup> clarified that allicin applies hepaprotective action counter to hepatic toxicity of cells that are acetaminophen-stimulated perchance owing to the molecular pathways of inhibiting endo hepatic metabolism purulent stress linked with intrahepatic TLR4/NF-κB pathway.

## Conclusions

In this comprehensive review, it is stated that allicin has lots of significant effects on diverse cell lines such as Gram-positive and Gram-negative bacteria, fungi, and yeast. The cytotoxic effects and their pathways are summarized by gathering studies that worked on that subject. More investigations of allicin which are about toxicity properties of allicin are needed to provide users security and should primarily be focalized on the assessment of toxicity effects that are long-term and genotoxicity.

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## Author contributions subject and rate:

- Esma Nur Bülbül (85%): Design the research, data collection and analyses and wrote the whole manuscript.
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