

## Garlic: A natural shield against detrimental effect of microorganisms.

Atif Liaqat<sup>1\*</sup>, Muhammad Farhan Jahangir Chughtai<sup>1</sup>, Kanza Saeed<sup>1</sup>, Adnan Khaliq<sup>1</sup>, Tariq Mehmood<sup>1</sup>, Samreen Ahsan<sup>1</sup>, Rabia Iqbal<sup>2</sup>

<sup>1</sup>Department of Food Science and Technology, Khwaja Freed University of Engineering and Technology, Rahim Yar Khan 64200, Pakistan

<sup>2</sup>Department of Food Science and Technology, Government College Women University, Faisalabad 38000, Pakistan

### Abstract

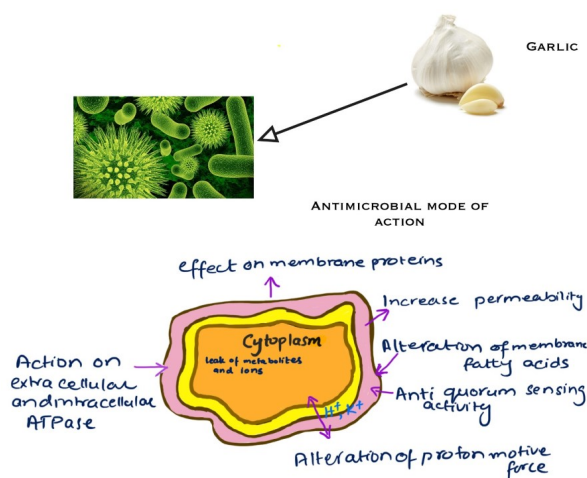
Garlic has a greater antimicrobial potential than other members of its family, due to its diverse profile of antimicrobial compounds, among which the most renowned are allicin, diallyl polysulfides and ajoenes. A unique Sulphur based compound allicin, found most abundantly in raw garlic. Exhibits antimicrobial potential and has been found equally effective against both gram-positive as well as, gram-negative bacteria. Allicin has the potential to hinder the bacterial biofilm formation, which is the leading cause of microbial resistance against antibiotic treatment leading chronic infections. Allicin eradicate biofilms by disrupting quorum sensing in microorganisms. Other bioactive compounds also exhibit similar inhibitory effects on microorganisms. These biological characteristics of garlic and garlic derived bioactive compounds can be used to intensify the effects of existing drugs and can also be used for the treatment of infections. In this review, we will summarize the effects of these bioactive compounds on pathogenic microorganism.

**Keywords:** Garlic, Allicin, Antimicrobial, Biofilm, Quorum sensing.

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### Introduction

History revealed that Central Asian soil is the origin of garlic. Afterwards, it has been expanded to west, south, and then finally in east. The mother land of garlic is said to be as Middle and West Asia. Garlic, a vegetable used for seasoning, contains a diverse range of phytochemicals having strong curative and antimicrobial characteristics. It is of great therapeutic importance and finds its place in numerous foods particularly meat ones because of its sharp odor, bitter taste, appetizer property and gives flavor to them. Bioactive compounds like allian, diallyl sulfide, alliin, ajonene render garlic their miraculous properties [1]. Polyphenols is a diverse group of complex chemical compounds with unique and extraordinary potential to act as antioxidant chain-breaker. These biologically active entities have the ability to shield against the damages caused by free radicals to DNA, cellular membrane and internal cell components. Further they exhibit antibacterial, antiallergenic, antithromobotic and anti-arthrogenic effects. These compounds have been found effective against pathogenic microorganisms like *Escherichia coli*, *Staphylococcus aureus*, *Salmonella typhi*, *Listeria monocytogenes*, *Candida albicans*, *Torulopsis glabrata*, *Vesicular stomatitis virus* responsible for numerous ailments in human body. In addition to it, these bioactive compounds reduce oxidative stress in body, preventing tumor formation, stimulate vasodilation and improve insulin secretion (Figure 1) [2].



**Figure 1.** Graphical Abstract-The effects of these bioactive compounds on pathogenic microorganism.

### Garlic: A Natural Therapeutic Herb

In the past few years, treatment of infectious diseases has become an alarming global concern due to proliferation of

drug-resistant bacteria. In order to treat infectious diseases new generation antibiotics are continuously being developed, and are part of infectious diseases treatment strategies; however, the increased microbial adaptability with extensive and uncontrolled use of such antibiotics has led to resistance in bacteria, leading to escalated drug-resistant ability attained through drug-target molecules mutations, cell membrane compositional changes, the efflux pumps overexpression, metabolizing enzymes production and biofilm formation [3]. Among all the above mention mechanisms, the biofilm comprises a large aggregated community of microbial cells protected by complex matrix, enabling the microbial cells to resist the detrimental effects of soldiers attack in our body (natural immunity) and antibiotics.

*Allium sativum* has long been used as a natural remedy against infectious maladies. Commonly known as garlic, has long been used as a natural remedy against infectious maladies [4]. Allicin is a chemically unstable compound and quickly vanishes once it comes into direct contact with human body plasma. Thus, making it troublesome for allicin to reach the target infected sites of the body in an active and effective form. Recent studies have proved that garlic derived sulfur-containing compounds, like Diallyl Disulfide (DAS2) and ajoene, restrict biofilm formation by restraining microbial communication signals (Quorum Sensing). Although, there are few studies which show that antimicrobial potential of these bioactive compounds is not as effective in comparison to the medical antibiotics utilized in clinical settings [5,6]. Numerous studies support the fact that herbs and their derivative bioactive compounds not only exert inhibitory effect on biofilm generation, but also have antibiotic activity [7].

### **Allicin**

In raw garlic, allicin is the most profound characteristic sulfur-containing compound. It is an alliin derived compound. There are numerous research references that support that allicin is a broad-spectrum antimicrobial that has been found to be effective against Gram-positive and negative bacteria. It also has deadly impact against multidrug-resistant bacteria [8]. In addition to it, allicin exhibits anti-parasitic, antiviral, and anti-fungal potential [9]. Allicin exhibits antimicrobial activity through the mechanism of S-allylmercapto recasting of thiol-containing proteins, which ultimately leads to the initiation of lethal events, like glutathione level drop, the induction of protein aggregation and crucial enzymes inactivation [10]. Vaporized allicin exhibited strong antimicrobial activity against pathogenic bacteria responsible for lungs infection [11]. Additionally, topical application of allicin has proved to effectively kill methicillin-resistant *S. aureus* stains (MRSA) leading to improved treatment of skin infection.

### **Mode of Action and Antimicrobial Properties**

A broad-spectrum biocide, allicin has been found effective in killing microbial as well as malfunctioned human cells. It is highly reactive thiosulfinate with the ability to oxidise thiol groups, the nature of the reaction is similar to the thiol-

disulfide exchange mechanism. The oxidation of thiol group results in the formation of adduct S-thioallyl and the entire procedure is regarded as S-thioallylation [12]. In stage 2, the adduct reacts with a second thiol group of protein resulting in the formation of disulfide bridge. Residual S-thioallyl transforms into allylmercaptane. High molecular weight protein thiols and low molecular weight glutathione both are targeted by S-thioallylation. S-mercaptogluthathione (thioallylated glutathione) a substrate for the enzyme glutathione reductase is unable to act as an oxidation-reduction buffer, but it recycles S-mercaptogluthathione to allylmercaptane and glutathione through an NADPH mediated reaction [13]. Consequently, the shunt pathway which is a key source of NADPH in cellular metabolism is pivotal to resist against allicin, rendering it the ability to control cellular growth [14].

According to a study [15] regarding antibacterial potential of solo garlic to evaluate it against *E. coli*, *S. aureus*, solo black garlic was found to be effective particularly when it is fermented for about a month prior use. In another 8 days storage study of ground pork, activity of garlic against *coliforms* and *Pseudomonas spp.* was evaluated and positive results of fresh garlic, dehydrated garlic and garlic essential oil were recorded [16]. In a study regarding development of polylactic acid active film containing extracts of wild garlic and its antimicrobial potential against *E. coli* and *S. aureus*, results proved that polylactic acid film with natural extracts retards the growth of foodborne pathogenic bacteria [17]. Gao et al. (2019) used traditional Chinese laba garlic and isolated three antimicrobial fractions from it. Activity was tested against *E. coli* and *S. aureus* growth and the results proved that peptides isolated from Laba garlic possess promising antimicrobial potential comparable to antibiotics [18].

### **Effects on Quorum Sensing (QS) and Biofilm Formation**

Bacteria have a barricade system also known as biofilm formation, which restrain the entry of disinfectants, host immune molecules and antibiotics into the bacterial cell membrane. This is a leading cause of induced drug-resistance of microbial cells [19]. Additionally, Quorum Sensing molecules, like N-Acyl homoserine lactone mediate intercellular communication for biofilm formation by bacterial population. In order to inhibit biofilm formation, we need to understand the underlying mechanism of microbial Quorum Sensing. Various studies have been conducted about exploration of natural products that could be an effective remedy against biofilm formation. Omid et al., have screened few components from garlic extract to identify Qs Inhibitors (QSIs) that effectively inhibited biofilm formation. Mechanism involved in the process comprises prevention of biofilm formation by hindering initial bacterial adhesion and secretion of extracellular polymeric substances [20]. In addition to regulate Quorum Sensing allicin halts the release of virulence factors [21]. Similarly, ajoene blocks virulence factors production induced by Quorum Sensing, resulting in inhibition of biofilm formation [22]. Diallyl disulfide inhibits the

*Pseudomonas spp.* biofilm formation by preventing the virulence factor production through QS regulation when used in a concentration of 0.16-1.28 mg/ml. In addition to it, diallyl disulfide hamper the formation of biofilm by stifling the QS-related genes expression [19]. Moreover, in case of *S. aureus* biofilm formation QS system, a thioester group containing peptidic compound acts as an autoinducer of process. Diallyl disulfide may also inhibit microbial communication network through reacting with the autoinducer thioester group. These bioactive compounds contribute to mitigate the detrimental impacts of these resistant microorganisms on human health and food systems, these natural compounds can be expected to transcend the problem of drug resistance development primarily caused by biofilm formation [23].

## Conclusion

Various bioactive compounds derived from garlic proved to have broad spectrum antimicrobial potential. In particular, allicin and its derivative compounds have been profoundly studied for their antimicrobial activity, which have shown the inhibitory activity against microorganisms as well as their biofilm formation *via* inhibiting Quorum Sensing. Development of stable allicin derivatives will lead to the development of exclusive compounds with distinguished antimicrobial activity, more potent impeding potential against biofilm formation and eradication of drug-resistant bacteria.

## References

- Prajapati SK, Mishra G, Malaiya A, et al. Antimicrobial Application Potential of Phytoconstituents from Turmeric and Garlic. In *Bioactive Natural Products for Pharmaceutical Applications*. Springer, Cham. 2021; 409-35.
- Chand B. Antibacterial effect of garlic (*Allium sativum*) and ginger (*Zingiber officinale*) against *Staphylococcus aureus*, *Salmonella typhi*, *Escherichia coli* and *Bacillus cereus*. *J Micro Biotech Food Sci*. 2021;2:2481-91.
- López D, Vlamakis H, Kolter R. Biofilms. *Cold Spring Harb Perspect Biol* 2010; 2: a000398.
- Fuchs AL, Weaver Jr AJ, Triplet BP, et al. Characterization of the antibacterial activity of Bald's eyesalve against drug resistant *Staphylococcus aureus* and *Pseudomonas aeruginosa*. *PloS one*. 2018; 13: e0208-108.
- Alabdullatif M, Ramirez-Arcos S. Biofilm-associated accumulation-associated protein (Aap): A contributing factor to the predominant growth of *Staphylococcus epidermidis* in platelet concentrates. *Vox sanguinis*. 2019; 114:28-37.
- Li WR, Ma YK, Shi QS, et al. Diallyl disulfide from garlic oil inhibits *Pseudomonas aeruginosa* virulence factors by inactivating key quorum sensing genes. *Appl Microbiol Biotechnol*. 2018; 102: 7555-64.
- Hasibul K, NakayamaImaohji H, Hashimoto M, et al. T. DTagatose inhibits the growth and biofilm formation of *Streptococcus mutans*. *Mol Med Rep*. 2018; 17(1): 843-51.
- Loi V, Huyen NTT, Busche T, et al. Antelmann H. *Staphylococcus aureus* responds to allicin by global S-thioallylation—role of the Brx/BSH/YpdA pathway and the disulfide reductase MerA to overcome allicin stress. *Free Radic Biol Med*. 2019; 139: 55-69.
- Getti GTM, Poole PL. Allicin causes fragmentation of the peptidoglycan coat in *Staphylococcus aureus* by effecting synthesis and aiding hydrolysis: A determination by MALDI-TOF mass spectrometry on whole cells. *J Med Microbio*. 2019; 68: 667-77.
- Müller A, Eller J, Albrecht F, et al. Allicin induces thiol stress in bacteria through S-allylmercapto modification of protein cysteines. *J Biol Chem*. 2017; 291:11477-90.
- Reiter J, Levina N, Van der Linden M, et al. Diallylthiosulfinate (Allicin), a volatile antimicrobial from garlic (*Allium sativum*), kills human lung pathogenic bacteria, including MDR strains, as a vapor. *Molecules*. 2017; 22: 1711.
- Gruhlke MC. Thiol-modification as important mode of action for allicin from garlic (*Allium sativum*). In *Multidisciplinary Digital Publishing Institute Proceedings*. 2019; 11: 27.
- Horn T, Bettray W, Slusarenko AJ et al. S-allylmercaptogluthathione is a substrate for glutathione reductase (EC 1.8. 1.7) from yeast (*Saccharomyces cerevisiae*). *Antioxidants*. 2018; 7: 86.
- Leontiev R, Hohaus N, Jacob C, et al. A comparison of the antibacterial and antifungal activities of thiosulfinate analogues of allicin. *Sci Rep*. 2018; 8:1-19.
- Setiyoningrum F, Herlina N, Afiati F, et al. Antibacterial activities of Solo garlic. In *IOP Conference Series: Materials Science and Engineering*. 2021 Jan; 1011: 012067. IOP Publishing.
- Kunová S, Lopašovský L, Haščík P, et al. Microbiological Quality of Ground Pork during Storage after Application of Garlic. *Scientific Papers: Animal Science & Biotechnologies*. 2019; 52.
- Radusin T, Torres-Giner S, Stupar A, et al. Preparation, characterization and antimicrobial properties of electrospun polylactide films containing *Allium ursinum* L. extract. *Food Packag Shelf Life*. 2019; 21, 100357.
- Gao X, Chen Y, Chen Z, et al. Identification and antimicrobial activity evaluation of three peptides from laba garlic and the related mechanism. *Food Funct*. 2019; 10: 4486-96.
- Høiby N. A short history of microbial biofilms and biofilm infections. *Apmis*. 2017; 125: 272-5.
- Ranjbar-Omid M, Arzanlou M, Amani, et al. Allicin from garlic inhibits the biofilm formation and urease activity of *Proteus mirabilis* in vitro. *FEMS microbio letters*. 2015;362:fnv049.
- Xu Z, Zhang H, Yu H, et al. Allicin inhibits *Pseudomonas aeruginosa* virulence by suppressing the rhl and pqs quorum-sensing systems. *Can J Microbiol*. 2019; 65: 563-74.

22. Jakobsen TH, Warming AN, Vejborg RM, et al. A broad range quorum sensing inhibitor working through sRNA inhibition. *Sci Rep.* 2017; 7: 1-12.
23. Vasquez JK, Tal-Gan Y, Cornilescu G, et al. Simplified AIP-II peptidomimetics are potent inhibitors of *Staphylococcus aureus* AgrC quorum sensing receptors. *Chembiochem: A European j chem bio.* 2017; 18: 413.

**\*Correspondence to**

Atif Liaqat

Department of Food Science and Technology,  
Khwaja Freed University of Engineering and Technology,  
Rahim Yar Khan 64200, Pakistan.  
E-mail: [atif.liaqat@kfueit.edu.pk](mailto:atif.liaqat@kfueit.edu.pk)