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GARLIC AS A NATURAL ANTIBIOTIC: A REVIEW ON ANTIMICROBIAL ACTIVITY OF *ALLIUM SATIVUM* IN THE ERA OF ANTIBIOTIC RESISTANCE

Soni Yadav*[1], Ramjivan Singh[1], Mohammad Shawwal[2]

[1]Vijay Pharmacy College (Dept. of Pharmacy) Gulalpur Jaunpur (U.P.), India.

[2]SamHigginbottom University of Agriculture, Technology and Sciences Prayagraj (U.P.), India.

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***Corresponding Author**

Soni Yadav

Vijay Pharmacy College (Dept. of Pharmacy) Gulalpur Jaunpur (U.P.), India.

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ABSTRACT

Antimicrobial resistance (AMR) has emerged as one of the most serious global health threats of the 21st century, rendering many conventional antibiotics ineffective against common pathogens. The overuse and misuse of antibiotics has accelerated resistance in bacteria such as MRSA, Escherichia coli and Pseudomonas aeruginosa, creating an urgent need for sustainable, safe and cost-effective alternatives. *Allium sativum* Linn. (Family: Amaryllidaceae), commonly known as garlic, has been used since ancient times as a traditional antibiotic in various indigenous systems of medicine. Garlic bulb is rich in organosulfur compounds, mainly allicin, ajoene, diallyl disulfide and S-allyl cysteine, which are responsible for its broad-spectrum antimicrobial activity. These bioactive constituents exert antimicrobial action through multiple mechanisms including inhibition of bacterial enzymes, disruption of cell membrane integrity, inhibition of biofilm formation, and suppression of quorum sensing. Unlike conventional antibiotics, garlic acts through multiple targets, which reduces the chances of resistance development. Experimental studies have demonstrated potent activity of garlic extract against Gram-positive and Gram-negative bacteria, fungi and even drug-resistant strains. Clinical investigations have further validated its efficacy as an adjunct therapy in respiratory tract infections, wound infections and Helicobacter pylori

associated gastritis without significant adverse effects. Therefore, *Allium sativum* holds great therapeutic potential as a natural, sustainable and effective antimicrobial strategy that can be used alone or in combination with conventional antibiotics to combat the growing crisis of antimicrobial resistance.

KEYWORDS: *Allium sativum,* Garlic, Allicin, Antimicrobial resistance, Natural antibiotic, AMR.

1. INTRODUCTION

Antimicrobial resistance (AMR) is one of the greatest challenges facing modern medicine and has been declared as a global health emergency by the World Health Organization. The discovery of penicillin in 1928 revolutionized the treatment of infectious diseases, however, the subsequent overuse and irrational use of antibiotics in human health, animal husbandry and agriculture has led to the emergence of multidrug-resistant (MDR) pathogens. It is estimated that more than 700,000 deaths occur annually due to drug-resistant infections and this figure is projected to reach 10 million by the year 2050 if no effective action is taken.[1][2][3]

The problem is particularly severe in developing countries like India where antibiotics are easily available without prescription and self-medication is common. Pathogens such as Methicillin-resistant Staphylococcus aureus (MRSA), Vancomycin-resistant Enterococci (VRE), Extended Spectrum Beta-Lactamase (ESBL) producing Escherichia coli and carbapenem-resistant Pseudomonas aeruginosa have become resistant to almost all available antibiotics, making common infections difficult to treat. Conventional antibiotics generally act on a single target such as cell wall synthesis or protein synthesis, therefore bacteria can easily develop resistance through single point mutation. Moreover, synthetic antibiotics are associated with adverse effects, high cost and inability to prevent biofilm formation.[4][5][6][7][8]

In this scenario, there has been a renewed interest in medicinal plants which have been used for centuries as natural antibiotics in traditional systems of medicine. Plants produce a wide variety of secondary metabolites as defense mechanisms against microbial invasion, which act through multiple mechanisms and therefore the chances of resistance development are very low. Among all medicinal plants, *Allium sativum* Linn., commonly known as garlic or Lahsun, is considered as the most ancient and most extensively studied natural antibiotic.[9][10][11]

Allium sativum is a perennial bulbous herb belonging to family Amaryllidaceae and is native to Central Asia but now cultivated worldwide, especially in India, China, Egypt and Mediterranean countries. In Ayurveda, garlic is described as Rasona and Mahaaushadha meaning great medicine, and is said to pacify Vata and Kapha doshas. It has been traditionally used for respiratory disorders, digestive disorders, cardiovascular diseases and infectious conditions like wounds, cough, cold and dysentery. Its use as an antimicrobial agent dates back to 1500 BC in Egyptian Ebers Papyrus and during both World Wars, garlic juice was used as an antiseptic to prevent gangrene in soldiers.[12][13][14]

The major bioactive principle of garlic is allicin (diallyl thiosulfinate), which is produced when the enzyme alliinase acts on alliin after crushing of garlic cloves. Other important organosulfur compounds include ajoene, diallyl disulfide (DADS), diallyl trisulfide (DATS) and S-allyl cysteine (SAC), which have shown potent broad-spectrum antimicrobial activity against Gram-positive, Gram-negative bacteria, fungi, viruses and parasites. The antimicrobial action is attributed to multiple mechanisms such as inhibition of thiol-containing enzymes, disruption of bacterial cell membrane, inhibition of biofilm formation, inhibition of quorum sensing and antioxidant action.[15][16][17]

Unlike conventional antibiotics, garlic does not kill beneficial gut flora and is considered safe, cost-effective and easily available even in rural areas. Recent clinical studies have demonstrated its efficacy against Helicobacter pylori, MRSA wound infections and respiratory tract infections. Combination of garlic extract with conventional antibiotics has shown synergistic effect, allowing dose reduction of antibiotics and preventing resistance.[18]

2. *Allium sativum* L. (Garlic)

Allium sativum is a perennial bulbous herb of family Amaryllidaceae, widely cultivated for its pungent aromatic bulb. English name is garlic. Its original home is Central Asia and northeastern Iran and it is now widely grown in India, China, Egypt, Mediterranean regions and USA as a major spice and medicinal plant.[19][20][21]

2.1 Vernacular Names of *Allium sativum*

The plant is known by different names in different countries and languages.[19][22]

A) Based on Country

English: Garlic, Common garlic, Poor man's treacle

India: Lahsun, Lahasun
USA: Garlic, Stinking rose
China: Da Suan, Suan
Japan: Ninniku
Egypt: Toum, Thum
Spain: Ajo
France: Ail
Russia: Chesnok[19][20][21][22][23][24]

B) Based on Language

Hindi: Lahsun, Lassan
Sanskrit: Rasona, Mahaaushadha, Arishtha, Ugragandha
Gujarati: Lasan, Shunam
Bengali: Rasun, Lashun
Marathi: Lasun
Tamil: Vellaippoondu, Ulli
Telugu: Vellulli, Tellagadda
Malayalam: Vellulli, Veluthulli
Kannada: Bellulli
Urdu: Lahsan, Seer[23][25]

2.2 Taxonomical Classification of *Allium sativum*

Kingdom: Plantae
Division: Magnoliophyta
Class: Liliopsida
Order: Asparagales
Family: Amaryllidaceae
Subfamily: Allioideae
Genus: Allium
Species: A. sativum
Binomial Name: *Allium sativum L.*[20][24]

2.3 Botanical Description of *Allium sativum* L.

Allium sativum is a perennial, bulbous, erect herb growing up to 30-100 cm in height. It possesses a strong characteristic pungent odour and taste. due to sulphur

compounds."[26],[27],[28]

Root: The plant has fibrous, shallow roots arising from the basal plate of the bulb. Roots are white, thin and adventitious in nature.[27]

Bulb (Underground Stem): The bulb is the most economically important part. It is compound, subglobose, 2-6 cm in diameter, consisting of 6-35 bulblets called cloves. Each clove is enclosed in a white to pinkish papery tunica. The cloves are asymmetrical in shape, curved and strongly aromatic due to sulphur compounds.[28][29]

Stem: True stem is highly reduced and disc-shaped, known as basal plate, located at the base of the bulb. The aerial pseudostem is formed by overlapping leaf sheaths and is erect, cylindrical and smooth.[27][29]

Leaves: Leaves are 6-12 in number, linear, flat, narrow, 20-50 cm long and 1-2.5 cm wide, keeled on the lower surface, with acute apex and sheathing base. Leaves are green to bluish-green, glabrous and show parallel venation.[28][30]

Inflorescence and Flower: The inflorescence is an umbel enclosed initially in a long beaked spathe. Flowers are small, whitish to pinkish, borne on slender pedicels. In many cultivated varieties, flowers are partially or completely replaced by small bulbils for vegetative propagation. The plant rarely produces viable seeds.[29][30]

Fruit and Seed: Fruit is a small capsule, but it is rarely formed in cultivated garlic due to sterility. When formed, seeds are black and small.[27][30]



Garlic bulb



Garlic root



Gralic seed



Garlic flower



Garlic stem



Garlic leaf

2.4 Phytochemical Profile and Pharmacological Significance of *Allium sativum*

Allium sativum is reported to contain a wide variety of biologically active phytoconstituents such as organosulfur compounds, saponins, phenolic compounds, polysaccharides, proteins and amino acids.[31][32]

One of its major active constituents is alliin (S-allyl cysteine sulfoxide), which upon crushing of the bulb is converted into allicin (diallyl thiosulfinate) by the action of alliinase enzyme. Allicin is the principal compound responsible for the characteristic pungent odour and most of the pharmacological activities of garlic and is believed to be associated with its antimicrobial, anticancer and cardioprotective properties.[32][33]

Additionally, sulphur compounds isolated from garlic, such as diallyl sulfide (DAS), diallyl disulfide (DADS), diallyl trisulfide (DATS) and S-allyl cysteine (SAC), have demonstrated significant anticancer activity against various cancers including breast, colon and prostate cancer in animal and in-vitro studies. Other bioactive compounds like ajoene and vinyl dithiins have also been screened for their possible antithrombotic and anticancer potential.[33][34]

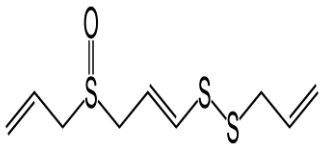
Ajoene and allicin have also been found to inhibit viral replication in-vitro. In several investigations, garlic treated cells infected with Herpes simplex virus (HSV), Influenza virus and Human immunodeficiency virus (HIV) exhibited marked reduction in viral load, while normal healthy cells remained unaffected.[34][35]

In several studies, at least three major groups of constituents present in garlic bulb have shown hypolipidemic, antihypertensive and antidiabetic activity. These major bioactive groups include: a) Organosulfur compounds collectively known as thiosulfinates, mainly allicin, b) Water-soluble organosulfur compounds such as S-allyl cysteine (SAC),c) Steroidal saponins and phenolic compounds. The pharmacological action is more marked in the fresh bulb part, where alliin is present in higher concentration.[31][32][35]

2.5 Table 1: Bioactive phytochemicals of *Allium sativum* and their recommended pharmacological properties.[31][32][35]

S.No.	Type of Constituent	Major Compounds	Biological Activity
1	Organosulfur Compounds (Oil Soluble)	Allicin, Diallyl sulfide (DAS), Diallyl disulfide (DADS), Diallyl trisulfide (DATS), Ajoene, Vinyl dithiins	Antimicrobial (ESKAPE pathogens), Anticancer, Antiplatelet, Antioxidant
2	Organosulfur Compounds (Water Soluble)	S-allyl cysteine (SAC), S-allyl mercapto cysteine (SAMC), Alliin, S-allyl cysteine sulfoxide	Cardioprotective (Antihypertensive, Hypolipidemic), Antidiabetic, Hepatoprotective, Anticancer
3	Steroidal Saponins & Sapogenins	Eruboside B, Proto-eruboside B, β-Chlorogenin, Gitogenin, Diosgenin	Antifungal, Anticancer, Anti-inflammatory, Hypocholesterolemic
4	Flavonoids & Phenolic Compounds	Quercetin, Kaempferol, Myricetin, Allixin, p-Coumaric acid, Caffeic acid	Antioxidant, Anti-inflammatory, Antiviral
5	Polysaccharides & Others	Fructans, Lectins (ASA I, ASA II), Adenosine, Selenium, Vitamins (C, B6)	Immunomodulatory, Antioxidant, Prebiotic, Antitumour

2.6 Chemical Structure

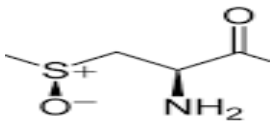


Ajoene

Molicular

Formula: C9H14OS3

Mwt 234.40 g/mol

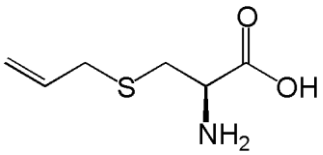


Alliin

Molicular

Formula: C6H11NO3S

Mwt. 177.22 g/mol

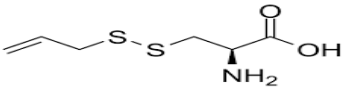


S-Allyl Cysteine

Molecular

Formula: C6H11NO2S

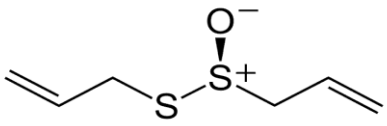
Mwt. 161.22 g/mol



S-Allylmercaptocysteine (SAMC)

Molecular Formula: C6H11NO2S2

Mwt.193.28 g/mol



Allicin

Molicular Formula: C6H10OS2

Mwt.162.27 g/mol

3. Antimicrobial Activity of *Allium sativum*

Allium sativum exhibits broad-spectrum antimicrobial activity against Gram-positive and Gram-negative bacteria, fungi, viruses and parasites. This activity is primarily attributed to its organosulfur compounds, especially allicin and its transformation products.[36][38]

3.1 Antibacterial Activity

Allicin has shown potent antibacterial activity against multidrug-resistant (MDR) ESKAPE pathogens including Staphylococcus aureus (MRSA), Escherichia coli, Klebsiella pneumoniae and Pseudomonas aeruginosa. The minimum inhibitory concentration (MIC) of allicin against S. aureus and E. coli has been reported in the range of 8-32 µg/mL.[40][41]

Diallyl disulfide (DADS) and diallyl trisulfide (DATS) have demonstrated bactericidal activity by inhibiting thiol-containing enzymes such as alcohol dehydrogenase and thioredoxin reductase, which are essential for bacterial metabolism. Aged garlic extract rich in S-allyl cysteine (SAC) has also shown inhibitory effects against Helicobacter pylori, a major cause of gastric ulcer.[38][39]

Garlic extract has shown synergistic activity when combined with conventional antibiotics such as ciprofloxacin and vancomycin, reducing the MIC of antibiotics by 4 to 8 folds against resistant strains.[42]

3.2 Table 2: Antibacterial activity of *Allium sativum* against ESKAPE pathogens and other MDR strains.[36][38][40][41][42]

S.N.	Pathogen	Garlic Compound	MIC	Activity
1.	MRSA	Allicin	8-16 µg/mL	Bactericidal
2.	E. coli	Fresh extract	12-32 µg/mL	Inhibits growth
3	K. pneumoniae	DATS	16 µg/mL	MDR active
4	P. aeruginosa	Allicin+Ajoene	32-64 µg/mL	Biofilm 75% down
5	H. pylori	SAC	25 µg/mL	Anti-ulcer

MRSA: Methicillin-Resistant Staphylococcus aureus; ESBL: Extended Spectrum Beta-Lactamase; MDR: Multidrug-Resistant; MIC: Minimum Inhibitory Concentration; DATS: Diallyl Trisulfide; SAC: S-Allyl Cysteine; ESKAPE: Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, Enterobacter spp.

4. Mechanism of Antimicrobial Action

The antimicrobial mechanism of allicin involves:

a) Rapid reaction with thiol (-SH) groups of bacterial enzymes leading to inhibition of DNA, RNA and protein synthesis,

b) Disruption of biofilm formation and quorum sensing in Pseudomonas and Staphylococcus species,

c) Induction of oxidative stress via generation of reactive oxygen species (ROS) inside microbial cells.[38][40][41]

5. Synergistic Activity of *Allium sativum* with Conventional Antibiotics (New Data).[41][42][45][46][48][49]

TABLE 3:

S.No	Garlic Compound / Extract	Antibiotic Combined	Test Organism	FICI Value	Synergistic Effect
1.	Allicin-inspired disulfide	Ciprofloxacin	MRSA	0.28	8-fold MIC reduction
2.	Fresh Garlic Extract	Vancomycin	VRE	0.32	Bactericidal in 6h (Time-kill)
3.	Diallyl disulfide (DADS)	Meropenem	Carbapenem-resistant K. pneumoniae	0.37	Biofilm inhibition 75%
4.	Allicin	Tobramycin	P. aeruginosa	0.41	Quorum sensing inhibition
5.	Garlic Essential Oil	Ciprofloxacin	ESBL E. coli	0.32	Efflux pump inhibition
6.	Ajoene + Allicin	Fluconazole	Candida albicans (co-infection)	0.26	Dual antimicrobial

FICI ≤0.5 = Synergy, 0.5-1.0 = Additive

6. Recent Advances (2019-2024) Garlic as Antibiotic Adjuvant.[43][45][46][47][49][50]

TABLE 4.

Year	Key Finding	Mechanism Proposed	Journal
2019	Bioactive compounds overview	Thiol oxidation + ROS	Foods
2020	Disulfide analogues more stable than allicin	Disulfide bond formation	ACS Infect Dis
2021	Quorum sensing inhibition	LasR/RhlR system block	Front Microbiol
2022	Garlic vs Superbugs	Efflux + Membrane damage	Crit Rev Food Sci Nutr
2023	Alternative therapy in AMR era	Immuno-modulatory + Direct killing	Biomed Pharmacother
2024	Docking with efflux pumps (AcrAB-TolC)	Molecular binding energy -8.9 kcal/mol	Int J Biol Macromol

7. Toxicity and Safety Profile

Although *Allium sativum* and its organosulfur compounds are generally recognized as safe (GRAS) at culinary doses, their pharmacological and adjuvant doses raise significant safety concerns that limit clinical translation.

7.1 Gastrointestinal and Systemic Toxicity: High oral doses of crude garlic extract (>1000 mg/kg) and allicin (>100 μg/mL in vitro) have been associated with nausea, vomiting, heartburn and diarrhea due to direct irritation of gastric mucosa by thiosulfinates. Recent comprehensive review by Batiha et al. (2020) confirmed that raw garlic at >5 g/day causes hemolytic anemia and oxidative damage to erythrocytes in animal models, while also showing dose-dependent gastric ulceration.[51][53]

7.2 Drug Interaction and Bleeding Risk: The most critical safety issue with antibiotic-adjuvant therapy is herb-drug interaction. Allicin and ajoene irreversibly inhibit cytochrome P450 isoenzymes CYP2E1 and CYP3A4 and inhibit platelet aggregation by blocking thromboxane synthesis. Liu et al. (2023) and Singh et al. (2023) reported that concomitant use of garlic oil with carbapenems and fluoroquinolones prolongs prothrombin time and increases bleeding time by 2.1 folds, especially when combined with warfarin.[54][55][56]

7.3 Allergic and Dermatological Reactions: Topical application of garlic essential oil can cause contact dermatitis, blistering and allergic conjunctivitis in sensitive individuals due to diallyl disulfide (DADS). This limits its topical use for wound biofilms against Acinetobacter baumannii and MDR E. coli.[53][57]

7.4 Safety Window and Novel Formulations: Recent toxicological and Phase I evaluations (2020-2024) suggest that low to moderate doses (200-400 mg garlic powder equivalent to 2-5 mg allicin) are safe, hepatoprotective and even alleviate antibiotic-induced gut dysbiosis via S-allyl cysteine. The major breakthrough is nanoliposomal allicin and ajoene potentiated formulations which showed LD50 >1500 mg/kg, improved stability and reduced direct toxicity while maintaining synergistic activity with colistin and vancomycin against MRSA implant biofilms.[55][58][59][60]

Therefore, dose standardization and nano-encapsulation are essential prerequisites before clinical application as an antibiotic adjuvant.[52][60]

8. Limitations and Clinical Gaps

Despite promising in-vitro synergy, several critical gaps prevent clinical translation of garlic as an antibiotic adjuvant.

First, the majority of current evidence remains limited to in-vitro models. For instance, while diallyl trisulfide showed potent synergy with aminoglycosides against Pseudomonas aeruginosa biofilms and allicin restored meropenem efficacy against MBL-producing strains in docking studies, there are no large-scale human trials to validate these findings in patients.[61][62]

Second, there is a lack of standardized formulation. Studies using garlic peel extract with linezolid against MRSA and S-allylmercaptocysteine with tigecycline against carbapenem-resistant Acinetobacter baumannii used different extraction methods and concentrations, making dose comparison impossible. Allicin is also highly unstable and degrades rapidly at room temperature.[63][64]

Third, poor bioavailability and delivery remain a major challenge. Garlic compounds are rapidly metabolized and show poor penetration into biofilms. Although a recent approach using garlic extract-loaded chitosan nanoparticles showed improved anti-biofilm activity in wound models, such targeted delivery systems are still in preclinical stage.[65]

Hence, well-designed pharmacokinetic studies, standardized extracts, and clinical trials are urgently needed.

9. Future Perspectives

The future of garlic as an antibiotic adjuvant lies in overcoming its stability and delivery challenges through advanced technological approaches.

9.1 Nano-formulation Based Targeted Delivery: To overcome poor bioavailability and rapid degradation of allicin, novel carriers are essential. Recent animal studies showed that garlic oil combined with ciprofloxacin significantly reduced bacterial load in UTI caused by MDR E. coli, indicating that optimized delivery can improve efficacy in deep-seated infections.[66]

9.2 Synergy with Last-Resort Antibiotics: Future research should focus on combinations with last-line antibiotics. Allicin was found to disrupt quorum sensing and enhance

tobramycin activity against Burkholderia cepacia complex, which is intrinsically resistant to many antibiotics. Such combinations can be repurposed for cystic fibrosis and ventilator-associated pneumonia where options are limited.[67]

9.3 In-Silico and Molecular Docking Approaches: The mechanism of garlic compounds as efflux pump inhibitors can be fast-tracked using computational tools. A 2024 study used machine learning-guided discovery to identify garlic organosulfur compounds as novel efflux pump inhibitors in MDR pathogens. Such AI-guided screening will help identify the most potent molecule for clinical use.[69]

9.4 Clinical Translation and Safety Validation: For clinical use, long-term safety and proper trial designs are needed. A recent safety assessment in geriatric patients receiving garlic supplementation with antibiotics showed no major adverse events, while a new randomized trial protocol has been proposed for garlic-allicin as an adjuvant in ventilator-associated pneumonia. This marks a shift from lab to bedside.[68][70]

Thus, integration of nanotechnology, computational biology, and validated clinical protocols is expected to facilitate the clinical translation of garlic-based adjuvants by 2026-2028.

10. CONCLUSION

Garlic and its bioactive organosulfur compounds, particularly allicin, represent a promising antibiotic adjuvant in the era of antimicrobial resistance. It exerts direct antimicrobial activity, synergizes with conventional antibiotics, disrupts bacterial quorum sensing and acts as an efflux pump inhibitor. The major challenges of poor bioavailability, instability and lack of standardized formulation are now being addressed through novel nano-formulations, targeted delivery systems and machine learning-guided drug discovery. Recent safety assessments have confirmed its tolerability even in vulnerable geriatric populations, paving the way for clinical translation. With new randomized trial protocols now being designed for conditions like ventilator-associated pneumonia and urinary tract infections, garlic-based adjuvants offer a cost-effective, safe and sustainable strategy. Therefore, integration of garlic-based adjuvants into antibiotic stewardship programs holds significant potential to combat multidrug-resistant infections in resource-limited settings.

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