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Allicin Against Infection: Evaluating Garlic's Role in UTI Prevention and Treatment

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Abstract: *Urinary tract infections (UTIs) are among the most common microbial diseases worldwide, especially in women. The increasing occurrence of antibiotic-resistant bacteria such as Escherichia coli, Proteus mirabilis, and Klebsiella pneumoniae has made treatment more complicated and created a need to explore natural therapeutic alternatives. Garlic (Allium sativum), a traditional medicinal plant, has been recognized for centuries for its strong antibacterial and healing properties. The major active compound in garlic, allicin, is a sulphur containing molecule that exhibits antibacterial, antifungal, and antiviral effects. Allicin works by inhibiting bacterial enzyme activity, damaging the cell membrane, and inducing oxidative stress, all of which contribute to the destruction of microbial cells. Several in vitro studies have confirmed that garlic extract effectively inhibits major UTI-causing bacteria, even those resistant to conventional antibiotics. Additionally, garlic prevents bacterial adhesion to bladder epithelial cells and inhibits biofilm formation, which helps reduce the recurrence of infections. Moreover, when garlic is used in combination with traditional antibiotics; it enhances their antibacterial effects and reduces the required dosage. Because of its natural origin, safety, affordability, and easy availability, garlic is considered a promising natural alternative for the prevention and treatment of urinary tract infections. Further research, especially clinical studies, is needed to determine the standardized dosage, formulations, and long-term safety of garlic-based therapies. The inclusion of garlic in modern medical treatment could provide an effective and sustainable strategy to combat urinary tract infections and antibiotic resistance*

Keywords*:* Allicin, Garlic (Allium sativum), Urinary Tract Infection (UTI), Antimicrobial activity, Biofilm inhibition, Antibiotic resistance

I. INTRODUCTION

Urinary tract infection (UTI) represents the most prevalent bacterial infection primarily affecting women, with approximately 50% experiencing at least one episode during their lifetime [1]. It is an infection affecting any part of the urinary system, including the kidneys, ureters, bladder, or urethra, is called a Urinary Tract Infection (UTI). It represents the second most prevalent infectious disease in community healthcare settings. Urinary tract infections (UTIs) are classified as uncomplicated or complicated. Their pathogenesis is multifactorial, involving host biological and behavioral factors, along with characteristics of the infecting uropathogens [2]. UTIs are more common in women than men due to the shorter female urethra, which promotes bacterial ascent into the bladder, and the influence of gastrointestinal pathogen colonization in the vaginal area [3]. Repeated urinary tract infections (RUTIs) are characterized by three or more episodes within one year or two or more episodes within six months. It is estimated that 20–30% of women who experience a UTI develop recurrent infections, and about 25% of these progress to frequent recurrences. Urinary tract infections are usually caused by bacteria, most often Escherichia coli (E. coli). Common signs include needing to urinate often and urgently, burning or pain while urinating, urine that appears cloudy or has a strong smell and pain in the abdominal pain [4]. In Japan, herbal medicines are more popular than conventional pharmaceuticals, with garlic being widely used for its therapeutic benefits, particularly in urinary tract infections

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(UTIs). The ureter transports urine from the renal pelvis to the bladder through peristaltic waves, while age-related changes in the kidneys lead to reduced size, diminished blood flow, and loss of glomerular function. By the age of 80, kidney mass decreases by nearly one-third, renal blood flow and filtration decline significantly, and about 40% of glomeruli become non-functional. These changes, along with reduced bladder capacity and weaker muscles, increase the risk of kidney diseases, dehydration, and UTIs in the elderly population. Pregnant women may transmit UTIs to infants and children, while postmenopausal women are at higher risk of infection due to estrogen deficiency, characterized by an increased colonization of Escherichia coli and a decline in Lactobacillus spp. within the vaginal flora.

Since ancient times, medicinal plants have been esteemed as a divine gift to humanity due to their vital role in the prevention and treatment of numerous severe diseases and disorders. Medicinal plants such as clove (Syzygium aromaticum), cardamom (Elettaria cardamomum), ajwain (Carum copticum), black pepper (Piper nigrum), peppermint (Mentha piperita), and ginger (Zingiber officinale) are widely used for the treatment of various diseases and physiological disorders. Their volatile oils possess significant therapeutic properties and are also incorporated into pharmaceutical and personal care products, including tablets, creams, and dental care formulations such as mouthwashes. In developing countries, including Togo, medicinal plants are widely employed, especially in rural areas; as a key resource for addressing public health issues. Despite their extensive use, information on the abundance, distribution, and accessibility of these plants remains scarce and poorly documented. Among these, garlic stands out as one of the oldest cultivated horticultural crops in the Old World. Historical records indicate that garlic was referenced in Egyptian and Indian civilizations around 5,000 years ago, and there is compelling evidence of its use by the Babylonians approximately 4,500 years ago[5]. It is widely utilized for the treatment and management of various diseases and pathophysiological conditions. Allium sativum (garlic), belonging to the Liliaceae family, has been valued for centuries across diverse cultures worldwide for its distinctive flavor and therapeutic properties. The edible bulb is widely utilized as a culinary spice, condiment, and dietary supplement [6].Traditionally, garlic has been employed in the management of bacterial infections, including piles, cough, and rheumatism, as well as in mitigating tumours, cardiovascular disorders, and age-related ailments [7].Garlic is well known for its antibacterial, antifungal, and antiviral properties [8].

Allicin, a flavour molecule with a number of pharmacological characteristics, including antibacterial effectiveness, is found in Allium sativum, also known as garlic. Numerous physiological activities in microorganisms, including RNA synthesis and lipid biosynthesis, are inhibited by allicin. Because it inhibits acetyl-CoA synthase, allicin also prevents acetate from being incorporated into fatty acid biosynthesis. This is important because in bacterial systems, allicin reversibly inhibits all enzymes that convert acetate to acetyl-CoA through non-covalent binding [9]. Garlic's antibacterial properties are also linked to the suppression of microbes' thiol LL-containing enzymes [10].

"This review critically examines the available evidence on garlic in the management and avoidance of UTIs, with particular emphasis on the antimicrobial activity of allicin and its potential clinical applications."

CHEMICAL COMPOSITION OF ALLICIN:

Allium sativum, or garlic, is a great source of vital nutrients and bioactive substances. Proteins (6.3%), carbs (29%), minerals (0.3%), essential oils (0.1–0.4%), lipids, vitamin C, and sulfur-containing substances make up its chemical composition. Ascorbic acid, or vitamin C, is especially abundant in green garlic. Its distinctive scent and several medicinal qualities are mostly caused by the presence of sulphur compounds like allicin.

Garlic has a variety of biological properties, such as antiviral, antifungal, antibacterial, and anti-protozoal properties. Additionally, it exhibits anticancer, antioxidant, and cardioprotective qualities, contributing to its significant medicinal value. Apart from its pharmaceutical importance, the sticky juice from garlic bulbs is used as an adhesive for repairing glass and porcelain, while garlic-derived polysulfides are employed as natural insecticides and pesticides to protect plants from infections and insect damage.

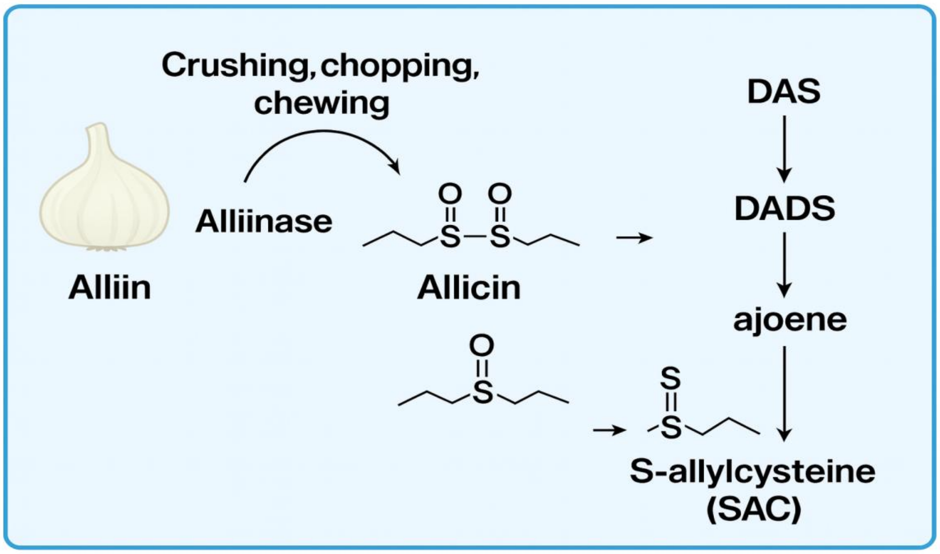

Fig. 1.1: Chemical Composition of Allicin

Garlic (Allium sativum) contains a sulfur-containing compound called alliin. When garlic is crushed, chopped, chewed, dried, or exposed to water or microbes, the enzyme alliinase converts alliin into allicin, which makes up most of garlic's active thiosulfinates.

Allicin is highly reactive and unstable, and it quickly breaks down into other active sulfur compounds, such as diallyl sulfide (DAS), diallyl disulfide (DADS), dithiins, and ajoene. At the same time, γ-glutamyl cysteine is converted into S-allylcysteine (SAC) via a separate pathway. These compounds together give garlic its antimicrobial, antioxidant, and therapeutic properties. The formation of allicin and its derivatives is key to garlic's ability to fight bacteria, fungi, and viruses, making it a promising natural agent for the prevention and treatment of urinary tract infections (UTIs) [11].

Compound	Type	Key Function
Allicin	Thiosulfinate	Antimicrobial, antioxidant, therapeutic
Diallyl Disulfide (DADS)	Organosulfur	Antimicrobial, cardiovascular benefits
Diallyl Trisulfide (DATS)	Organosulfur	Antimicrobial, anticancer potential
Ajoene	Sulfur compound	Antithrombotic, antimicrobial
Dithiins	Sulfur compound	Antioxidant, antimicrobial
S-allylcysteine (SAC)	Organosulfur	Amino acid antioxidant, Neuroprotective, Cardioprotective

Table 1: Chemical derivatives of allicin and associated pharmacological activities

Medicinal Plants and Allicin in UTI Management:

Medicinal plants are rich sources of bioactive compounds, including flavonoids, alkaloids, glycosides, phenols, saponins, steroids, sterols, tannins, and terpenoids, which provide multiple health benefits. The use of these phytochemicals for preventing or treating diseases, such as urinary tract infections (UTIs), has been practiced for centuries. Research on natural, non-chemical UTI treatments has focused on various stages of infection, including bacterial colonization, adherence to epithelial cells, and tissue invasion. While no single study has fully explained how medicinal herbs cure UTIs, evidence suggests that secondary compounds in these plants can inhibit bacterial growth, reduce colonization in the urinary tract, act as natural diuretics to Clear the bladder and repair the lining of the bladder, reduce pain and inflammation, and provide antioxidant and immune-boosting effects.

Many secondary metabolites found in medicinal plants, including alkaloids, flavonoids, glycosides, phenols, saponins, steroids, terpenoids, tannins, hydrocarbons, phlobatannins, and other phytochemicals that directly contribute to their

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antimicrobial activity, are responsible for these antibacterial qualities. Plant extracts' antibacterial properties have been investigated utilising techniques such as disc diffusion, agar well diffusion, and minimum inhibitory concentration (MIC) determination. Nevertheless, little is known about the precise antibacterial action of particular phytochemicals. Because the synergistic impact of several bioactive chemicals increases the effectiveness of managing antibiotic resistance, the usage of medicinal plants may also assist lower antibiotic resistance.

TYPES AND CLINICAL FEATURES OF URINARY TRACT INFECTIONS (UTIs):

One of the most prevalent bacterial diseases is a urinary tract infection (UTI) and can be broadly classified into upper and lower urinary tract infections based on the anatomical site of involvement. The pathophysiology, clinical presentation, and complications vary based on the infection's location and intensity.

1. Upper Urinary Tract Infections :

Upper urinary tract infections primarily affect the kidneys and ureters and are associated with more severe clinical manifestations. Common conditions include acute pyelonephritis, chronic pyelonephritis, interstitial nephritis, renal abscess, and perirenal abscess.

• Pyelonephritis: Pyelonephritis refers to an infection of the kidney, typically resulting from the ascending spread of bacteria from the lower urinary tract or due to urinary tract obstruction. Obstructions may cause retrograde urine flow into the ureters and kidneys, increasing susceptibility to infection.

• Acute Pyelonephritis: Characterized by sudden infection of one or both kidneys, acute pyelonephritis often involves the lower urinary tract. Clinical features include pyuria, fever, flank pain, and malaise.

• Chronic Pyelonephritis: This condition represents a long-standing pathological alteration in the kidneys, which may or may not result from persistent infection can lead to renal scarring, impaired renal function, and recurrent infections over time.

2. Lower Urinary Tract Infections:

Lower urinary tract infections primarily involve the bladder, urethra, & prostate. They are generally less severe than upper tract infections but can significantly affect quality of life. Common lower urinary tract infections consists cystitis, urethritis, and prostatitis.

• Cystitis: Cystitis is a bacterial infection of the urinary bladder, often arising from ascending infection from the urethra. Clinical manifestations typically include frequent urination, urgency, dysuria, and cloudy or hematuric urine.

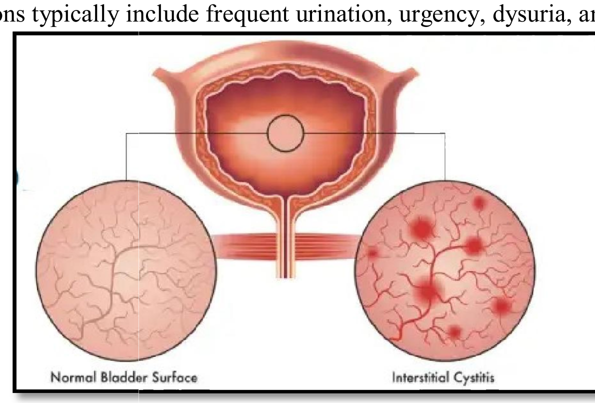

Fig.1.2: Cystisis [12]

• Urethritis: Urethritis refers to infection of the urethra, the tubular structure responsible for urine excretion. Patients commonly present with dysuria, urethral discharge, and irritation.

• Prostatitis: In males, prostatitis involves infection or inflammation of the prostate gland, presenting with pelvic pain, dysuria, fever, and lower urinary tract symptoms[13].

Both upper and lower UTIs are categorised as complicated or uncomplicated based on underlying risk factors:

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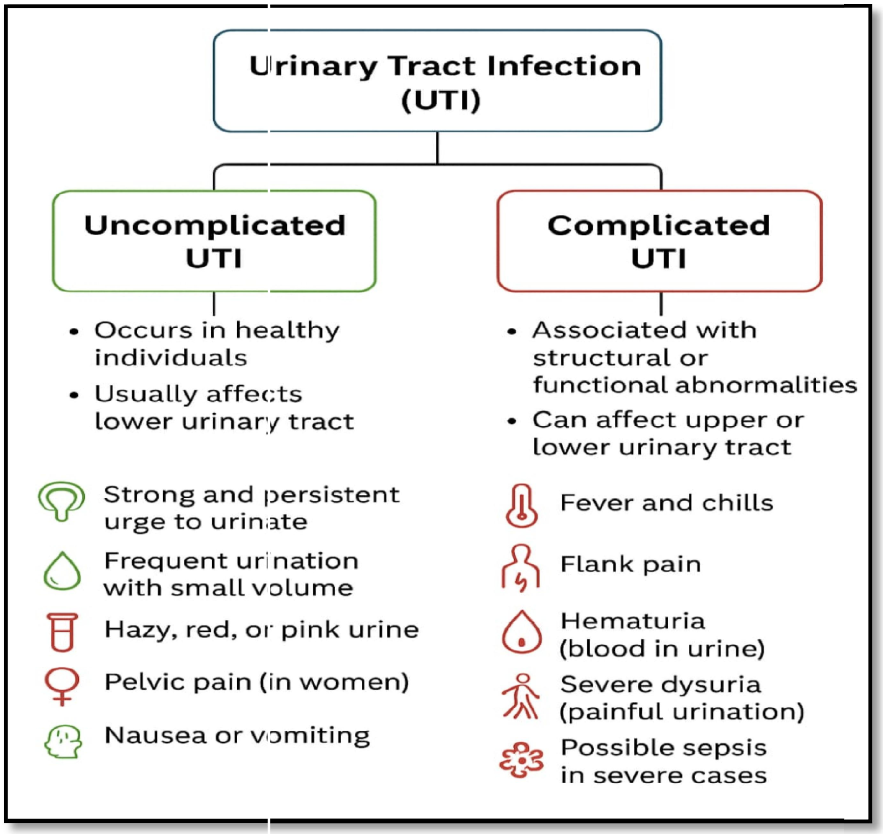

Fig.1.3: Types and Clinical Findings of Urinary Tract Infection (UTI)

Complicated UTI: When there are anatomical or functional problems in the urinary tract, a severe urinary tract infection develops, such as indwelling catheters or renal calculi. Host-related predisposing factors including advanced age, catheterization, diabetes mellitus, and spinal cord injury increase the risk of complicated UTIs. Clinically, complicated UTIs may present as prolonged cystitis or hemorrhagic cystitis.

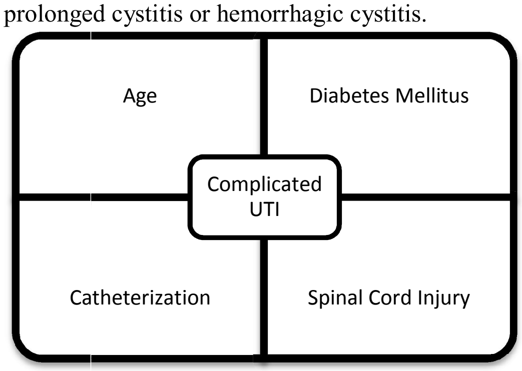

Fig.1.4: Host-related risk factors [14]

Uncomplicated UTI: In a urinary system that is both physically and functionally normal, an uncomplicated UTI develops. It usually affects the lower urinary system, which includes the bladder and urethra, and manifests as uncomplicated cystitis that lasts for one to five days. These infections have the potential to spread to the upper urinary tract, including the kidneys and ureters, if treatment is not received.

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Stages of urinary tract infection:

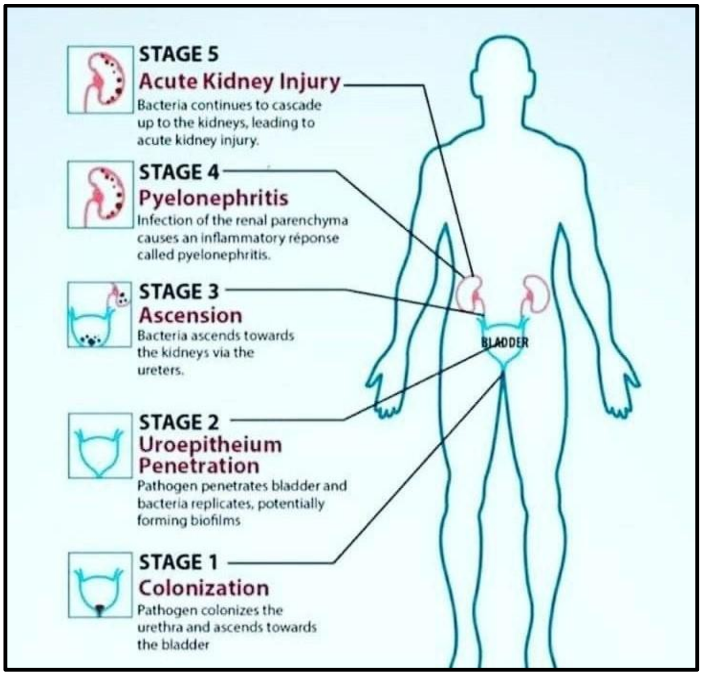

Fig.1.5: Stages of urinary tract infection [15]

Causes of UTI:

Urine may contain fluids, salts, and waste products, but it is usually free of bacteria, viruses, and fungi. Microorganisms, mostly bacteria from the digestive tract, are the source of infection. The most frequent source of infection is E. coli, which is usually found in the colon. Catheter-associated UTIs are most frequently caused by E. coli. Numerous bacteria, including Proteus mirabilis, P. aeruginosa, Streptococcus faecalis, Staphylococcus aureus, Klebsiella pneumoniae, Mycobacterium tuberculosis, Actinomycetes, and Candida, can cause urinary tract infections.

Symptoms of Urinary Tract Infection (UTI):

The clinical presentation of urinary tract infection (UTI) varies based on the site, severity, & progression of the infection. The most commonly observed symptoms include:

1. Dysuria: Painful, burning sensation while urination.
2. Suprapubic and lower back pain.
3. Fever and general malaise.
4. Urinary urgency: Sudden and compelling need to void urine.
5. Urinary hesitancy: Difficulty or delay in initiating urination.
6. Polyuria: Increased frequency of urination, often with passage of small volumes.
7. Pyuria: Presence of pus cells, resulting in cloudy or turbid urine.
8. Dyspareunia: Pain experienced during sexual intercourse.
9. Pelvic discomfort, soreness, or cramping.
10. Nausea and vomiting.
11. Urinary incontinence: Involuntary leakage of urine.
12. Hematuria: Presence of blood or reddish discoloration in urine.
13. Costovertebral angle pain: Pain or tenderness on the sides of the lower back, indicating kidney involvement [16].

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PATHOGENESIS OF URINARY TRACT INFECTION (UTI):

Source of Infection (Intestinal flora, mainly E. coli)
↓
Bacterial Entry through Urethral Opening
↓
Colonization of Periurethral Area
↓
Ascension of Pathogens to the Bladder (Cystitis)
↓
Adhesion to Uroepithelial Cells (via Fimbriae/Pili)
↓
Bacterial Multiplication and Biofilm Formation
↓
Host Immune Response → Inflammation, Dysuria, Urgency
↓
Ascending Spread to Ureters and Kidneys (Pyelonephritis)
↓
Renal Scarring / Chronic or Recurrent UTI (if untreated)[17]

ANTIMICROBIAL EFFECTS OF GARLIC:

Since ancient times, humankind has encountered a wide variety of diseases, with their origins often surrounded by speculation. During the middle Ages, illnesses were commonly attributed to supernatural causes, particularly demonic influence. However, a major breakthrough occurred in the 19th century when Robert Koch scientifically demonstrated that bacteria were responsible for causing and transmitting anthrax, thereby establishing the germ theory of disease. Historical records suggest that the antimicrobial properties of garlic were first described by Louis Pasteur, who reported its ability to inhibit bacterial growth. During World War I, garlic extracts were utilized for their antibacterial and antiseptic properties. Since then, numerous scientific investigations have been conducted to evaluate and validate the antibacterial potential of garlic [18].

Herbal active ingredients have been demonstrated to either kill bacteria or stop the growth of microorganisms. Garlic may prevent the pathogenesis because it can kill a variety of pathogens, according to some research. The results of a study shows that hamburgers containing garlic extract have antimicrobial qualities. Additionally, garlic extract can be utilized as a natural addition and as a flavor [19]. An in vitro study revealed that garlic extract exhibited concentration-dependent antibacterial activity, with the active compound diallyl disulphide (DADS) demonstrating significant potency, underscoring the potential of garlic-derived compounds as novel antibacterial agents [20].

Uropathogenic Escherichia coli (UPEC) is a highly infectious bacterium commonly related with urinary tract infections (UTIs). Depending on the severity and underlying conditions, UPEC infections can be classified as either complicated or uncomplicated. UTIs represent one of the most common bacterial infections of the urinary system and frequently occur in neonates, preschool-aged girls, sexually active women, and elderly men and women. In recent years, recurrent UTIs have been increasingly reported among children, indicating repeated or persistent infections. Improper or incomplete use of antibiotics may contribute to the recurrence or persistence of these infections.

Diallyl sulphide and diallyl disulphide, two components of garlic, have been shown to have dose-dependent bactericidal effects on H. pylori cultures. The reduced N-acetyltransferase activity seen in the bacterial cytosols and suspensions after exposure to these substances is connected to this impact. By dramatically lowering the fungal burden and mortality in Swiss albino mice, a niosomal formulation of diallyl sulphide proved effective against experimental candidiasis [21]. Diallyl disulphide may have strong antifungal effects in the treatment of candidiasis because it pro-oxidizes Candida species [22]. According to a study, diallyl disulphide has potent antifungal properties that cause

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Candida species to die. In a similar vein, pure allicin has been demonstrated to successfully impede the formation of hyphal cells, suggesting its potential as a substitute medicinal agent for the treatment of dermatophytosis [23]. Resistant to methicillin Allicin may be useful against isolates of Staphylococcus aureus. Allicin and other thiosulphinates found in garlic extract have antibacterial qualities via blocking Acetyl-CoA synthase [25, 26]. Methicillin-resistant Staphylococcus aureus (MRSA) infection in diabetic mice was studied in relation to the inhibitory potential of two important garlic-derived chemicals, diallyl sulphide and diallyl disulphide. Malondialdehyde levels in the kidney and spleen were dramatically raised by MRSA infection and significantly decreased after treatment with garlic components. These results imply that under diabetic situations, garlic bioactives provide significant protection against infection. Diallyl sulphide's strong antibacterial activity was further verified by another study.

MECHANISM OF ACTION OF ALLICIN:

1. Formation of Allicin: Allicin is produced when garlic (Allium sativum) is crushed or chopped. The enzyme alliinase converts alliin into allicin, which is the primary bioactive compound responsible for its antimicrobial activity.
2. Reaction with Thiol-Containing Enzymes: Allicin reacts with thiol (–SH) groups in cysteine residues of proteins and enzymes, forming S-thioallylated adduct. This alters enzyme structure and inhibits catalytic activity, disrupting essential processes like energy metabolism, redox balance, and DNA transcription in microbial cells.
3. Oxidative Stress Induction: Allicin generates reactive oxygen species (ROS), leads to oxidative stress. This damages DNA, proteins, and lipids, further impairing microbial viability.
4. Disruption of Membrane Integrity: Being lipophilic, allicin penetrates phospholipid membranes, increasing permeability and causing leakage of cytoplasmic contents. This destabilizes ion gradients and nutrient transport, leading to cellular dysfunction.
5. Intracellular Redox Imbalance: Allicin depletes intracellular thiols such as glutathione (GSH), disturbing redox homeostasis. Microbial cells become more susceptible to oxidative damage and enzyme inhibition.
6. Multi-Target Action and Low Resistance Risk: Allicin simultaneously affects enzymes, membranes, and redox systems. Its broad, non-specific mechanism reduces the likelihood of microbial resistance, enhancing its potential as a therapeutic agent [27, 28].

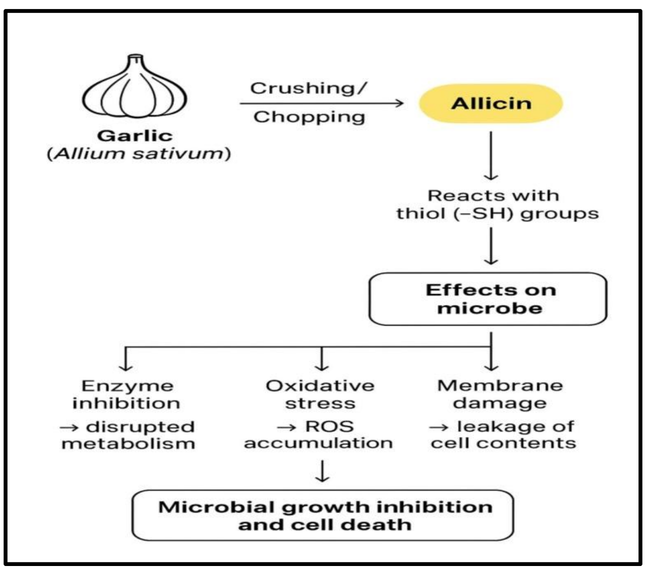

Fig.1.6: Mechanism of Action of Allicin

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EFFECT OF ALLICIN ON UROPATHOGENS:

Uropathogens including Escherichia coli, Proteus mirabilis, and Klebsiella pneumoniae are the main causes of urinary tract infections (UTIs), which are among the most common bacterial illnesses worldwide. The demand for new and efficient treatment options has increased due to the rising prevalence of antibiotic-resistant bacteria. Because of its strong and wide-ranging antibacterial action against both Gram-positive and Gram-negative bacteria, allicin—the main bioactive sulfur-containing component derived from garlic (Allium sativum)—has drawn a lot of interest.

Allicin, a biologically active sulfur compound derived from garlic (Allium sativum), exhibits a strong inhibitory effect against a variety of uropathogens responsible for urinary tract infections (UTIs). These include Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Enterococcus faecalis, and Pseudomonas aeruginosa. The antimicrobial mechanism of allicin primarily involves its interaction with thiol (-SH) groups present in bacterial enzymes, which leads to enzyme inactivation, metabolic disruption, and eventual cell death. Allicin is especially efficient against uropathogenic E.coli (UPEC), the most frequent cause of UTIs, according to several studies demonstrated that subinhibitory concentrations of allicin significantly reduced UPEC biofilm formation, adhesion, and motility, thereby impairing its colonization potential within the urinary tract. This anti-biofilm activity is crucial, as biofilms are often associated with chronic and recurrent UTIs.

Additionally, allicin alters bacterial cell membrane permeability, resulting in leakage of cytoplasmic contents and inhibition of essential enzyme activities [29]. It also interferes with bacterial quorum sensing in Gram-negative species such as Pseudomonas aeruginosa, leading to suppression of virulence factors like pyocyanin and elastase. In Proteus mirabilis, allicin inhibits urease enzyme activity, preventing urine alkalinization and reducing crystal formations, which are common in catheter-associated UTIs.

Moreover, allicin demonstrates synergistic effects when combined with conventional antibiotics such as ciprofloxacin and gentamicin, enhancing their activity against multidrug-resistant uropathogens [30]. This synergism results from allicin's ability to increase bacterial cell wall permeability, facilitating antibiotic penetration. The compound's multifaceted action affecting membrane integrity, enzymatic function, and quorum-sensing pathways makes the development of bacterial resistance less likely. Therefore, allicin holds great promise as a natural antimicrobial candidate for both the prevention and treatment of urinary tract infections.

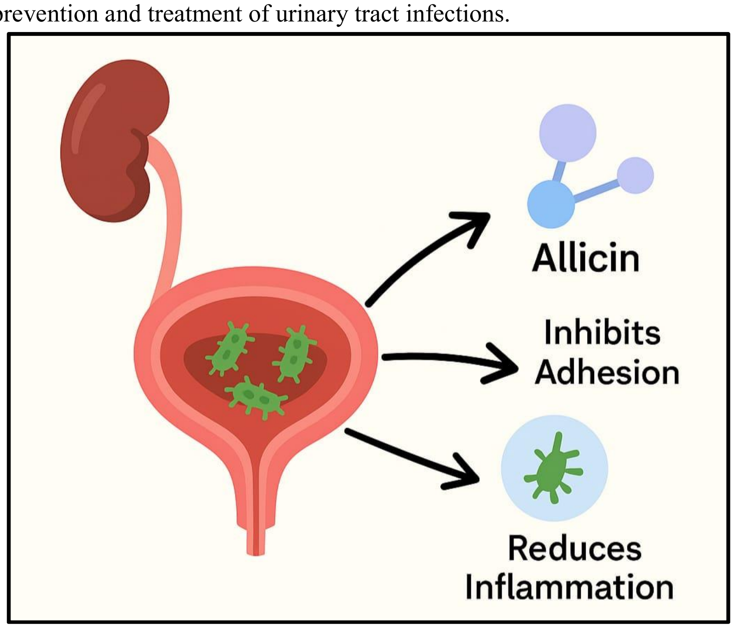

Fig.1.7: Effect of Allicin on Uropathogens

SYNERGISTIC INTERACTION OF ALLICIN:

Allicin, the bioactive compound derived from fresh garlic (Allium sativum), has emerged as a potent natural antimicrobial agent with significant therapeutic potential, particularly when used in combination with conventional antibiotics. Its antimicrobial activity is largely attributed to its ability to react with thiol (-SH) groups in essential bacterial enzymes, such as alcohol dehydrogenase, thioredoxin reductase, and RNA polymerase, leading to protein inactivation and disruption of vital cellular processes. Unlike many conventional antibiotics that target a single bacterial pathway, allicin can simultaneously affect multiple cellular systems, including protein synthesis, DNA replication, redox balance, and enzyme activity. This multifaceted mode of action not only makes allicin inherently bactericidal but also provides a strong basis for synergistic interactions when combined with standard antibiotics.

When used together with antibiotics, allicin enhances their bactericidal effects in a manner that goes beyond simple additive activity. Allicin exhibits strong synergistic activity with fluoroquinolones, including ciprofloxacin and enoxacin, against gram-negative bacteria such as Pseudomonas aeruginosa and Escherichia coli. Similarly, combinations with vancomycin, clarithromycin, and linezolid demonstrate pronounced synergy against gram-positive bacteria such as Staphylococcus aureus, including methicillin-resistant strains (MRSA), and Enterococcus faecalis, including vancomycin-resistant enterococci (VRE) [31]. The complementary mechanisms of action underlie this synergy: fluoroquinolones inhibit bacterial DNA replication by targeting DNA gyrase and topoisomerase enzymes, beta-lactams interfere with cell wall synthesis, and aminoglycosides disrupt protein translation, while allicin simultaneously inactivates key thiol-containing enzymes and proteins. This multi-targeted approach overwhelms bacterial defence systems, making it particularly effective against multidrug-resistant organisms where monotherapy often fails.

The clinical Implications of allicin-antibiotic synergy are especially significant for infections caused by extended-spectrum beta-lactamase (ESBL)-producing E. coli, which are commonly implicated in urinary tract infections (UTIs) and exhibit resistance to multiple classes of antibiotics. Fresh garlic extract has been shown to display remarkable synergistic effects with beta-lactams (ampicillin, cephalosporins), fluoroquinolones (ciprofloxacin, levofloxacin), aminoglycosides (amikacin, gentamicin), and carbapenems (imipenem, meropenem) against ESBL-producing E. coli urinary isolates. Quantitative assessment using fractional inhibitory concentration (FIC) indices consistently confirms values below 0.5 for all tested combinations, indicating true synergy rather than additive effects. The synergistic combinations also significantly reduce the minimum inhibitory concentrations (MICs) of antibiotics, allowing lower doses to achieve effective bacterial killing. Lowering antibiotic doses can reduce toxicity and side effects, which is particularly important for drugs like aminoglycosides that can be nephrotoxic or ototoxic at high concentrations.

Beyond direct antibacterial activity, allicin has been shown to interfere with bacterial resistance mechanisms at the molecular level. It can suppress the expression of key ESBL-encoding genes, including SHV, TEM, and CTX-M, thereby reducing the production of enzymes that degrade beta-lactam antibiotics. Allicin also demonstrates anti-biofilm activity, inhibiting the formation and maintenance of bacterial biofilms. Biofilms protect bacteria from environmental stresses and antibiotics, and their disruption by allicin enhances bacterial susceptibility to treatment. This effect has been observed in E. coli, Pseudomonas aeruginosa, and Staphylococcus aureus, suggesting that allicin could be particularly useful for chronic infections where biofilms contribute to persistent or recurrent disease. By combining antimicrobial activity, resistance gene suppression, and biofilm inhibition, allicin acts as a multi-functional agent that complements conventional antibiotics and strengthens overall treatment efficacy [32].

In addition to its antibacterial properties, allicin demonstrates low toxicity in mammalian cells, making it a safe adjunctive therapy. Its natural origin, widespread availability, and cost-effectiveness further support its use in combination therapies, particularly in resource-limited settings where access to newer antibiotics may be restricted. By combining allicin with existing antibiotics, it may be possible to restore the efficacy of drugs that have become less effective due to resistance, effectively extending the useful lifespan of current antimicrobial agents. This strategy is particularly important in the context of global antibiotic resistance, which poses a growing threat to public health and increases morbidity, mortality, and healthcare costs worldwide.

Overall, the synergistic interaction between allicin and conventional antibiotics represents a multifaceted approach to managing bacterial infections. By targeting multiple bacterial pathways simultaneously, lowering required antibiotic doses, inhibiting biofilm formation, and suppressing resistance gene expression, allicin-antibiotic combinations provide a powerful, low-toxicity, and cost-effective alternative to conventional monotherapy. These findings underscore the potential of allicin not only as an adjunctive agent in the treatment of drug-resistant infections, such as UTIs caused by ESBL-producing E. coli, MRSA, and VRE, but also as a component of broader strategies aimed at mitigating the ongoing global antibiotic resistance crisis.

EVIDENCE-BASED EVALUATION OFGARLIC DERIVED ALLICIN IN THE PREVENTION AND TREATMENT OF UTI:

• In Vitro Anti-Biofilm and Anti-Crystallization Effects:

A major complication of catheter-associated urinary tract infections (CAUTIs) arises from Proteus mirabilis, a urease-positive pathogen known for biofilm formation and crystalline encrustation of catheters. The ability of allicin to prevent these events was investigated using a synthetic bladder model that mimicked natural infection conditions. In this experiment, purified allicin was tested at sub-MIC concentrations (2–8 µg/mL) against clinical P. mirabilis isolates obtained from catheterized patients. The study demonstrated that allicin effectively inhibited urease activity, delayed the pH rise in synthetic urine, and suppressed struvite ($MgNH_4PO_4 \cdot 6H_2O$) and carbonate apatite crystal formation in a dose-dependent manner.

The presence of allicin significantly prolonged the time to catheter blockage: control catheters were obstructed at 48 hours, whereas 2, 4, and 8 µg/mL of allicin extended blockage times to 61, 74, and 92 hours, respectively. Microscopic and biochemical analyses revealed substantially lower magnesium and calcium deposition on allicin-treated catheters compared with untreated controls. These findings demonstrated that allicin not only interferes with urease-mediated alkalinization but also directly reduces crystal nucleation and growth on catheter surfaces [33].

Complementary in vitro assays using P. mirabilis lysate as a urease source confirmed that allicin suppresses ion precipitation and turbidity, further verifying inhibition of crystal formation. Optical density and pH measurements over time revealed that allicin maintained near-neutral pH in synthetic urine and reduced magnesium and calcium precipitation significantly ($p < 0.05$). These inhibitory effects were comparable to those achieved by iodoacetic acid, a known urease inhibitor, confirming that allicin acts on urease enzyme systems through interaction with cysteine residues in the active site. Together, these findings indicate that allicin could serve as an alternative or adjunctive agent in the prevention of catheter-associated UTIs by controlling Proteus biofilm and encrustation.

• In Vitro Evidence of Antimicrobial Spectrum Expansion

Beyond individual pathogen studies, comparative investigations have highlighted the wide antimicrobial spectrum of garlic extracts in urinary isolates. Using both nutrient and MacConkey agar systems, aqueous garlic extracts demonstrated inhibition across different clinical bacterial species relevant to urinary tract infections, including E. coli and K. pneumoniae. The large inhibition zones observed in these experiments, comparable to or greater than those produced by standard antibiotics, underscore the potential of garlic's thiosulfinate compounds as natural antibacterial agents.

The antimicrobial efficacy in these in vitro studies is attributable to allicin's ability to penetrate bacterial cell membranes, react with sulfhydryl-containing enzymes, and disrupt essential metabolic processes. However, since this review focuses solely on empirical evidence, it is sufficient to note that reproducible inhibition was achieved under standardized laboratory conditions using both crude and purified preparations of garlic and allicin. The repeatability across independent in vitro experiments supports the reliability of these findings for translational consideration.

• In Vivo and Immunomodulatory Evidence

Although fewer in vivo studies directly examine garlic or allicin in urinary infection models, multiple animal experiments have elucidated its systemic immunomodulatory and anti-inflammatory roles that could influence infection outcomes. Experimental data derived from mouse and rat models demonstrated that garlic extracts can enhance immune cell proliferation and regulate cytokine expression. In particular, garlic consumption stimulated lymphocyte and macrophage cytotoxic activity, promoted T-cell proliferation, and increased counts of immune cells in bone marrow and spleen tissues. These immunostimulatory effects were observed following oral administration or injection of aqueous and protein fractions of garlic extracts.

Garlic-derived compounds, including allicin, were also shown to modulate cytokine production. In treated mice, allicin inhibited proinflammatory Th1 cytokines such as TNF-α and IL-1β while promoting anti-inflammatory cytokines like IL-10, thereby helping maintain immune homeostasis [34]. Furthermore, in vivo models revealed that different doses of garlic oil could differentially shift T helper responses: low doses favored Th1-type immunity, whereas high doses promoted Th2 type responses. This dual modulation could be therapeutically relevant, as it enhances immune protection against infection while preventing excessive inflammation.

Although these in vivo studies did not exclusively involve urinary tract models, they establish biological plausibility that garlic constituents enhance host defence mechanisms. By regulating cytokine balance, promoting macrophage activity, and suppressing oxidative stress, allicin may support clearance of bacterial pathogens during urinary infection and mitigate tissue inflammation that contributes to recurrent UTI pathology.

Role of Garlic in Reducing Recurrence of Urinary Tract Infection:

Recurrent urinary tract infection (rUTI) is a long-standing medical problem that affects many people, especially women. In this condition, the infection comes back even after it seems to have been cured. Even when antibiotics are used correctly, some bacteria survive inside the urinary tract or bladder wall and cause the infection to return. One of the main reasons for recurrence is that these bacteria remain hidden inside the bladder and stay inactive for a while. When conditions become favourable, they become active again and cause a new infection.

Traditional treatments for rUTI usually depend on long-term use of antibiotics. These can help reduce the number of infections for some time, but they are not a permanent solution. Long-term antibiotic use may lead to side effects, disturbance of healthy bacteria, and development of antibiotic resistance. Therefore, it is important to find natural and safe ways to stop the infection from coming back. Garlic is one natural option being studied because it may help in reducing recurrence by acting on the reasons that cause infections to reappear.

The capacity of bacteria to adhere to the bladder wall and create biofilms—thin protective layers that render bacteria immune system and antibiotic resistant—is the primary cause of recurrence. By dissolving these protective biofilms and stopping germs from adhering to the bladder lining once more, garlic may be beneficial. It is more difficult for bacteria to thrive and spread infection when biofilms are reduced or eliminated.

Some bacteria can also hide inside the bladder cells in a dormant form. These bacteria do not show up in normal urine tests and can resist many antibiotics. By preventing these hidden bacteria from becoming active again, garlic may help reduce the chance of relapse. This means that garlic does not just remove bacteria temporarily it may also help stop the infection from returning. Continuous use of antibiotics for prevention often causes side effects and resistance, which is a major concern. Because of this, non-antibiotic and natural approaches are needed. Garlic can be one such option since it acts on the main processes that cause recurrence rather than working like a typical antibiotic. Using garlic or its natural compounds as a supportive method may help reduce repeated infections and lower the dependence on antibiotics.

Prevention of recurrence should also include improving the body's natural defences and maintaining a healthy urinary environment. Garlic may support this by helping reduce inflammation and improving bladder health, which together make the urinary tract less likely to get reinfected. Although current evidence mainly comes from laboratory and theoretical studies, there are strong scientific reasons to believe that garlic can help reduce recurrence. Bacterial

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persistence, intracellular survival, and biofilm formation are the main causes of repeated infections, and these are the same processes that garlic can affect. Therefore, garlic could play an important role in lowering the recurrence of urinary tract infections.

Future studies should focus on confirming this effect through proper clinical research that measures recurrence rates over time. If future findings support these results, garlic may become a safe, natural, and effective option for preventing recurrent urinary tract infections and reducing the need for long-term antibiotic use [35].

Therapeutic Role of Garlic in Urinary Tract Infections

Traditionally used to treat a variety of illnesses, including urinary tract infections (UTIs), garlic (Allium sativum) is a potent natural antibacterial agent. A study assessed the efficacy of garlic extract against a number of UTI-causing bacteria, including Proteus mirabilis, Escherichia coli, Staphylococcus aureus, and Pseudomonas aeruginosa. These organisms are the primary uropathogens responsible for kidney and bladder infections. The agar well diffusion method was used to investigate the antibacterial activity of garlic extract at various doses. The findings demonstrated that garlic extract was efficient against every tested bacterium, with E. coli showing the greatest zone of inhibition (around 22 mm).

The minimum inhibitory concentration (MIC) was approximately 50 mg/mL, indicating that even a small quantity of garlic extract could suppress bacterial growth. The antibacterial activity was found to be dose-dependent, meaning higher concentrations produced stronger inhibitory effects.

The main active compound responsible for this effect is allicin, a sulfur-containing molecule formed when garlic is crushed. Allicin reacts with thiol (–SH) groups in bacterial enzymes, thereby inhibiting their activity, damaging the cell membrane, and ultimately leading to bacterial death. Garlic also prevents bacteria from adhering to the bladder wall and forming biofilms, which are protective layers that cause recurrent infections. Its natural anti-inflammatory properties help reduce bladder irritation and strengthen the body's immune defences system.

Overall, garlic extract shows significant antibacterial effects against UTI-causing pathogens and can be used as a supportive or alternative therapy for urinary tract infections. Due to its safety, low cost, and easy availability, garlic is considered a promising natural agent for the prevention and treatment of UTIs [36].

Garlic: Safety Profile and Possible Side Effects

Garlic (Allium sativum) is commonly used as food and medicine. It is safe for most people when eaten in normal amounts, but using too much or taking it as a strong supplement can sometimes cause mild side effects. The most common problems are stomach pain, nausea, heartburn, gas, or loose motion (diarrhoea). These effects are not serious and usually stop when the amount of garlic is reduced. Garlic has natural sulfur compounds like allicin and ajoene.

These help kill harmful germs but also cause a strong smell. Eating large amounts of raw garlic for a long time can lead to bad breath, body odour, or minor skin rashes, especially in people who are sensitive to it. Some research shows that garlic can slow blood clotting because of its natural chemicals. People who are taking blood-thinning medicines (such as aspirin or warfarin) or those who are planning to have surgery should be careful. They should avoid taking high-dose garlic supplements, as this might increase bleeding risk during or after surgery.

Even with these mild effects, garlic is still a safe and useful natural remedy when used properly. Using controlled or standardized garlic products helps reduce stomach irritation while keeping its health benefits. In general, garlic is safer than chemical antibiotics and can be used for long-term prevention of infections and to support good health [37].

II. CONCLUSION

Urinary tract infections (UTIs) are a major health problem around the world, especially because many bacteria are becoming resistant to antibiotics. This review shows that garlic (Allium sativum) and its main active compound, allicin, have strong antibacterial, anti-biofilm, and immune-boosting effects. They work well against common UTI-causing bacteria such as E. coli, Proteus mirabilis, and Klebsiella pneumoniae. Allicin fights infections by damaging bacterial membranes, blocking certain enzymes, and causing oxidative stress. This multi-action effect helps stop bacteria from developing resistance easily.

When allicin is used along with regular antibiotics, it can improve their effect and help treat drug-resistant infections, including those caused by ESBL-producing bacteria. Garlic also prevents bacteria from forming biofilms and sticking to urinary tract surfaces, which helps reduce repeated UTIs. However, most research so far has been done in labs and on animals, with only a few studies in humans. More clinical research is needed to decide the right dosage, best form, and long-term safety of garlic use.

Overall, garlic is a natural, safe, low-cost, and easily available remedy that shows great potential for preventing and treating UTIs. With more clinical proof, garlic-based treatments could become a useful alternative or addition to antibiotics, especially in areas with limited medical resources, helping to improve patient health and reduce antibiotic resistance.

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