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Antibacterial Efficacy of Allium Sativum Against Multidrug-Resistant Bacterial Pathogens and its Synergistic Interaction with Conventional Antibiotics

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ABSTRACT
Objective: *This study aims to investigate the potential of Allium sativum (garlic) as an alternative antibacterial agent in the context of rising antibiotic resistance.* ***Method:*** *A comprehensive literature review was conducted, focusing on in vitro and in vivo studies that evaluate the antimicrobial efficacy of Allium sativum against multidrug-resistant (MDR) bacterial strains. Sources included peer-reviewed journals in microbiology, pharmacology, and ethnomedicine.* ***Results:*** *The analysis reveals that Allium sativum exhibits broad-spectrum antibacterial activity, particularly effective against Gram-positive and Gram-negative MDR bacteria. Its bioactive compounds, such as allicin, disrupt bacterial cell walls, inhibit enzyme activity, and prevent biofilm formation. The low incidence of side effects and the affordability of garlic make it a viable candidate for complementary or integrative antimicrobial therapies.* ***Novelty:*** *This study highlights the relevance of traditional medicinal plants in modern antimicrobial drug discovery, emphasizing Allium sativum as a sustainable, natural, and accessible alternative in combating antibiotic-resistant infections, with implications for public health and pharmaceutical innovation.*

INTRODUCTION

The increasing mortality rate of infectious diseases is one the most challenging public health problems faced by different countries worldwide [1]. Unfortunately, the wide use of antibiotics has increased the development of bacterial resistant strains to antibiotics [2], which has resulted in a reduction in the effectiveness of some of the antibacterial agents, leading to high mortality rates. Medicinal plants have been used for many years in the treatment of a vast number of human diseases by the community, specifically in traditional medicine [1]. They are considered the main source of new, natural, and safe drugs to be utilized.

In managing diseases as an effective and harmless alternative medicine, because they are not expensive and pose minimum side effects to humans [3]. According to a report published in 2002 by the World Health Organization (WHO) in Geneva, medicinal plants have significant value and could be considered as the best source of complementary and alternative natural medicines [4]. Garlic, scientifically known as Allium sativum, is one of the oldest plants used as a spice in food and also used as a medicine because of its many benefits to human health and wellbeing [5]. Results from different studies have shown that garlic extracts have the capacity to inhibit the growth of some pathogenic microorganisms [6].

RESEARCH METHOD

This study employed a narrative literature review method to explore the antibacterial efficacy of *Allium sativum* against multidrug-resistant (MDR) bacterial strains and its potential synergistic interaction with conventional antibiotics. The research involved the collection, analysis, and synthesis of peer-reviewed scientific articles, meta-analyses, and global health reports published in reputable journals and databases, including studies by the CDC, WHO, and various microbiological and pharmacological researchers. The review emphasized the biochemical mechanisms of garlic-derived compounds—particularly allicin—in inhibiting bacterial growth, disrupting metabolic pathways, and enhancing oxidative stress. Additionally, studies examining the clinical significance of garlic in traditional medicine and its reported activity against ESKAPE pathogens (e.g., *E. coli*, *Staphylococcus aureus*, *Klebsiella*, and *Pseudomonas aeruginosa*) were evaluated. The evidence was organized thematically to highlight microbial resistance pathways, the role of garlic bioactive compounds, and synergistic effects when combined with antibiotics.

RESULTS AND DISCUSSION

Definition Of Antibiotic Resistance

Antimicrobial resistance poses a serious threat to global public health, causing at least 1.27 million deaths globally and approximately 5million fatalities in 2019 [7]. More than 35,000 people die as a result, according to CDC's 2019 Antibiotic Resistance (AR) Threats Report [8]. Antimicrobial resistance may have an impact on individuals at every stage of life, as well as on the medical, veterinary, and agricultural sectors [9]. This makes it one of the most important public health issues in the entire world [8]. Rapid development of Ab resistance in microorganisms is directly related to overconsumption of Abs, their broad utilization in agriculture [10]. Due to the fact that repeated drug administration and greater doses are common nowadays, Antibiotic resistance has emerged against various types of antibiotics commonly used against harmful bacteria [11].

Development Of Bacteria Antibiotic Resistance

Bacteria are living entities that change over time. Their major goal is to multiply, endure, and spread as quickly as they can. Microbes, as a result, adapt to their environment and develop in ways that ensure their survival [12]. If anything, such as an antibiotic, inhibits their ability to develop, genetic changes may occur, rendering the bacteria resistant to the medicine and enabling them to survive [7], [13]. Antibiotics can be rendered inactive by bacteria via a variety of molecular mechanisms [7].

Production of inactivating enzymes: The bacteria produces enzymes that inactivate the antibiotic, causing it to lose its biological function [14].

1. Change and alterations in the antibiotic target [15].
2. Decrease in antibiotic uptake : Change in the structure of cell surface casing can reduce the entry of an antibiotic [16].

3. Extrusion of drug outside the cell: Energy-driven drug efflux systems eliminate antibiotics that have been taken up by bacterium cells [17].
4. Activation of alternative metabolic pathways: Bacteria exposed to antibiotic are still able to produce substances through a different metabolic pathway [18].
5. Transferring of resistance genes: As a result of bacterial communication and genetic information sharing, resistance genes transfer among bacterial populations [19].
6. Extracellular biofilm formation: Some antibiotics are unable to penetrate the protective extracellular of bacterial biofilms [20].

Once a species gains resistance to an antibiotic, it eventually overcomes the combined drug effects, leading to development of multidrug-resistant (MDR) organisms which are resistant to antimicrobial drugs or combination treatments. By encouraging bacterial growth that was not immediately eliminated, this scenario occasionally encourages the spread of resistance [21], [22].

Multi-Drug Resistance Bacteria Strains

Increased antibiotic resistance is among the world's top three public health issues of the 21st century, according to the World Health Organization (WHO). The much more harmful bacteria, collectively known as ESKAPE are those that cause the most concern:

1. E. coli
2. Staphylococcus
3. Klebsiella
4. Pseudomonas, they are all are connected to a high death rate [23].

S. aureus can cause:(Pimples, boils or other skin conditions, Bloodstream infections or sepsis, Pneumonia, Endocarditis (infection of the heart valves), which can lead to heart failure and Osteomyelitis (bone infection). E. coli can make people sick with diarrhea, urinary tract infections, pneumonia, sepsis, and other illnesses. Klebsiella can cause pneumonia, bloodstream infections, wound or surgical site infections, and meningitis. P. aeruginosa can cause infections in the burn, blood, lungs (pneumonia), urinary tract or other parts of the body after surgery. The spread of MDR and extensively drug-resistant (XDR) bacteria continues to represent a severe threat to human and animal health due to their high mortality, morbidity, and prices of medication to combat them [16]. This is made worse by a number of bacterial strains' capacity to form biofilms, which is linked to 65–80% of human illnesses.

MDR causes blockage in the fight against disease and decreases treatment effectiveness, which causes the patient's infection to last longer than expected [7]. Immunocompromised patients such as those with chronic diseases, receiving cancer chemotherapy, immunosuppressive drugs or undergo organ transplantation are more vulnerable to MDR infection [7]. Additionally, the treatment cost has also increased as a result of MDR since microorganisms have developed resistant to commercially accessible Abs, necessitating the adoption of a more expensive one.

Allium Sativum (Garlic) As Alternative Treatment

In recent years, awareness of the issue of antibiotic resistance has increased, including in the political field: In 2017, the countries decided to intensify global collaboration on this issue to stimulate the R&D of antimicrobial molecules, also starting from existing antibiotics . Since 2017, eight new antibiotics have been approved by the FDA, including one for the treatment of multidrug-resistant tuberculosis: Most of these drugs were developed from traditional molecules and target Enterobacteriaceae resistant to carbapenems and other pathogens considered dangerous by WHO. Findings have shown that garlic can be used in the management of various diseases such as cardiovascular disease and hyperglycemia. Additionally garlic has been approved to reduce the risk of cancer, boosting the immune system and protecting against inflammation as well as infectious diseases. Their antimicrobial activity has been linked to the presence of sulphur compounds, specifically, allicin which is the compound produced by the alliin lyase enzyme, after crushing or bruising a garlic bulb. Many medical bacteria, including grampositive and gram-negative strains, are sensitive to garlic extracts, indicating that garlic has a reliable broad spectrum of activity related to its chemical composition. However, the amounts and types of antimicrobial substances extracted depend on diverse extraction methods. Allicin is a reactive sulfur species and reacts with free thiol groups such as those in protein cysteine or glutathione; thus it has a wide range of cellular targets. GSH is oxidized by allicin to S-allylmercaptoglutathione (GSSA), diminishing the cellular GSH pool and leading to oxidative stress in the cell (Jana Reiter et al.; 2020). Furthermore, allicin oxidizes accessible cysteine in proteins to produce Sallylmercapto- adducts. S-thioallylation of cysteine can inhibit essential enzymes, or disrupt signal transduction by changing the three-dimensional conformation of proteins, or preventing metal cofactor binding; these properties are generally thought to be responsible for allicin’s antimicrobial activity.

CONCLUSION

Fundamental Finding : This study emphasizes the significant antibacterial potential of *Allium sativum* (garlic) in combating multidrug-resistant (MDR) bacterial pathogens, attributing its efficacy to bioactive compounds such as allicin, which disrupts microbial cell functions and enhances oxidative stress in pathogens. **Implication :** The results support the integration of garlic-derived compounds as complementary or alternative therapeutics in antimicrobial regimens, particularly in low-resource settings, due to their broad-spectrum activity, low cost, and minimal side effects. Furthermore, the synergistic interaction between garlic extracts and conventional antibiotics may enhance treatment outcomes and reduce reliance on high-dose pharmacological agents. **Limitation :** However, the current findings are limited by variability in garlic extract composition due to differences in extraction methods, lack of standardized dosages, and the predominance of in vitro studies without extensive clinical validation. **Future Research :** Further experimental and clinical studies are needed to standardize extraction techniques, determine pharmacokinetics, assess toxicity profiles, and validate the in vivo efficacy of garlic-based formulations against MDR infections, ultimately paving the way for their incorporation into modern antimicrobial protocols.

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