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Navigating Antibiotic Resistance in *Staphylococcus aureus*: Mechanisms, Strategies, and Future Perspectives, A Mini Review

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ABSTRACT

The review article addresses the significant issue of antibiotic resistance, focusing on *Staphylococcus aureus* (*S. aureus*) infections and its potential threat to public health. It highlights the challenges in treating these infections due to the diverse nature of *S. aureus* strains and emphasizes the global impact of antimicrobial resistance [AMR]. The review discussed the genetic diversity and antibiotic resistance genes in *S. aureus*, particularly the MRSA strain.

Introduction:

Staphylococcus aureus [*S. aureus*] is a bacterium that frequently causes an infection in humans and is also able to acquire resistance to several antibiotics that are regularly used in bacterial infection [1]. In some countries like China, up to 40% of these infections are instigated by *S. aureus*. The major issue is that *S. aureus* infections are difficult to treat because it has several common and rare types, making it difficult to find effective *S. aureus* treatments [2]. Antimicrobial resistance [AMR] is a major problem in healthcare and it means the medicine isn't effective anymore against infectious bacteria [3].

Regular use of antibiotics makes them less effective in treating infections. In some places, like Europe, they limit administering antibiotics to animals because it can lead to AMR. When bacteria, like *S. aureus, Salmonella*, and *K. pneumoniae*, become resistant, it's difficult to treat the infections [4]. For example, there's a type of *S. aureus* called MRSA, which doesn't respond to common antibiotics. In Europe, attempts were made to control MRSA. However, MRSA remains a substantial issue in various areas [5]. To circumvent public health issues, the World Health Organization [WHO] acclaims to improve healthcare, and developing new drugs against resistant microbes [6]. This review highlights the probable threat of *S. aureus* in raw milk to human health. Investigating their genetic diversity, and how they resist antibiotics helps us to understand their pathogenicity.

Antibiotic Revolution and Resistance:

In the 1940s, antibiotics like Penicillin were a big breakthrough in treating infections. But, bacteria started getting resistant to these antibiotics. Antibiotics were considered a miracle cure against bacteria in the 1940s and 1950s. Antibiotics, once seen as a solution, became a problem due to overuse and bacteria developing resistance [7]. In the 1960s, antibiotic concerns grew. In the US, investigations into the pharmaceutical industry led to more standardized drug trials and global regulations. In the UK, issues arose about antibiotic use in agriculture, especially in milk production. Books like Silent Spring and research highlighted antibiotic resistance spreading between different bacteria and species. People started seeing antibiotic resistance as environmental pollution with resistant microbes. The fear of "superbugs" emerged, describing bacteria resistant to many drugs [8].

Mechanisms and Evolution of Antibiotic Resistance in *S. aureus*:

The genetic determination of resistance to many antimicrobial agents is thought to have advanced erstwhile to the era of antibiotic chemotherapy. Antibiotic resistance in *S. aureus* comprises many mechanisms which are drug efflux, expression, or mutation of target proteins, leading to its rapid evolution which requires innovative approaches to develop novel treatment methodologies [9] [Figure 2].

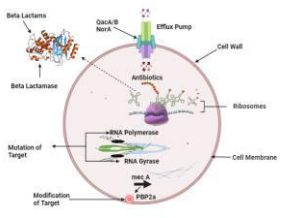

Figure 1. Mechanisms and Evolution of Antibiotic Resistance in *S. aureus*.

Advanced Genetic Analysis of Bacteria:

Scientists used a special method called pulsed-field gel electrophoresis [PFGE] to study bacteria. They took samples, created a gel to separate the bacteria's DNA, and looked at the patterns to identify different types of bacteria. To recognize the genes of bacteria researchers, investigate their DNA sequence. They used different approaches and databases to investigate the genes, proteins, and other fragments of the DNA [10]. They also studied the procedure that how the bacteria becomes able to resist the regular use of conformist antibiotics. Using a database called CARD, scientists found 18 genes in bacteria [*S. aureus]* that make it resistant to regularly used antibiotics. They confirmed the presence of a specific gene, mecA, which showed that the bacteria were MRSA, a type that's resistant to antibiotics [11]. Scientists used advanced methods and databases to find these genes and understand the mechanism of how the bacteria resist medicines.

Antibiotic-resistant Development Mechanism:

Regular use of antibiotics in humans, and animals contaminate the water, dairy, and agricultural products. This results in the perseverance of drug residues or resistance genes in the food products obtained from livestock and agriculture which leads to Antibiotic-resistant development [12] [Figure 2].

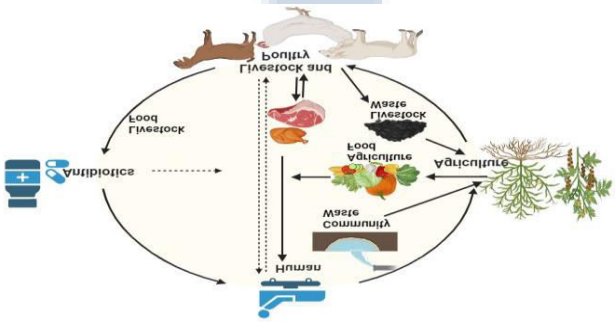

Figure 2: Mechanism of Antibiotic-resistant Development.

Strategies Against *S. aureus*, Prevent Infections and Ensuring Safety:

To prevent *S. aureus* infections, scientists are exploring different strategies. They are seeking natural alternatives to antibiotics like phytochemicals to control *S. aureus* without causing antibiotic resistance. Nanoparticles, probiotics, plant compounds [cinnamaldehyde], and vaccines are being explored as alternatives to antibiotics which successfully prevent bacterial infection without any harm to ARM and are completely safe for body health [13].

Health Awareness Initiatives:

World Antimicrobial Awareness Week from November 18-24 aims to prevent antimicrobial resistance. Despite efforts, there are concerns about public awareness of these health issues.

Scientists extracted DNA from bacteria like *S. aureus* in meat samples using special kits [14]. They identified bacteria-related genes and tested for bacteria using color and enzyme reactions. Antibiotic effectiveness against *S. aureus* in raw meat was also checked using paper discs. Out of 452 meat samples, 96 had *S. aureus*, most common in beef. Testing 96 strains found many were

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resistant to antibiotics, with most resistance against kanamycin and telithromycin. Nearly all strains were resistant to multiple drug classes, some to up to 10 different classes [15].

Antibiotic Resistance Causes, Challenges, and Solutions:

Antibiotic resistance happens when microbes become too strong for the medicines we use. This mainly occurs because we use antibiotics too much, not just in healthcare but also in farming and the environment. Poor hygiene and bad animal care can also spread these microbes. It's not just about how many antibiotics we use; things like clean water, and healthy food. Resistance doesn't just come from bacteria changing on their own; they can also get stronger by sharing genes. Contaminated water is a major way these genes spread, especially in places with bad water quality [16]. There are things we can do now to control antibiotic resistance. In hospitals, better infection control can make a big difference. In Australia, they reduced certain infections a lot in 12 years through national efforts. We can also reduce antibiotic use in animals like Denmark and the Netherlands did, and some big US companies are making positive changes [17]. Imported foods and travel can bring resistant microbes, so it's important to be cautious about what we eat and take preventive measures during travel to avoid spreading these microbes.

National and International Initiatives:

The issue of antibiotic resistance is getting worse. Some bacteria, like MRSA and VRE, are not responding to many antibiotics, making it difficult to treat infections in the United States and Europe. Overusing antibiotics is a big reason. Advertisements and online sales also make it easy for people to ask for specific, expensive antibiotics. This misuse of antibiotics creates more resistant bacteria, making infections tougher to treat [18]. To tackle this problem, many countries are working together to monitor resistant bacteria. Different programs like EARSS collect important information on antibiotic resistance. Doctors use Antibiotic Stewardship Programs wisely, like 'Start Smart, Focus' in the UK. Another method, 'care bundle,' improves use by starting small, adjusting based on tests, and ensuring the right dosage for the shortest time [19]. Education and feedback to doctors are crucial for effective antibiotic use.

Future Infectious Threats:

Formulating for the future of various infectious diseases involves forecast and bearing in mind factors such as climate change, population growth, and economic challenges. Experts have created different scenarios, imagining situations where reduced immunity, social inequalities, and human movement lead to disease outbreaks. These scenarios help in planning for public health to be better prepared for the future. It's essential to note that not all these scenarios will happen, and efforts in public health can prevent some of them [20].

Conclusion:

Antibiotic resistance is a major health problem. Some microbes, like *S. aureus*, can cause infections that are difficult to treat because they get used to the medicines. This happens not just in people but also in animals. The medicines we use to treat infections aren't working as well anymore. Scientists are observing various alternatives, like vaccines, nanoparticles, probiotics, and plant compounds [cinnamaldehyde] to control the bacterial infections that are resistant to conformist antibiotics and difficult to treat. In the future, researchers are investigating alternative medicines and phytochemicals to prevent bacteria that have become resistant, like *S. aureus*.

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