**Egyptian Journal of Veterinary Sciences**

**https://ejvs.journals.ekb.eg/**

# Antibiotic Resistant *Staphylococcus aureus*, Its Prevalence, Isolation and Prevention Techniques

**Ahmed N. Elashry*, Esmat I. El-Said*, Salah F. Abd ElAal, Mohamed A. Bayomi and Eman N. Abdelfatah**

*Department of Food Control, Zagazig Univeristy, Zagazig City, 44511, Sharkia Governorate, Egypt*

**Abstract**

STAPHYLOCOCCUS is one of the major causes of human infection that normally presents on mucous membranes and skin but can become pathogenic under some conditions and cause bacteremia, cellulitis, sepsis, urinary tract infection (UTI), and pneumonia. *Staphylococcus aureus* (*S. aureus*) is considered the most dangerous species, as it shows different mechanisms of pathogenicity. The severity of diseases that it causes is due to the production of several putative virulence factors and possession of antibiotic resistance genes such as *mec*A, *van*A, staphylococcal exotoxins, and other factors that facilitate the initiation of disease process, immune evasion, and host tissue destruction. It is a highly adaptable bacterium that develops resistance to the majority of antibiotics on the market. Drug resistance in *S. aureus* has gradually risen over the last few decades as the pathogen has evolved and antibiotics have been abused. The emergence of antimicrobial resistance in *S. aureus* posed a major veterinary and public challenge worldwide. *S. aureus* being a highly versatile pathogen, can quickly acquire resistance genes. The development of resistance in bacteria predates the era of antibiotic use. This review aims to highlight - AMR *S. aureus*, its prevalence, ecology, and antimicrobial resistance and, to explore recently effective prevention and control strategies to mitigate its impact on public health.

**Keywords**: *S. aureus*, AMR, SEs, Mec genes, SFP.

## Introduction

*S. aureus* is a versatile bacterium distributed everywhere and highly adaptable within the host. It colonizes the skin and mucous membrane of different body parts like, gastrointestinal tract (GIT), perineum, pharynx and anterior nares [1]. It has a considerable influence on public health as it can cause several infectious diseases in humans [2]. The potency of *S. aureus* relies on its ability to produce plenty of highly virulent factors like the production of staphylococcal enterotoxins (SES) and other factors that initiate the disease, hiding the pathogen from immunity attack and leading to host cell destruction. As well as the emergence of several antibiotic-resistant genes like *mec*A and *van*A which decrease treatment efficacy [3]. The deployment of staphylococcal infection and the emergence of multidrug resistant (MDR) *S. aureus* are of great concern in food quality control and public health [4]. It is considered one of the coagulase-positive microorganisms (m.os), multidrug - resistant, can produce heat-stable enterotoxins (SEs), and has the ability to cause cross-contamination on food processing utilities, basically through surfaces that come in contact with foods and food handlers [5]. Contamination of *S. aureus* has been recognized as one of the leading causative agents of diverse severe clinical infections in humans of account to their high incidence as food-borne illness outbreaks worldwide [6]. Nowadays, the deployment of antibiotic-resistant pathogens has increased, and the availability of new antibiotic drugs has decreased, posing a great challenge to public health. However, the use of antibiotics in farm animals is significant and has been discussed for selecting resistant microorganism , with the animals acting as reservoirs for resistant pathogens and having the ability to transmit them through consumption and food products [7]. Lately, *S. aureus* has been reported to be the 2nd worldwide pathogen that is responsible for antimicrobial

*Corresponding authors: Esmat I. Elsaeid, E-mail: esmatawad2@yahoo.com Tel.: +201010531873
(Received 16 March 2025, accepted 24 April 2025)
DOI: 10.21608/ejvs.2025.368801.2705

resistant (AMR)-associated deaths, with methicillin-resistant *S. aureus* (MRSA) alone causing over 100,000 mortalities ascribed to AMR in 2019 [8]. MRSA are the main human pathogens that exhibit greater virulence and resistance to different antibiotics. Causing numerous infections, from mild to fatal conditions [9].

*Reservoir and staphylococcus transmission*

Human nostrils are considered the greatest reservoir for *S. aureus* [10], followed by milking animals' skin, mucus membrane and udder which are considered as essential reservoirs[11]. The infected animals excrete bacteria in their milk and it can be also transmitted by insects, utensils, or handlers' coming in contact with the contaminated milk, other environmental transmission routes are less frequent [12]. *S. aureus* can survive in the environment but to ensure its survival, it needs animal colonization [13]. Infectious strains of staphylococcus genus usually transmit through the community, hospital and animals as bacteria can be transmitted easily between humans and animals especially in farm environments [14]. It can contaminate milk, milking utensils, and finally, processing plants and dairy products, as it was known it has a great ability to form biofilms which help in its resistance to antimicrobials and protection from sanitizers [15]. Foods - produced from raw milk, in particular, are of great importance considering that Staphylococcus spp. are most commonly identified as mastitis-causing microorganisms [16]. As in Egypt, populations usually consume raw milk and dairy products like raw milk cheese, laban rayed, and yoghurt. Which may be manufactured, handled, and stored under unhygienic practices [17]. Furthermore, foods that come from animal origin can be a cause of staphylococcal food poisoning via secreting SEs [18] when a high number of *S. aureus* cells are found in the food. The toxins are thermostable and, once produced could persist in heated or fermented foods, whereas viable cells decline in number, reaching undetectable levels [19]. During the production chain, contamination of dairy products with MRSA could be incriminated by animal, human, and environmental sources [20].

*Associated infections in animals and human*

*In animals:*

*S. aureus* is one of the most prevalent pathogens in veterinary medicine, and it can be considered a major cause of mastitis in dairy animals [21]. It can also cause different diseases, that vary in severity from small abscesses to clinical and sub-clinical mastitis as a contagious pathogen and may lead to chronic infection which can't be cured easily [22]. Infection of mammary gland with *S. aureus* is still a pressing issue for the dairy industry all over the world because of its pathogenicity, persistence in cow environment, colonization on skin or mucosal epithelial tissue, contagiousness, and limited therapeutic efficacy of many applied antimicrobials agent [23]. Misuse and haphazard use of these antibiotics may end with presence of antibiotics residues which in turn lead to development of drug-resistant bacteria and lead to treatment failure [24]. Misuse of antibiotics and roughly handled animals can lead to infection with - plenty of pathogenic microorganisms as *S. aureus* [25].

*In humans*

*S. aureus* is one of the significant pathogens that triggers a variety of diseases in humans including, pneumonia, endocarditis, and bacteraemia [26]. As well as cellulitis, impetigo, abscess, folliculitis, and highly contagious skin infection [27]. On the other hand, other diseases can be induced by staphylococcal toxins that are secreted by many strains of pathogenic *S. aureus* as toxic shock syndrome, Staphylococcal food poisoning (SFP), and scalded skin syndrome [28]. Eating food contaminated with SEs, leads to SFP, which appear as nausea, abdominal cramps and vomiting within 2-8 h. [29]. Toxins of *S. aureus* may also result in a syndrome called toxic shock syndrome which is characterized by rash, fever, life threatening low blood pressure, and finally failure of many organs [27]. More than 24 genes are responsible for *S. aureus* enterotoxicity for instance, (SEA, SEI, SEE, SEG and SEIZ). Recently new genes of SEs are discovered as sel26 and sel33 [30]. According to the International Nomenclature Committee for Staphylococcal Superantigens (INCSS), Staphylococcus strains to be classified as SEs producing, their toxin should exhibit emetic toxicity. And other toxins that are not related to emetic activity are named staphylococcal enterotoxin-like [31]. Although the latest researches revealed that the SEs considered as enterotoxins, depending on their molecular structure, they do not demonstrate any emetic potential in primates as recommended by the INCSS [32]. Contamination of food with staphylococcal toxins poses a risk to consumer due to its stability at high temperatures and wide range of pH 4–7.4 [33]. The infective dose of *S. aureus* to reach a level of foodborne toxicity and cause disease is $10^5$–$10^6$ CFU/g [34].

*Pathogenicity and effects on response to treatment*

*S. aureus* to infect humans and animals needs virulence factors that help it to hide from the immune system, attach to the host cells and

harm it [35]. So, plenty of virulence factors are secreted by *S. aureus*. Adherence and exotoxins are the primary virulence factors [36]. Infection caused by *S. aureus* needs more than one virulence factor, except in the case of toxic shock syndrome [37]. *S. aureus* has an important method to maintain its infection by producing biofilms [38]. Biofilms are a case of a matrix made from proteins, polysaccharides and extracellular DNA that encloses communities of bacteria and protect them from phagocytic cells. Biofilms are produced by three main steps: attachment, proliferation, and separation [39]. For pathogenesis, *S. aureus* can hide from the host immune system by the peptidoglycan layer, which decreases opsonisation so the pathogen can escape from the phagocytic cell [40]. *S. aureus* colonizes host cells efficiently due to its secretion of adherence materials, which help it interface with host cells [41]. Also, it has elaborated strategies to counter antimicrobial peptides and the complement system [42]. Toxins, proteins of the cell surface, enzymes, and adherence proteins of *S. aureus* help it to hinder innate immunity and the efficacy of drugs, which increases the ability of this microbe to cause infection [43].

*Antimicrobial resistant S. aureus*

Antibiotic resistance is a natural phenomenon that predates the use of antibiotics in human and veterinary medicine, as well as in agricultural practices [44]. It has become a significant dangerous issue for public health worldwide [45]. The criticality of Staphylococcus strains did not depend only on its epidemiological and clinical importance but also on their ability to overcome the efficacy of antibiotics [46]. Thus, *S. aureus* is considered an infamous microbe due to its ability to resist a wide range of antibiotics and the development of MDR worldwide [47]. The first antibiotic resistant *S. aureus* strain was discovered in mid-1940, and it resisted penicillin by producing a penicillinase enzyme that hydrolysed penicillin [48]. After this time, methicillin was introduced as a treatment of penicillin resistant *S. aureus*, and then the resistance against methicillin was discovered within a year of using it as a drug of choice against *S. aureus* infection [47]. After the failure of penicillin and methicillin to cure *S. aureus* infection, plenty of antibiotics were used, but *S. aureus* unfortunately resists these antibiotics too [49]. Increased usage of vancomycin against MRSA infections led to emergence of vancomycin resistant *S. aureus* [50]. Resistance of *S. aureus* to vancomycin highly increased producing vancomycin resistant *S. aureus* (VRSA); its resistance may be due to acquired transposon Tn1546 [51]. It is worth mentioning that *S. aureus* can tolerate antibiotics by several mechanisms, like modification of some proteins, upregulation of drugs outflow, this resulted in trying to find new treatment modalities. On the other hand, recent studies found an interesting phenomenon called cross-protection, where exposure of m.o. to abiotic stressors, during different product processing such as cold temperatures, acidity, or osmotic extremes, induces resistance to commonly used antibiotics [52]. Over the last 4 decades, the research suggested that AMR in east Africa is related to human-animal contact as they use a high level of antibiotics in small production systems, ignoring the withdrawal time from recently treated animals that are used for human consumption of milk and meat products. This account is one of the major reasons for treatment failure of infectious diseases [53]. Although global production has been rapidly growing and has moved increasingly, over using or abusive usage of antimicrobial agents as an integral part of production may lead to the risk of presence of antibiotic residues in foods. When humans consume it, the antibiotic residues will accumulate in the body and may cause numerous side effects, such as transfer of antibiotic-resistant bacteria to humans, reproductive disorders, allergy, bone marrow toxicity, hepatotoxicity, and kidney failure [54]. The emergence of resistant bacteria in food leads to the use of antimicrobials in the food processing chain, indicating that these bacteria can contaminate food, humans, and animals and pass their genes to other bacteria. MRSA strains pop up as one of antimicrobial resistant bacteria. It's endemic in many hospitals worldwide and identified in food- producing animals and people in contact with them [55]. In the last few decades, multidrug resistant staphylococci, especially MRSA, have shown their ability for zoonotic transmission, and their deployment has increased dramatically due to bacterial adaptation, evolution, and antibiotic overuse for therapy or prophylaxis [56]. Its morbidity rate is one hundred times that of tuberculosis (TB), while its mortality rate is more than that of HIV-AIDS [57]. The vulnerability of MRSA to antimicrobial variables depends on its source, whether animal or human source, and usually the isolated MRSA strains are MDR. For instance, in a study done by scientists found that all isolated MRSA strains were resistant to 6-11 antimicrobials, unveiling a variable rate of resistance to cefoxitin, amoxicillin, tetracycline and enrofloxacin. While all isolates were

susceptible to gentamicin, vancomycin, and tobramycin [58]. Although MRSA is prevented from entering food chain by the pasteurization of milk, its fate in dairy products from fresh milk is unknown [20]. MDR *S. aureus* strains, especially MRSA are related to the containing of a DNA fragment called Staphylococcal Cassette Chromosome mec (SCCmec), which carries the *mecA* gene responsible for encoding a protein called Penicillin Binding Protein 2A (PBP2A) that has low affinity to the β-lactam ring. The synthesis of this protein allows bacteria that carry SCCmec to build the bacterial cell wall even in the presence of β-lactams antibiotics, granting resistance to most antimicrobials in this group [59]. Thirteen different types of SCCmec have been discovered, and *mecC* (a *mec*A homolog), has also been found to confer resistance to penicillinase-resistant penicillin [60]. The SCCmec element carries genes that control mec gene expression (*mecR1* and *MecI* [encoding *MecI*-repressor protein]) and acts as a carrier for the exchange of genetic information among Staphylococcus strains [61]. It can resist the tetracycline group by several mechanisms that provide tetracycline resistance. Due to the *tet*M gene, which develops ribosomal protection because tetracycline is a bacteriostatic compound that binds to 30S ribosomal subunits and blocks protein production [62]. MRSA and VRSA are debilitating bacteria that cause a high percentage of deaths globally and for which there are no effective treatment options. They considered MDR bacteria that resist too many types of available antibiotics. Lately, VRSA strains increased in Africa and Asia, resistance mostly caused by *vanA* and SCCmec II. Control of MRSA is very important to prevent the emergence of more VRSA strains [63].

*S. aureus isolation techniques*

The gold standard isolation technique is culture based method due to its efficacy and sensitivity, but it needs a long time for judgement which limits its usage in food industry [64]. Plate culture techniques for isolation and identification, Gram staining, and biochemical tests as (urease, methyl red, catalase, coagulase, and citrate and sugar fermentation) and non-selective pre-enrichment were used for Staphylococcus species identification, and they took several days for analysis [65]. Then, further identification with immunological methods and molecular techniques. For instance, plate culture can be done by using 10 ml of milk or 10 grams from dairy products, placed with 90 ml of tryptic soya broth (TSB) and 6.5% NaCl in a stomacher bag, then homogenized for 2 minutes then in the same broth we made ten-fold serial dilution. 1 ml from each dilution was poured in Baird- Parker (BPA) media supplemented with egg yolk tellurite. Plated 1 ml of milk on BPA media to detect less than 10 CFU per g or ml of sample. Other milk products should be enriched for 24 h at 35°C and, then take one loopful of the enriched culture and incubated aerobically at 35 °C for 24-48 h [20]. It is worth mentioning that, the most widely molecular method used in detecting *S. aureus* is polymerase chain reaction (PCR) by amplification of *nuc* gene, the coagulase gene a 500- to 650-bp fragment of the coa gene and a 416-bp fragment of the nuclease (*nuc*) gene were amplified [66] or 16 s rRNA. Also used for detection of AMR genes by using specific primers associated with antimicrobial resistance. PCR is considered the gold- standard technique to detect methicillin resistant gene as *mec*A and other resistant genes like *erm*C, *bla*Z, *erm*A, *van*A, and *tet*M [67]. An attractive method instead of this traditional one is molecular methods as real -time PCR (RT-PCR) that is used in quantitative gene detection. For example, using RT-PCR in the detection of different resistant genes such as (*mec*A, *van*B, and *erm*B) and virulence genes that belong to resistant species like staphylococcus [68].Many techniques are developed like clustered regularly interspaced short palindromic repeats (CRISPR)--based diagnostics and loop-mediated isothermal amplification (LAMP) to test MRSA in food, and these techniques are promising for more accurate and short time results [69]. Plenty of methods are used to identify AMR in Staphylococcus species phenotypically such as agar disc diffusion and broth micro-dilution methods; they are the most used techniques to detect AMR strains isolated from food. The MALDI- TOF-MS method can be used to detect AMR bacteria as, extended-spectrum β-lactamases [70]. Recently, antibiotic susceptibility tests can be replaced by developed biosensors. For example, resistance to vancomycin, methicillin, ampicillin, and erythromycin can be accessed by gauging the impedance produced by *S. aureus* cultured on plastic microchips [71]. Biosensors used in many fields now as those used in detection of toxins, m.os, and AMR genes due to their short time analysis, specificity, and ease of use. They are composed of 2 main components: a biological element that interacts with the target of interest, and a transducer that produces a measurable signal from this bio-recognition. There are types of transducer (optical, piezo-electrical, and electrochemical) and different bio-receptor as (antibodies and DNA probes,

enzymes etc...) [72]. Using biosensors to detect AMR genes needs DNA to be extracted first before application of biosensors. Gene's detection by biosensors takes less than 2h for hybridization between the DNA probe and the target gene. The *mec*A gene for example, can be detected within 1 h by using ssDNA probes Mounted on N-doped porous carbon materials within the limit of 3.6 FM [73]. *S. aureus* in milk and infant formula can be seen by the naked eye using colorimetric biosensors developed by some scientists, and this technique combines specific aptamers that bind *S. aureus* cells with gold nanoparticles, and the phenomenon of localized surface plasmon resonance. When conditions are optimized, *S. aureus* can be seen within 30 min., but this is limited detection as the detection limit was 8.4 × $10^4$ CFU/mL in infant formula and 7.5 × $10^4$ CFU/mL in milk. These biosensors can be used to assess the microbiological safety of food in a short time through detecting pathogens directly in food. Although further optimizations are needed to meet end-users compliance [74].

*Prevention and treatment of S. aureus*

Rapid techniques for microbiological isolation and analysis are needed for prevention of *S. aureus* and its SEs from food chain. So, monitoring programs, prevention techniques, GMP and biosecurity with judicious use of antibiotics should be executed from farm to distribution. Hygienic standards to deal with raw food such as milk to prevent contamination with *S. aureus*. On the other hand, consumers should have know potential risks and good sanitation procedures to prevent contamination [75]. It is important to know that antibiotics are indispensable in treating bacteria, for instance, treatment of MRSA strains is still effective by using teicoplanin, and glycopeptide antibiotics. As well as new generations of cephalosporins as ceftaroline which have broad spectrum antibiotic activity to overcome the limitation of cefazoline [76]. For these reasons, maximum limit of antibiotics residues in foodstuffs might be demonstrated to decrease AMR. However, detecting antibiotics in foodstuffs is still an explicit challenge [77]. Recently, nano-drugs have been used as an alternative choice to antibiotics to cure MDR, and highly persistent *S. aureus* related to bovine recurrent and subclinical mastitis [78]. On the other side, alternative techniques to classical antibiotics are used to decrease AMR, including bacteriophages, which can be used as antimicrobial agents [79]. The pros of using bacteriophagesthat bacteriophages are very specific to their host, auto -replicate, can recognize MDR bacteria and lysis it and their safety [80]. Probiotics can also be used in producing supplements and food products as a substitute for antibiotics. However, using it in food is more efficient than in supplements because food act as a buffering media for probiotics and serves as source of nutrient that help in efficacy, viability and multiplication of probiotics [81]. The most applied M.O used as probiotics in industry are lactic acid bacteria (LAB) [82]. Recently, many researchers reported that moringa oleifera leaf extract (MOLE) as an alternative to antibiotics. It contains flavonoids, sterols, tannins, and tocopherols. So, it has antioxidant activity and used as an anti-cancer, anti-carcinogenic, anti-hypersensitivity and, anti-obesity [83]. MOLE has antimicrobial activity as it causes microbial protein denaturation and leads to cell wall damage of bacteria [83]. Also, it contains tannins which inactivate bacterial enzymes [84]. As well as alkaloids that inhibit bacterial multiplication by stopping enzymes needed for DNA replication and cause disruption of cell walls by damaging peptidoglycan of bacterial cell walls [85].

## Conclusion

*S. aureus* contamination is a great issue worldwide. Its prevalence significantly increased, especially MRSA strains, which resist several types of antibiotics, which resulted in treatment failure and it becomes persistet in host cells. Its toxins resulted in many mild to severe symptoms. To avoid staphylococcus contamination and its SEs, strict preventive measures are required from farm to dairy product processing and storage. Good hygienic practice (GHP), good manufacturing practice (GMP), and hazard analysis and critical control points (HACCP) should be applied to provide safe products for consumers.

*Acknowledgement:*

The authors wish to express their gratitude to the Department of Food Hygiene, Safety, and Technology, Faculty of Veterinary Medicine, Zagazig University, Egypt.

*Funding statement*

There is no external funding for the present study.

*Declaration of Conflict of Interest*

The authors declare that there is no conflict of interest.

*Ethical approval*

This research was conducted in compliance with Zagazig University's guidelines.

## References

1. Den Heijer, C.D.J., van Bijnen, E.M.E., Paget, W.J., Pringle, M., Goossens, H., Bruggeman, C.A. and Stobberingh, E.E. Prevalence and resistance of commensal *Staphylococcus aureus*, including methicillin-resistant *S. aureus*, in nine European countries: a cross-sectional study. *The Lancet Infectious Diseases*, **13** (5); 409-415(2013). https://doi.org/10.1016/S1473- 3099(13)70036-7.
2. Luzzago, C., Locatelli, C., Franco, A., Scaccabarozzi, L., Gualdi, V., Viganò, R., Sironi, G., Besozzi, M., Castiglioni, B., Lanfranchi, P. and Cremonesi, P. Clonal diversity, virulence-associated genes and antimicrobial resistance profile of *Staphylococcus aureus* isolates from nasal cavities and soft tissue infections in wild ruminants in Italian Alps. *Veterinary Microbiology*, **170**(1), 157-61(2014). https://doi. org/10.1016/j.vetmic.2014.01.016
3. Holden, M.T.G., Feil, E.J., Lindsay, J.A., Peacock, S.J., Day, N.P.J., Enright, M.C. and Atkin, R. Complete genomes of two clinical *Staphylococcus aureus* strains: evidence for the rapid evolution of virulence and drug resistance. *Proceedings of the National Academy of Sciences of the United States of America*, **101**(26), 9786-9791(2004). https://doi.org/10.1073/ pnas.0402521101
4. Sri Prabakusuma, A., Zhu, J., Shi, Y., Ma, Q., Zhao, Q., Yang, Z. and Huang, A. Prevalence and antimicrobial resistance profiling of *Staphylococcus aureus* isolated from traditional cheese in Yunnan, China. *3 Biotech.*, **12**, 1-15 (2022). https://doi.org/10.1007/s13205-021-03072-4
5. Naorem, R.S., Blom, J. and Fekete, C. Genome-wide comparison of four MRSA clinical isolates from Germany and Hungary. *Peer Journal*, **9**, e10185 (2021).
6. Nouws, S., Bogaerts, B., Verhaegen, B., Denayer, S., Laeremans, L., Marchal, K., Roosens, N.H.C., Vanneste, K.D. and Keersmaecker, S.C.J. Whole genome sequencing provides an added value to the investigation of staphylococcal food poisoning outbreaks. *Frontiers in Microbiology*, **12**, 750278 (2021).
7. Nordstrom, L., Liu, C. M. and Price, L. B. Foodborne urinary tract infections: a new paradigm for antimicrobial-resistant foodborne illness. *Frontiers in microbiology*, **4**, 29 (2013).
8. Murray, C.J.L., Ikuta, K.S., Sharara, F., Swetschinski, L., Robles Aguilar, G. and Gray, A. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *Lancet*, **399** 629–655 (2022).
9. Barcudi, D., Sosa, E. J., Lamberghini, R., Garnero, A., Tosoroni, D., Decca, L. and Sola, C. MRSA dynamic circulation between the community and the hospital setting: New insights from a cohort study. *Journal of Infection*, **80**(1), 24-37 (2020).
10. Moreillon, P. and Que, Y. A. Infective endocarditis. *Lancet*, **363**, 139-149(2004).
11. Asperger, H., Zangerl, P., Roginski, H., Fuquay, J. and Fox, P. *Staphylococcus aureus*. *Encyclopedia of Dairy Sciences*, 2563-2569 (2003).
12. Capurro, A., Aspan, A., Ericsson Unnerstad, H., Persson Waller, K. and Artursson, K. Identification of potential sources of *Staphylococcus aureus* in herds with mastitis problems. *Journal of Dairy Science*, **93**, 180–191 (2010).
13. Haag, A., Fitzgerald, J. and Penades, J. *Staphylococcus aureus* in animals. *Microbiology Spectrum*, **7**, 1–18(2019).
14. Teramoto, H., Salaheen, S. and Biswas, D. Contamination of post-harvest poultry products with multidrug resistant *Staphylococcus aureus* in Maryland-Washington DC metro area. *Food Control*, **65**,132–135 (2016).
15. Emiliano, J. V. D. S., Fusieger, A., Camargo, A. C., Rodrigues, F. F. D. C., Nero, L. A., Perrone, Í. T. and Carvalho, A. F. D. *Staphylococcus aureus* in dairy industry: Enterotoxin production, biofilm formation, and use of lactic acid bacteria for its biocontrol. *Foodborne Pathogens and Disease*, **21**(10), 601-616 (2024).
16. Gajewska, J., Zakrzewski, A., Chajęcka-Wierzchowska, W. and Zadernowska, A. Meta-analysis of the global occurrence of *S. aureus* in raw cattle milk and artisanal cheeses. *Food Control*, **147**, 109603 (2023).
17. Al-Ashmawy, M.A., Sallam, K.I., Abd-Elghany, S.M., Elhadidy, M. and Tamura, T. Prevalence, molecular characterization, and antimicrobial susceptibility of methicillin-resistant Staphylococcus aureus isolated from milk and dairy products. *Foodborne Pathogens and Disease*, **13**, 156-162 (2016).
18. Szczuka, E., Porada, K., Wesołowska, M. and Łęska, B. Occurrence and Characteristics of *Staphylococcus aureus* Isolated from Dairy Products. *Molecules*, **27**(14), 4649 (2022).
19. Rajkovic, A. *Staphylococcus*: Food poisoning. Pages 133-139 in *Encyclopedia of Food and Health*. Elsevier (2016). https://doi.org/10 .1016/B978-0-12-384947-2.00655-3.
20. Papadopoulos, P., Papadopoulos, T., Angelidis, A. S., Boukouvala, E., Zdragas, A., Papa, A. and Sergelidis, D. Prevalence of *Staphylococcus aureus* and of methicillin-resistant *S. aureus* (MRSA) along the production chain of dairy products in north-western Greece. *Food Microbiology*, **69**, 43-50 (2018).
21. Pal, M. Mastitis: A major production disease of dairy animals. *Agriculture World*, **4**, 46-51 (2018).
22. Magro, G. Bovine *Staphylococcus aureus* mastitis: from the mammary immune response to the bacteria virulence genes. Phd Thesis, Università Degli Studi Di Milano, Milan, Italy (2017).
23. Reynard, P., Foucras, G., Fitzgerald, J.R., Watts, J.L., Koop, G. and Middleton, J.R. Knowledge gaps and research priorities in *Staphylococcus aureus* mastitis control. *Transboundary and Emerging Diseases*, **65**, 149–165 (2018).
24. Sergelidis, D. and Angelidis, A. S. Methicillin-resistant *Staphylococcus aureus*: a controversial food-borne pathogen. *Letters in Applied Microbiology*, **64**(6), 409-418 (2017).

25. Pal, M., Kerorsa, G., Marami, L. and Kandi, V. Epidemiology, pathogenicity, animal infections, antibiotic resistance, public health significance, and economic impact of *Staphylococcus aureus*: A comprehensive review. *American Journal of Public Health Research*, **8**, 14-21 (2020).

26. Tong, S., Davis, J., Eichenberger, E., Holland, T. and Fowler, V. *Staphylococcus aureus* infections: Epidemiology, pathophysiology, clinical manifestations, and management. *Clinical Microbiology Reviews*, **28**, 603–661 (2015).

27. Bush, L. *Staphylococcus aureus* infections. *MSD manual* (2019).

28. Lin, J., Lin, D., Xu, P., Zhang, T., Ou, Q., Bai, C. and Yao, Z. Non-hospital environment contamination with *Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus*: proportion meta-analysis and features of antibiotic resistance and molecular genetics. *Environmental Research*, **150**, 528–540(2016).

29. Murray, R. Recognition and management of *Staphylococcus aureus* toxin-mediated disease. *Internal Medicine Journal*, **35**, 106–119(2005).

30. Cieza, M. Y. R., Bonsaglia, E. C. R., Rall, V. L. M., Dos Santos, M. V. and Silva, N. C. C. Staphylococcal enterotoxins: description and importance in food. *Pathogens*, **13**(8), 676 (2024).

31. Lina, G., Bohach, G. A., Nair, S. P., Hiramatsu, K., Jouvin-Marche, E. and Mariuzza, R. Standard nomenclature for the superantigens expressed by *Staphylococcus*. *Journal of Infectious Diseases*, **189,**2334–2336(2004).

32. Umeda, K., Nakamura, H., Yamamoto, K., Nishina, N., Yasufuku, K., Hirai, Y., Hirayama, T., Goto, K., Hase, A. and Ogasawara, J. Molecular and epidemiological characterization of staphylococcal foodborne outbreak of *Staphylococcus aureus* harboring seg, sei, sem, sen, seo, and selu genes without production of classical enterotoxins. *International Journal of Food Microbiology*, **256,**30–35(2017).

33. Al-Nabulsi, A. A., Osaili, T. M., AbuNaser, R. A., Olaimat, A. N., Ayyash, M., Al-Holy, M. A. and Holley, R. A. Factors affecting the viability of *Staphylococcus aureus* and production of enterotoxin during processing and storage of white-brined cheese. *Journal of Dairy Science*, **103**(8), 6869-6881(2020).

34. Ertas, N., Gonulalan, Z., Yildirim, Y. and Kum, E. Detection of *Staphylococcus aureus* enterotoxins in sheep cheese and dairy desserts by multiplex PCR technique. *International Journal of Food Microbiology*, **142**(1–2), 74–77(2010).

35. Foster, T. Immune evasion by *Staphylococci*. *Nature Reviews Microbiology*, **3**, 948–958 (2005).

36. Costa, R., Batistao, F., Ribas, M., Sousa, M., Pereira, O. and Botelho, M. *Staphylococcus aureus* virulence factors and disease. In A. Mendez-Vilas, Microbial Pathogens and Strategies for Combating Them. *Science, Technology and Education*, **1**, Badajoz, Formatex (2013).

37. Ferry, T., Perpoint, T., Vandenesch, F. and Etienne, J. Virulence determinants in *Staphylococcus aureus* and their involvement in clinical syndromes. *Current Infectious Disease Reports*, **7**, 420–428(2005).

38. Otto, M. Staphylococcal Biofilms. *Microbiology Spectrum*, **6**, 3–23(2018).

39. Thurlow, L., Hanke, M., Fritz, T., Angle, A., Aldrich, A., Williams, H. and Horswill, A. R. *Staphylococcus aureus* biofilms prevent macrophage phagocytosis and attenuate inflammation in vivo. *Journal of Immunology*, **186**, 6585–6596(2012).

40. O'Riordan, K. and Lee, J. C. *Staphylococcus aureus* capsular polysaccharides. *Clinical Microbiology Reviews*, **17**(1),218-234(2004).

41. Foster, T. J., Geoghegan, J. A., Ganesh, V.K. and Höök, M. Adhesion, invasion and evasion: the many functions of the surface proteins of *Staphylococcus aureus*. *Nature Reviews Microbiology*, **12**(1),49-62(2014).

42. Chavakis, T., Preissner, K.T. and Herrmann, M. The anti-inflammatory activities of *Staphylococcus aureus*. *Trends in Immunology*, **28**(9),408-418(2007).

43. Zecconi, A. and Scali, F. *Staphylococcus aureus* virulence factors in evasion from innate immune defenses in human and animal diseases. *Immunology Letters*, **150**(1-2), 12-22. 24(2013).

44. Chang, Q., Wang, W., Regev-Yochay, G., Lipsitch, M. and Hanage, W.P. Antibiotics in agriculture and the risk to human health: how worried should we be? *Evolutionary Applications*, **8**, 240–247 (2015).

45. WHO. Antimicrobial resistance: global report on surveillance. *World Health Organization*, Geneva, Switzerland (2014).

46. De Souza, M., de Oliveira, C., Annes, I., Castro, S., Rocha, B. and Silva, C. Antibiotic Resistance in staphylococcus species of animal origin. In *Antibiotic Resistant Bacteria - A Continuous Challenge in the New Millennium*, pp. 273–303(2012).

47. Basset, P., Feil, E.J., Zanetti, G. and Blanc, D.S. The Evolution and Dynamics of Methicillin-Resistant *Staphylococcus aureus*. In *M. Tibayrenc (Ed.), Genetics and Evolution of Infectious Disease*; (pp. 669-688(2011). London: Elsevier.

48. Jeljaszewicz, J., Mlynarczyk, G. and Mlynarczyk, A. Antibiotic resistance in Gram-positive cocci. *International Journal of Antimicrobial Agents*, **16**, 473–478(2000).

49. Emmerson, A.M. and Jones, A.M. The quinolones: Decades of development and use [Internet]. Vol. **51**, *Journal of Antimicrobial Chemotherapy*, 12702699 (2003). [cited 2021 Jan 15]. p. 13-20. Available from: https://pubmed.ncbi.nlm.nih. gov/12702699/

50. Kirst, H.A., Thompson, D.G. and Nicas, T.I. Historical yearly usage of vancomycin. *Antimicrobial Agents and Chemotherapy*, **42**, 1303–1304(1998).

51. Javed, M. U., Ijaz, M., Fatima, Z., Anjum, A. A., Aqib, A. I., Ali, M. M. and Ghaffar, A. Frequency and antimicrobial susceptibility of methicillin and vancomycin-resistant *Staphylococcus aureus* from

bovine milk. *Pakistan Veterinary Journal*, **41**(4),463-468(2021).

52. Liao, X., Ma, Y., Daliri, E.B.M., Koseki, S., Wei, S. and Liu, D., Interplay of antibiotic resistance and food-associated stress tolerance in foodborne pathogens. *Trends in Food Science and Technology*, **95**, 97–106 (2020).

53. Erb, A., Stürmer, T., Marre, R. and Brenner, H. Prevalence of antibiotic resistance in *Escherichia coli*: overview of geographical, temporal, and methodological variations. *European Journal of Clinical Microbiology & Infectious Diseases*, **26**, 83-90 (2007).

54. Bacanli, M. and Basaran, N. Importance of antibiotic residues in animal food. *Food and Chemical Toxicology*, **125**, 462–466 (2019). https://doi.org/10.1016/j.fct.2019.01.033

55. Abolghait, S.K., Fathi, A.G., Youssef, F.M. and Algammal, A.M. Methicillin-resistant *Staphylococcus aureus* (MRSA) isolated from chicken meat and giblets often produces staphylococcal enterotoxin B (SEB) in non-refrigerated raw chicken livers. *International Journal of Food Microbiology.* **328**, 108669 (2020). https://doi.org/10.1016/j.ijfoodmicro .2020.108669.

56. Crespo-Piazuelo, D. and Lawlor, P.G. Livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA) prevalence in humans in close contact with animals and measures to reduce on-farm colonisation. *Irish Veterinary Journal*, **74**, 21 (2021).

57. Peterson, L. R. To screen or not to screen for Methicillin- resistant *Staphylococcus aureus*. *Journal of Clinical Microbiology*, **48**(3), 683–689 (2010).

58. Parisi, A., Caruso, M., Normanno, G., Latorre, L., Sottili, R., Miccolupo, A. and Santagada, G. Prevalence, antimicrobial susceptibility and molecular typing of methicillin-resistant *Staphylococcus aureus* (MRSA) in bulk tank milk from southern Italy. *Food Microbiology*, **58**, 36-42 (2016).

59. Otto, M. and Chatterjee, S.S. Improved understanding of factors driving methicillin-resistant *Staphylococcus aureus* epidemic waves. *Clinical Epidemiology*, **205**, 205(2013).

60. Baig, S., Johannesen, T. B., Overballe-Petersen, S., Larsen, J., Larsen, A. R. and Stegger, M. Novel SCCmec type XIII (9A) identified in an ST152 methicillin-resistant *Staphylococcus aureus*. *Infection Genetics and Evolution.* **61**, 74–76 (2018).

61. Liu, J., Chen, D., Peters, B. M., Li, L., Li, B., Xu, Z. and Shirliff, M. E. Staphylococcal chromosomal cassettes mec (SCCmec): A mobile genetic element in methicillin-resistant *Staphylococcus aureus*. *Microbial Pathogenesis*, **101**, 56-67 (2016).

62. Nguyen, F., Starosta, A.L., Arenz, S., Sohmen, D., Donh ¨ ofer, ¨ A. and Wilson, D.N. Tetracycline antibiotics and resistance mechanisms. *Biological Chemistry*, **395** (5), 559–575 (2014).

63. Wu, Q., Sabokroo, N., Wang, Y., Hashemian, M., Karamollahi, S. and Kouhsari, E. Systematic review and meta-analysis of the epidemiology of vancomycin-resistance *Staphylococcus aureus* isolates. *Antimicrobial Resistance & Infection Control*, **10**, 1-13(2021).

64. Gizaw, F., Kekeba, T., Teshome, F., Kebede, M., Abreham, T., Berhe, H.H. and Tufa, T.B. Multidrug-resistant *Staphylococcus aureus* strains thrive in dairy and beef production, processing, and supply lines in five geographical areas in Ethiopia. *Veterinary Sciences*, **10** (12), 663 (2023).

65. Ouoba, L.I.I., Mbozo, A.B.V., Anyogu, A., Obioha, P.I., Lingani-Sawadogo, H., Sutherland, J.P. and Ghoddusi, H.B. Environmental heterogeneity of Staphylococcus species from alkaline fermented foods and associated toxins and antimicrobial resistance genetic elements. *International Journal of Food Microbiology*, **311**, 108356 (2019).

66. Zdragas, A., Papadopoulos, T., Mitsopoulos, I., Samouris, G., Vafeas, G., Boukouvala, E., Ekateriniadou, L., Mazaraki, K., Alexopoulos, A. and Lagka, V. Prevalence, genetic diversity, and antimicrobial susceptibility profiles of *Staphylococcus aureus* isolated from bulk tank milk from Greek traditional ovine farms. *Small Ruminant Research*, **125**, 120e126 (2015).

67. Oliveira, R., Pinho, E., Almeida, G., Azevedo, N.F. and Almeida, C. Prevalence and diversity of *Staphylococcus aureus* and staphylococcal enterotoxins in raw milk from Northern Portugal. *Frontiers in. Microbiology*, **13**, 846653 (2022).

68. Burcham, Z.M., Schmidt, C.J., Pechal, J.L., Brooks, C.P., Rosch, J.W., Benbow, M.E. and Jordan, H.R. Detection of critical antibiotic resistance genes through routine microbiome surveillance. *PLoS One*, **14** (3), e0213280 (2019).

69. Yigci, D., Atçeken, N., Yetisen, A.K. and Tasoglu, S. Loop-mediated isothermal amplification-integrated CRISPR methods for infectious disease diagnosis at point of care. *ACS Omega*, **8** (46), 43357–43373 (2023).

70. March-Rosselló, G. A. Rapid methods for detection of bacterial resistance to antibiotics. *Enfermedades Infecciosas y Microbiología Clínica*(English Ed), **35**,182–188(2017).

71. Safavieh, M., Pandya, H.J., Venkataraman, M., Thirumalaraju, P., Kanakasabapathy, M. K., Singh, A. and Shafiee, H. Rapid real-time antimicrobial susceptibility testing with electrical sensing on plastic microchips with printed electrodes. *ACS Applied Materials and Interfaces Journal*, **9** (14), 12832–12840 (2017).

72. Novakovic, Z., Khalife, M., Costache, V., Camacho, M.J., Cardoso, S., Martins, V. and Vidic, J. Rapid Detection and Identification of Vancomycin-Sensitive Bacteria Using an Electrochemical Apta-Sensor. *ACS Omega*, **9** (2), 2841–2849 (2024)

73. Dai, G., Li, Z., Luo, F., Lu, Y., Chu, Z., Zhang, J. and He, P. Simultaneous electrochemical determination of *nuc* and *mecA* genes for identification of methicillin-resistant *Staphylococcus aureus* using N-doped porous carbon and DNA modified MOF. *Microchimica Acta*, **188**, 1–9 (2021).

74. Marin, M., Rizzotto, F., L´eguillier, V., P´echoux, C., Borezee-Durant, E. and Vidic, J., Naked-eye detection of *Staphylococcus aureus* in powdered milk and infant formula using gold nanoparticles. *Journal of Microbiological Methods*, **201**, 106578 (2022).

75. Léguillier, V., Pinamonti, D., Chang, C. M., Mukherjee, R., Kumar, H., Cossetini, A. and Vidic, J. A review and meta-analysis of *Staphylococcus aureus* prevalence in foods. *The Microbe*, 100131 (2024).

76. Esposito, S., Blasi, F., Curtis, N., Kaplan, S., Lazzarotto, T., Meschiari, M., Mussini, C., Peghin, M., Rodrigo, C., Vena, A., Principi, N. and Bassetti, M. New Antibiotics for *Staphylococcus aureus* Infection: An Update from the World Association of Infectious Diseases and Immunological Disorders (WAidid) and the Italian Society of Anti-Infective Therapy (SITA). *Antibiotics*, **12**(4), 742 (2023). https://doi.org/10.3390/antibiotics12040742

77. Liu, Y., Deng, Y., Li, S., Chow, F.W.N., Liu, M. and He, N. Monitoring and detection of antibiotic residues in animal derived foods: solutions using aptamers. *Trends in Food Science & Technology*, **125**, 200–235 (2022).

78. Wang, L., Hu, C. and Shao, L. The-antimicrobial activity of nanoparticles. *International. Journal of Nanomedicine*, **12**, 1227–1249(2017).

79. Zalewska-Piątek, B. and Piątek, R., Bacteriophages as potential tools for use in antimicrobial therapy and vaccine development. *Pharmaceuticals*, **14**(4),331 (2021).

80. Bai, J., Kim, Y. T., Ryu, S. and Lee, J. H. Biocontrol and rapid detection of foodborne pathogens using bacteriophages and endolysins. *Frontiers in Microbiology*, **7**, 474 (2016). https://doi:10.3389/fmicb.2016.00474

81. Homayoni, R.A., Vaghef-Mehrabany, E., Alipoor, B. and Vaghef-Mehrabany, L. The comparison of food and supplement as probiotic delivery vehicles. *Critical Reviews in Food Science and Nutrition*, **56**,896–909 (2016). https://doi.org/10.1080/10408398.2012.733894

82. Song, D., Ibrahim, S. and Hayek, S. Recent application of probiotics in food and agricultural science. In: *Everlon Cid Rigobelo (Ed) Probiotics*, 50121 (2012), Intech Open, https://doi.org/10.5772/50121

83. Gharsallah, K., Rezig, L., Rajoka, M. S. R., Mehwish, H. M., Ali, M. A. and Chew, S. C. Moringa oleifera: Processing, phytochemical composition, and industrial application. *South African Journal of Botany*, **160**, 180-193 (2023).

84. Malhotra, S.P.K. and Mandal, T.P. Phytochemical screening and in vitro antibacterial activity of Moringa oleifera (Lam.) leaf extract. *Archives of Agriculture and Environmental Science*, **3** (4), 367– 372 (2018).

85. Arodes, E.S., Cing, J.M., Sitompul, F., Kurniaty, L., Sunarti, L.S. and Siagian, F.E. Effectiveness of methanol extract of Moringa oleifera Lam. lead as antibacterial drug to bacterial triggers of urinary tract infections in vitro. *Journal of Complementary and Alternative Medical. Research*, **17** (1), 1–12 (2022).

## المكورات العنقودية الذهبية المقاومة للمضادات الحيوية: انتشارها، عزلها، واستراتيجيات الوقاية منها

**أحمد نوار العشري، عصمت إبراهيم السعيد*، صلاح فتحي عبدالعال، محمد عبدالحكيم بيومي وايمان نبيل عبدالفتاح**

قسم صحة وسلامة وتكنولوجيا الألبان، كلية الطب البيطري، جامعة الزقازيق، مصر.

**الملخص**

المكورات العنقودية هي أحد الأسباب الرئيسية للعدوى البشرية، حيث تتواجد عادةً على الأغشية المخاطية والجلد، ولكنها يمكن أن تتحول إلى مُمْرِضة تحت ظروف معينة وتسبب تسمم الدم، والتهاب النسيج الخلوي، والتعفن، والتهابات المسالك البولية، والالتهاب الرئوي. وتُعتبر المكورات العنقودية الذهبية أكثر الأنواع خطورةً، نظرًا لامتلاكها آليات متنوعة لاحداث المرض. تعتمد شدة الأمراض التي تسببها على إنتاج العديد من عوامل الضراوة وامتلاك جينات مقاومة للمضادات الحيوية مثل (mecA وvanA) ، والتي تسهل بدء عملية المرض، وتجنب الجهاز المناعي، وتدمير أنسجة المضيف .

تتميز هذه البكتيريا بقدرة عالية على التكيف، حيث طورت مقاومةً لغالبية المضادات الحيوية المتاحة في السوق. وقد ازدادت مقاومةالمكورات العنقودية للأدوية تدريجياً على مدى العقود الماضية مع تطور العامل الممرض وإساءة استخدام المضادات الحيوية. يشكل ظهور مقاومة مضادات الميكروبات في المكورات العنقودية تحدياً بيطرياً وصحياً عاماً كبيراً على مستوى العالم. ونظراً لكونها مُمْرِضة شديدة التنوع، يمكنها اكتساب جينات المقاومة بسرعة.

تهدف هذه الدراسة إلى تسليط الضوء على المكورات العنقودية الذهبية المقاومة للمضادات ، من حيث انتشارها، وبيئتها، ومقاومتها للمضادات الحيوية، واستكشاف استراتيجيات الوقاية والمكافحة الفعالة حديثاً لتخفيف تأثيرها على الصحة العامة.

**الكلمات الدالة:** المكورات العنقودية الذهبية ، مقاومة المضادات الحيوية ، التسمم الغذائي بالمكورات العنقودية.