Methicillin-Resistant Staphylococcus aureus (MRSA) and its Intersection with Animals

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ABSTRACT

Methicillin-resistant Staphylococcus aureus (MRSA) is a multidrug-resistant bacteria that poses a serious risk to public health. In addition to human populations, MRSA has become a problem in the context of animals, posing issues with reservoirs, interspecies transmission, and possible effects on veterinary and human treatment. This succinct study delves into the relationship between MRSA and animals, looking at important factors such genetic diversity, transmission patterns, and prevalence. The report addresses the several animal species—companion, livestock, and wildlife—that have been linked to MRSA colonization and infection. The bidirectional transmission of MRSA between people and animals is highlighted in particular, highlighting the need of a One Health approach in understanding and managing the intricate dynamics of this zoonotic infection. To understand the genetic processes underlying MRSA adaption and transmission across species borders, genomic research and molecular epidemiology are examined closely. Additionally, the paper evaluates how animals may serve as reservoirs for rare strains of MRSA and how they contribute to the pathogen's overall genetic diversity. The study also discusses the effects of MRSA on livestock production systems, veterinary treatment, and the dangers it presents to human and animal populations that live near to one another. The need of cooperative efforts between the human and veterinary healthcare sectors is emphasized in the discussion of strategies for monitoring, prevention, and control at the human-animal interface. To sum up, this multidisciplinary summary offers a concise examination of the intricate interactions that exist between MRSA and animals. It seeks to improve our comprehension of the complex dynamics of MRSA transmission in various animal populations by combining existing research and promoting an all-encompassing strategy to reduce the dangers related to this disease that is clinically relevant.

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1. INTRODUCTION

The bacteria Methicillin-Resistant *Staphylococcus aureus* (MRSA) has attracted a lot of interest in the medical community due to its resistance to antibiotics, including methicillin and other beta-lactam medications. The *Staphylococcus aureus* is a Gram-positive, human-host-adapted bacterium that is frequently discovered on people's skin and in their nasal passages. Though sometimes thought of as an opportunistic pathogen, it is also a commensal organism that may cause invasive infections of the skin. The first reports of methicillin-resistant *S. aureus* (MRSA) appeared in the early 1960s, not long after the drug's release. MRSA infection rates sharply rose in the late 1970s, mostly among hospitalized patients.
Another important development in the 1990s was the identification of MRSA infections among previously healthy persons contracted in the community (Weese 2010). The terms HA-MRSA (healthcare-associated) and CA-MRSA (community-associated) now apply to these two MRSA origins. MRSA has always been linked to diseases that affect people who get treatment, but it has now developed a presence in animals as well, posing new problems and causing concern in the veterinary and public health fields. This chapter explores the complex interactions between MRSA and animals, including the patterns of transmission, the distribution of reservoirs, and any possible effects on both animal and human health.

2. MRSA: A BRIEF OVERVIEW

MRSA is a strain of the bacterium *Staphylococcus aureus* (SA) that has shown and developed resistance to beta-lactam antibiotics, primarily methicillin. *Staphylococcus aureus* is a well-known nosocomial bacterium that causes epidemics in humans and cattle mastitis, according to studies (Biedenbach et al. 2004) (Barton et al. 2006). *S. aureus* includes different virulence factors like Panton-valentine leukocidin (PVL), certain enzymes such as proteases, lipases, and elastase, and slime factor i.e., biofilms, which promotes the mutilation of host tissues and proliferation to other sites (Gordon and Lowry 2008). The staphylococcal cassette chromosome mec (SCCmec), which carries the mecA gene, is the main mechanism via which MRSA spreads (Deurenberg et al. 2007). Five different kinds of SCCmec elements were identified, including types I, II, III, IV, V, and VI. Inappropriate antibiotic use, underdosing, and improper delivery play a significant influence in the development of resistance to antibiotics. MRSA has emerged as a significant contributor to infections that are hospital- and community-related, as well as isolated from milk (Livestock-associated) (Klein et al. 2007) (Devriese and Hommez 1975). The emergence of MRSA is largely attributed to the overuse and misuse of antibiotics, which has led to the selection of resistant strains. Initially recognized in human healthcare settings, MRSA infections are challenging to treat due to their resistance profile.

3. MRSA IN ANIMALS: AN EVOLVING CONCERN

In recent years, MRSA has been identified in a variety of animal species, both domestic and wild. The transmission of MRSA between humans and animals, as well as within animal populations, has been documented, highlighting the complex interplay between these reservoirs. The main known method of MRSA transmission between hosts is through direct physical contact with the source. The defining property of MRSA lineages is the capacity to spread to many hosts, including humans as well as animals. When a person comes into personal touch with an animal or their surroundings, LA-MRSA can spread to humans (Pantosti 2012). Before the Hungarian cow was identified as the root cause of livestock-associated MRSA transmission to its keeper by analyzing swabs taken from throat in 1961, LA-MRSA was solely confined to animals (Cefai et al. 1994). This report was the preliminary account of MRSA spreading from an animal to a man, demonstrating the potential for horizontally transmitting MRSA between humans & animals. Following that, several reports on numerous animal species, including poultry, pigs, cattle, sheep, goats, equines, and companion animals, were published by a variety of authors from different parts of the world. These findings showed that both MRSA strains either from animals or humans shared several clonal complexes (CCs) with multi-locus sequence types (STs), including CC5, CC1, CC8, CC9, CC59, CC22, CC30, CC45, CC97, CC130, and CC398. However, other HA-MRSA and CA-MRSA strains have also been identified, and they are comparable to other LA-MRSA strains that are shown in Fig. 1. Bovine mastitis is brought on by a human clone called ST1 that was discovered in animals (Grundmann et al. 2010). comparable to human clones CC398 and ST398 that cause diseases like HA-MRSA and CA-MRSA, animal clones of these strains induce comparable infections in humans (Witte et al. 2007). A global ST5 poultry clone was also

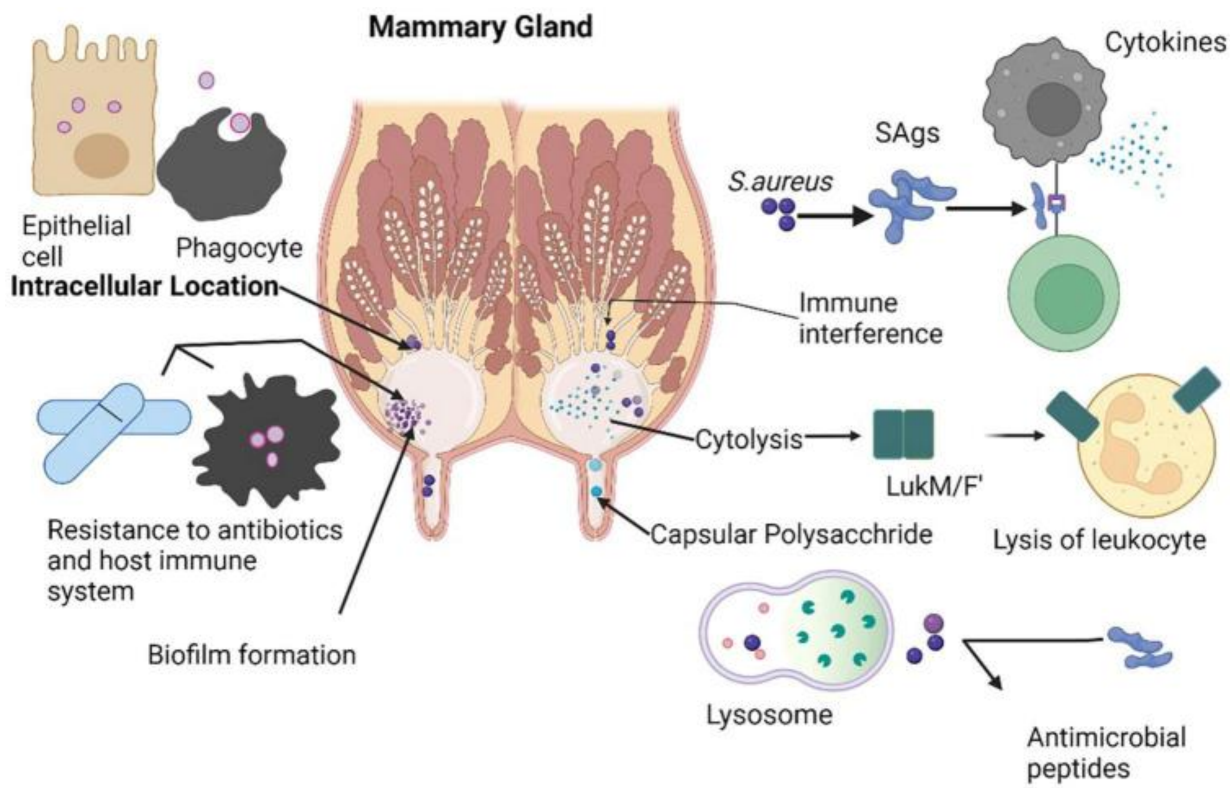

Fig. 1: Different strategies used by *Staph. aureus* to cause infection in mammary glands

discovered in individuals working on poultry farms (Lowder et al. 2009). Numerous studies have also established that MRSA may spread from companion animals to people. For instance, research by across the United States and Canada found that 18% of pet owners carried MRSA. Similar stress was observed in patients, hospital personnel, and nursing cats in different research conducted in a UK nursing home (Scott et al. 1988). The same MRSA lineage ST22 was spread from sick canines to veterinary staff members in research done at a veterinary facility (Baptiste et al. 2005). However, a household member in the Netherlands discovered that dogs were also occupied with a strain which is human PVL-positive CA-MRSA (Van Duijkeren et al. 2005). Another research by Shoaib et al. (2020) outlined the dangers connected to LA-MRSA transmission from companion animals. The owner's sex, the sample spot, and the dog's size were found to be insignificant risk factors for MRSA transmission. Amongst these risk factors, it was discovered that having access to the bedroom by a pet, veterinarians, body infection, use of antibiotics for longer periods and animal health records were also important risk factors for the transmission of MRSA to humans. According to a different study by Mulders et al. (2010) the type of slaughtering process, the surroundings of the abattoir, and farm employees who come into touch with live birds, are all important risk factors for MRSA transfer from poultry to humans.

4. TRANSMISSION DYNAMICS

Transmission of MRSA between animals and humans occurs through direct contact, environmental contamination, and shared living spaces. Companion animals such as dogs, cats, and horses have been found to carry MRSA, often without showing clinical signs of infection. S. aureus, in contrast, does not adapt to either dogs or cats as hosts. This is why *S. aureus* colonization in pets, including both methicillin-resistant and methicillin-susceptible strains, often lasts little more than a few weeks (Loeffler et al. 2010) (Morris et al. 2012). *S. pseudintermedius*, which can also be methicillin-resistant (MRSP), is the most prevalent commensal *Staphylococcus* in dogs and cats. MRSA is often obtained from people in dogs and cats. The strains discovered in animals closely resemble those discovered in residents of that area (Loeffler et al. 2010) MRSA colonization rates in cats and dogs typically vary from 0-4%, but they can reach as high as 7-9% in certain populations (Weese 2010). Contact with an MRSA-infected human, multiple courses of antibiotics, going to a veterinary facility, having surgery, or being hospitalized for a prolonged period of time are the main risk factors for MRSA colonization in dogs.7,8 The risk of MRSA colonization is also higher for veterinary professionals than it is for the general public (Weese 2010; Loeffler et al. 2010). Recent studies have revealed a frequency of 4–18% among veterinary staff compared to 1-3% in the general population (Weese 2010), highlighting the need of proper hand hygiene and glove use in the veterinary field. Livestock, including pigs, cows, and poultry, have also been identified as reservoirs of MRSA, raising concerns about potential foodborne transmission.

5. ZOONOTIC IMPLICATIONS

The zoonotic potential of MRSA cannot be understated. While MRSA strains in animals may differ from those in humans, the exchange of genetic material between species can lead to the emergence of novel strains with enhanced virulence and resistance traits. Individuals who work closely with animals, such as veterinarians, animal handlers, and pet owners, are at an increased risk of contracting MRSA infections. Although MRSA infections present in companion animals and food were once believed to spread more slowly, it is also becoming a severe issue for food sector companies and food animals. According to LA-MRSA is a significant contributor to mastitis in buffaloes and cows, which results in reduced or nonexistent milk output. poultry's infections such as chondronecrosis, septic conditions and comb necrosis are also caused by LA-MRSA . Nearly all pets such as dogs, cats, and horses, have the potential to spread LA-MRSA to people who come into contact with them directly or indirectly. Mastitis is a serious condition that affects dairy cows and is associated with excessive antibiotic usage, which results in significant economic losses. Among all other potential causes of mastitis across the world, *S. aureus* is the most common

pathogen. According to Grinberg et al. (2004), LA-MRSA is a significant factor in the pustular dermatitis that affects their milkers. However, none of the bovine MRSA clones, which cause subclinical mastitis in cattle, are often found in dairy cows (Aqib et al. 2018; Abdeen et al. 2021). MRSA was initially found in cattle in Belgium in milk samples in 1972, where it was presumed that it had been contaminated by the hands of the milkers (Lee 2003). According to (Holden et al. 2013), mammary gland's infection due to MRSA in calves reduces milk production and, in extreme cases, might result in the termination of milk production from the mammary glands.
Healthy poultry birds' cloaca and nares have also been shown to have LA-MRSA. It can result in pyoderma, omphalitis, UTI, arthritis, and otitis in poultry birds (Pickering et al. 2022). following the use of several antimicrobial drugs. MRSA of spa types t011 and t157 were discovered. While ST398 is a brand-new MRSA strain linked to livestock that is also present in poultry (Nemati et al. 2008). According to a different analysis, all MRSA isolates of chicken origin belonged to spa type t1456.

5.1. DIFFERENT DISEASES CAUSED BY MRSA IN DIFFERENT SPECIES

Numerous human illnesses, including acne, wound suppuration, food poisoning, urinary tract infection (UTI), endocarditis, otitis, pyogenic pneumonia, osteomyelitis, nosocomial infections, health-care associated infections, mastitis, and septicemia, may be brought on by MRSA strains (Boucher et al. 2008). Horses are susceptible to botryomycosis, a "peculiar disease" caused by bacteria that causes pyogenic inflammation of the spermatic cord and a localized purulent infection. Localized pyogenic infection, severe acute mastitis, and apparent toxemia in cattle and ewe. Similar to caseous lymphadenitis in sheep, anaerobic strains produce abscesses in sheep. Food poisoning and pustular dermatitis in cats and dogs. In pigs, exudative epidermatitis "greasy pig disease" and in avians, suppurative arthritis "Bumble-foot".

5.2. MRSA AND COMPANION ANIMALS

Most families now include pets like dogs, cats, and horses, especially in advanced countries like the USA and the UK (Chomel and Sun 2011). As a result, there is a substantial likelihood that these animals may colonize humans or infect them with MRSA (Mustapha et al. 2014). Dogs are more likely than cats to be infected or colonized with MRSA, according to Morgan (2008), and 1.5% of MRSA was found in samples from diseased companion animals in the UK. Infections of the skin and soft tissues are the most common way to present the diseases. EMRSA-15 (ST22) and EMRSA-16 (ST36) are the MRSA strains that have been isolated in the majority of UK hospitals (Ellington et al. 2010), whereas USA100 (ST5), which has been linked to HA-MRSA infections in humans, has been recovered from US pets (Ellington et al. 2010). Additionally, an MRSA clone (ST398) that was typical of farm animals was found in dogs and horses in a UK investigation (Loeffler et al. 2009). The majority of events and outbreaks of MRSA infections have been linked to problems following surgery and large stables (Weese et al. 2005; Morgan 2008). MRSA strains identified from horses were different from those recovered from people (Loeffler and Lloyd 2010). The prevalence of MRSA infection in different species of animals has been shown in Table 1.

Table 1: Prevalence of MRSA infection in different species of animals

Countries	Animals	Sample type	Prevalence(percentage)	References
Germany	Dog, cat, horses	Wounds	62.7, 46.4, 41.3	Vincze et al. 2014
Germany	cats	Clinical	10	Walther et al. 2008
Netherland	calves	Nasal samples	88, 28	Graveland et al. 2010
Belgium	Cows/broilers	Nasal/Cloaca	5.0, 5.0	

6. VETERINARY HEALTHCARE SETTINGS

Veterinary clinics and animal hospitals can serve as potential hotspots for MRSA transmission. In these settings, animals receiving medical treatment can act as reservoirs, while human-to-human transmission can exacerbate the problem. Implementation of rigorous hygiene and infection control measures is crucial to prevent MRSA spread within veterinary facilities.

7. ONE HEALTH APPROACH

The One Health approach, which recognizes the interconnectedness of human, animal, and environmental health, is paramount in addressing the MRSA challenge. Collaborative efforts between medical and veterinary professionals, researchers, and public health authorities are essential for understanding and mitigating the impact of MRSA on animals and its potential to affect human health.

8. FUTURE DIRECTIONS

As MRSA continues to adapt and evolve, ongoing research is needed to elucidate the dynamics of MRSA transmission in animal populations and its implications for human health. Improved surveillance, diagnostic tools, and antimicrobial stewardship programs are vital components in managing MRSA across species. according to a study, a post-antibiotic era, in which common diseases and mild infections might kill, is a very real prospect for the twenty-first century. According to the World Health Organization (WHO), the rise in antibiotic-resistant microorganisms is one of the biggest threats to public health.
A-lactam antibiotic and potassium clavulanate were discovered to be the most efficient combination against MRSA (De Araújo et al. 2013). According to several studies, phytochemicals have a significant organic potential to demonstrate antibacterial action and function as modulators of antibiotic resistance, either alone or in combination with antibiotics. According to (Lakshmi et al. 2013), plants' active secondary metabolites are responsible for the bulk of these healing benefits. According to (Coutinho et al. 2009), phytochemicals modify bacterial enzymes and inhibit efflux pumps in addition to altering active sites, increasing plasma membrane permeability, and inhibiting efflux pumps as shown in Fig. 2.

8.1. SYNERGISTIC EFFECT OF ANTIBIOTICS WITH NSAIDS

Numerous investigations have demonstrated that NSAIDs have antibacterial capabilities, however, the precise route of action is unknown. Diclofenac, aspirin, and ibuprofen have been found to exhibit antibacterial properties at 5 mg/ml against some gram-positive bacteria, except mefenamic acid. The only NSAID that is effective against gram-negative bacteria is aspirin because gram-negative bacteria have lipopolysaccharide, which is hydrophilic and hinders most medicines' metabolism. Antimicrobial medicines can penetrate gram-positive bacteria cells with ease since their cell walls lack lipopolysaccharides (Khalaf et al. 2015).

8.2. NANOPARTICLES AS THERAPEUTIC AGENTS

Metal nanoparticles (NPs) are increasingly common and affordable production materials that are finding many uses in the modern world due to their unique properties. The market for nanometals based on metal oxides was said to have reached USD 4.2 billion in 2016. The rising usage of metal-based nanoparticles in biomedical research is observed to be expected to enhance the need for NP manufacture by 2025 (Gudkov et al. 2022).

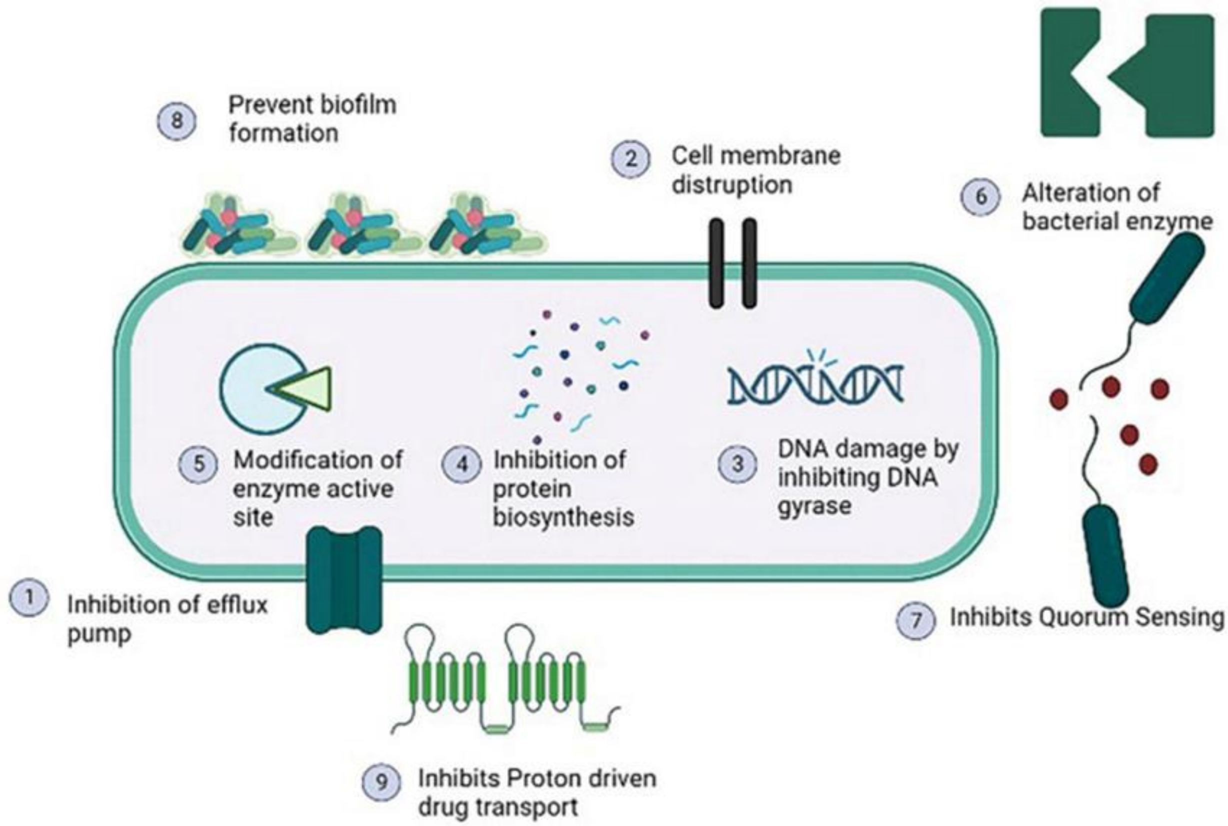

Fig. 2: Antibacterial mechanisms of various phytochemicals against methicillin resistant strain of *Staphylococcus aureus* (MRSA).

9. CONCLUSION

The emergence of MRSA in animals underscores the intricate relationship between human and animal health. Understanding the transmission dynamics, reservoirs, and zoonotic potential of MRSA is imperative for effective control and prevention strategies. By adopting a One Health approach, society can work collaboratively to address the challenges posed by MRSA and promote the well-being of both humans and animals. Methicillin-resistant *S. aureus* strain (MRSA) is a flexible and unpredictable pathogen with a variety of lineages shared by humans and animals, suggesting that it spreads from people to animals. The lineages CC398, CC9, CC130, CC97, and CC398 were those shared by humans and animals. Except for this, few HA-MRSA and CA-MRSA lineages were found in animals, although LA-MRSA lineages, which resemble HA-MRSA and CA-MRSA, were found. Because of its growing genetic adaptability and ubiquity in both animal and human populations, this disease poses a danger to public health. This disease has a wide variety of hosts, including people, food animals, pets, and many more. Work on effective MRSA vaccination and vaccine manufacturing is a further strategy.

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