

## ANNOTATION

**dissertation work of Aliyeva Gulnur Koziyevna  
on the topic «Intraspecific features and differences of resistance profiles of  
*Staphylococcus spp.* strains circulating in the Northern region of Kazakhstan»  
submitted for the degree of Doctor of Philosophy (PhD) in the specialty  
6D120200 - Veterinary Sanitation**

### **Relevance of the topic.**

Staphylococcal infections are diverse and include more than 100 nosological forms. Studies on the analysis of the species and properties of staphylococci living in the body of animals and poultry are limited. The topic of the dissertation work is relevant today, since the species spectrum and intraspecific features of staphylococci are little studied in veterinary practice, especially since there are a large number of works proving an increase in the virulent properties of coagulase-negative staphylococci (CNS), previously considered safe.

In recent years, the main problem is the wide spread of resistant staphylococci in Kazakhstan and around the world, as well as the decrease in the effectiveness of a number of antibiotics. Resistant clones that are stable in animals can be spread to humans through the food chain or through direct contact with animals.

Determination of antibiotic resistance by microbiological and molecular genetic methods provides a clear picture of the state of resistance of microorganisms to antibiotics, allows to predict the emergence of resistance to various groups of antimicrobial drugs, as well as to assess the spread of resistant strains at the local and regional levels.

**Purpose of the study:** to determine the resistance profile and interspecies features and species spectrum of strains of the subfamily *Staphylococcus* isolated from animals, birds and animal products.

### **To achieve this goal, the following tasks were set:**

1. Isolation and identification of *Staphylococcus spp.* strains from animals, birds and animal products in the northern region of Kazakhstan;
2. To study the main biological properties of staphylococcus isolates isolated from various biotopes (virulence factors, persistence, etc.), to study the species spectrum and determine interspecific features;
3. Determination of phenotypic resistance to antibacterial drugs and selection of resistant and multidrug-resistant strains of staphylococci;
4. Determination of the genetic profile of antibiotic-resistant strains of staphylococci.

**Object of study:** bacterial isolates of staphylococci isolated from various sources circulating in the Northern region of Kazakhstan.

**Subject of study:** antibiotic resistance and molecular genetic mechanisms of resistance of strains of *Staphylococcus spp.*

### **The main provisions submitted for protection:**

1. Species spectrum of staphylococci isolated from various biotopes of agricultural animals and birds of the northern region of Kazakhstan.

2. Types and combination of virulence factors of coagulase-positive and coagulase-negative types of staphylococci, interspecies features.

3. Phenotypic and genotypic resistance of staphylococcus species to various groups of antibacterial drugs.

#### **Scientific novelty of the work.**

For the first time, a comparative analysis of species characteristics and biological properties of various strains of staphylococci isolated from farm animals, birds and animal products was carried out. It has been established that the species composition of staphylococci is significantly diverse.

It has been shown that the vast majority of isolated strains of staphylococci, including KNS, have a certain set of virulence factors, regardless of the isolated source.

In addition, among the studied strains, isolates with a certain set of virulence factors were often identified. Most isolated staphylococci are capable of forming a biofilm.

For the first time in the northern regions of the republic, an analysis of the antibiotic resistance of staphylococcal strains isolated in livestock farms and products of animal origin was carried out, and data on the genetic virulence profile were obtained.

Sensitive, resistant and multi-resistant strains have been found. The greatest number of isolates are resistant to various antibiotics of the  $\beta$ -lactam group, while the least resistant isolates have been identified in the aminoglycoside and sulfonamide groups.

#### **The practical significance of the work.**

The results expand the understanding of the ecology of staphylococcus, the features and differences in the biological properties of staphylococcus strains isolated from various sources.

The work has not only fundamental but also practical significance in livestock production: data have been obtained showing the possibility of a wide distribution of various species of *S.aureus* and coagulase-negative staphylococci (CNS). The presence of virulence factors and multidrug-resistant strains among staphylococci that colonize animals and birds poses a potential threat to public health through animal products. Knowledge of bacterial resistance to antibiotics is critical to successful disease control. In the course of the work, the veterinary specialists of the farms showed great interest in determining the sensitivity / resistance to antibacterial drugs in the treatment of infectious animal diseases, especially cow mastitis.

#### **Relationship of work with research programs**

The work was carried out within the framework of 2 scientific projects:

- grant funding project of the Ministry of Education and Science of the Republic of Kazakhstan No. AP05131447 "Monitoring of antibiotic resistance of pathogens of enteropathogenic zoonanthropotic diseases of the Northern region of

Kazakhstan" under the budget program 217 "Development of science", subprogram 102 "Grant funding of scientific research";

- project "Analysis of the risks of the emergence of resistance to antibiotics in pathogenic microflora isolated from animals and from raw materials and products of animal origin" within the framework of the scientific and technical program BR10764944 "Development of methods for analytical control and monitoring of food safety" funded by the Ministry of Agriculture within the framework of the budget program 267 "Improving the availability of knowledge and scientific research", subprogram 101 "Program-targeted financing of scientific research and activities".

#### **Publication of research results**

On the topic of the dissertation, 9 articles were published, including 3 articles in publications recommended by the Committee for Quality Assurance in Education of the Ministry of Education of the Republic of Kazakhstan, 2 articles in journals that are part of the Russian Science Citation Index, and 2 articles were published in scientific publications included in the international databases Web of Science (Clarivate Analytics) and Scopus (Elsevier) - 86 percentiles and 15 percentiles in general veterinary medicine, as well as 2 articles published in the materials of international conferences. 1 utility model patent has been received, there are 2 acts of introduction into production and 1 act of introduction into the educational process.

#### **Degree of reliability of results**

The reliability of the data obtained is determined by a sufficient amount of research, the use of modern methods. The results of the research are reflected in the final report on the project AP05131447 "Monitoring of antibiotic resistance of pathogens of enteropathogenic zoonotic diseases in the Northern region of Kazakhstan" (reg. No. 0118RK00397, inventory No. 0220RK00538). Personal contribution.

The author took part in all stages of the study: the isolation and identification of isolates, the study of virulence factors, the formation of biofilms, the resistance of staphylococci to antibacterial drugs, as well as PCR studies. Review and analysis of literary sources, processing, analysis and interpretation of the results of the study were made by the author personally.

#### **Research results.**

1. 1811 samples of biological material from animals and birds delivered from farms, products of animal origin (raw materials and ready products) selected at retail outlets were studied, 342 staphylococcus isolates were isolated.

2. It has been established that the species composition of staphylococci is significantly diverse. Cultural, biochemical, molecular genetic and MALDI mass spectrometric methods identified 13 types of coagulase-positive and coagulase-negative staphylococci: *S. aureus*, *S. intermedius*, *S. chromogenes*, *S. sciuri*, *S. xylosus*, *S. cohnii*, *S. agnetis*, *S. fleurettii*, *S. simulans*, *S. arlettae*, *S. gallinarum*, *S. saprophyticus*, *S. hyicus*.

3. It was shown that the vast majority of isolated strains of staphylococci, including KNS, have a certain set of virulence factors, regardless of the source of isolation.

4. Most isolated staphylococcus isolates have been found to be capable of forming biofilms.

5. The analysis of antibiotic resistance of *Staphylococcus* strains circulating in livestock farms and animal products of the northern regions of the Republic was carried out. Resistant and polyresistant strains have been established. The largest number of isolates resistant to various antibiotics were found in the group of  $\beta$ -lactams, the least resistant strains - in the group of aminoglycosides - 11% and in the group of sulfonamides - 16.1%

6. Data on the genetic profile of virulence were obtained. For most of the studied antibacterial drugs ( $\beta$ -lactams, macrolides, and aminoglycosides), a reliable relationship has been established between the presence of genes encoding resistance and the data of the phenotypic method for determining sensitivity..

#### **Practical Suggestions**

1. In case of isolation of coagulase-negative staphylococci (*S. intermedius*) from pathological or biological material, conduct studies of their virulence factors as infectious agents.

2. In case of infectious diseases of animals, send the biomaterial to veterinary laboratories with indication of tests for sensitivity to antibacterial drugs of isolated pathogens and the issuance of a study protocol with recommendations on the choice of antibacterial drugs

#### **Scope and structure of the dissertation.**

The dissertation work is presented on 142 pages of computer text and consists of introduction, main part and conclusion. The text of the dissertation contains 50 tables, 42 figures, 2 formulas, 8 applications. The list of used literature consists of 223 sources.