

Mechanisms of Antimicrobial Action and the Development of Antimicrobial Resistance in Aquaculture

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Aquaculture has expanded significantly in recent years to meet the growing global demand for fish and shellfish. To increase productivity, many farming systems have higher stocking densities and a more intensive production model. However, crowding and environmental stress can suppress the fish's immune system, thus increasing vulnerability to infectious diseases. To deal with bacterial diseases, farmers use antibiotics. Antibiotics are very useful if used properly. However, if antibiotics are used excessively or as a precautionary measure, bacteria start adapting and surviving. Over time, they become more difficult to kill, complicating the treatment of infectious diseases. Studies have demonstrated that antibiotic residues can be detected in farmed fish and shrimp. In some instances, the amount of these antibiotics can go beyond the recommended safety level. Some of these resistant bacteria can infect humans either through contact with fish or through the consumption of contaminated fish.

Antimicrobial Agents

Antimicrobial agents are natural, synthetic, or semi-synthetic compounds that are microbicidal (kill microorganisms) or microbiostatic (inhibit the growth of microorganisms). In aquaculture, antibiotics specifically target bacterial pathogens. Antimicrobial agents can be grouped according to their mode of action, which includes inhibition of cell wall synthesis, disruption of cell membrane integrity, inhibition of protein synthesis, inhibition of nucleic acid synthesis, and interference with metabolic processes.

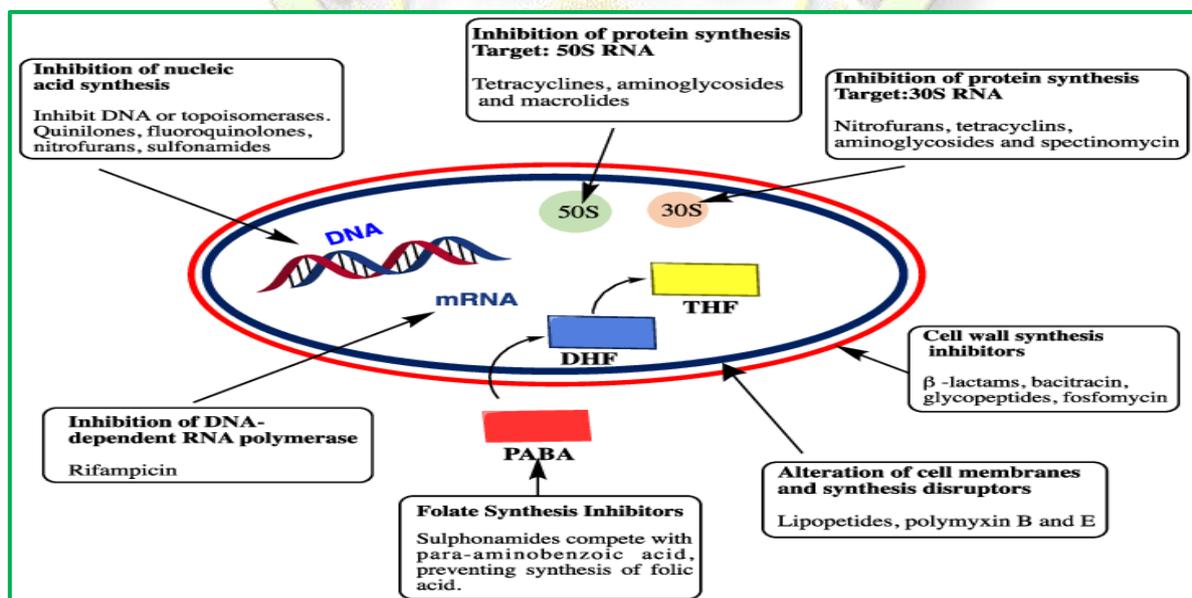


Fig. 1. Mechanism of action of antimicrobial agents in bacterial cells.

Origins of Antimicrobial Resistance

Antimicrobial resistance (AMR) can be defined as the ability of microorganisms to withstand the effects of antimicrobial agents that would otherwise inhibit or kill them, mainly as a result of selective pressure exerted by inappropriate use of antibiotics.

The main drivers of antimicrobial resistance (AMR) include:

- Inadequate or unjustified prescribing practices
- Empirical use of broad-spectrum antibiotics without a definitive diagnosis
- Overuse of antibiotics exerts selective pressure favouring resistant bacterial populations.

Resistance can be intrinsic (natural) or acquired.

1. Intrinsic Resistance - Present in all individuals of a species by nature. Not caused by previous exposure to antibiotics or horizontal gene transfer. Mechanisms include decreased membrane permeability and efflux pumps.

2. Acquired Resistance - Arises from horizontal gene transfer (transformation, conjugation, transposition) or chromosomal mutations.

Mechanisms of Antimicrobial Resistance

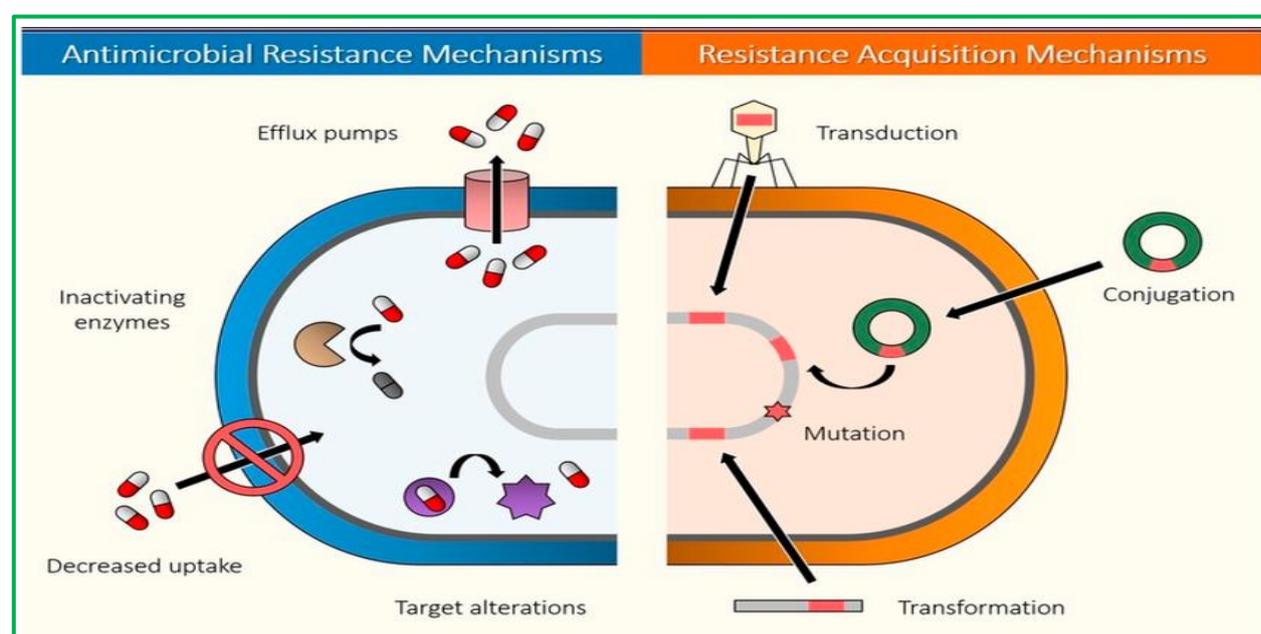


Fig. 2. Mechanisms of Antimicrobial Resistance and Genetic Acquisition in Bacteria

1. Enzymatic Drug Inactivation

A. Enzyme Inactivation - Bacteria have enzymes that inactivate or degrade antibiotics. Classic example: Production of β -lactamase by *Staphylococcus aureus*. β -lactamases cleave the β -lactam ring, making it impossible for the antibiotic to bind. Common in β -lactam resistance (penicillins and cephalosporins).

B. Enzyme-Mediated Drug Modification - Bacteria bring about chemical modifications of the antibiotic itself. Example: Aminoglycoside-modifying enzymes (such as acetyltransferases) inactivate antibiotics such as kanamycin.

2. Target Site Modification

A. **Target Modification by Mutation** - Random mutations in DNA lead to mutations in antibiotic target proteins. If the mutation occurs in the binding site of the drug, the drug will not be able to bind properly. Mutant bacteria will be able to survive and thrive in the presence of antibiotics.

B. **Enzyme-Mediated Target Modification** - Certain enzymes produced by the bacteria bring about chemical modifications of the target molecule for the antibiotic. Chemical modification of the target prevents binding. Example: erm gene methylates ribosomal RNA \rightarrow resistance to macrolides (such as erythromycin).

3. Efflux Pumps and Reduced Permeability- Efflux pumps actively remove antibiotics from the cell (e.g., TetA pumps for tetracycline). Porin mutations decrease antibiotic uptake (loss, modification, or reduced expression). Both methods lower intracellular antibiotic concentrations. Some bacteria naturally resist antibiotics using these mechanisms.

Alternatives to Antibiotics

There is an increasing need to identify safer and more sustainable alternatives to antibiotics in aquaculture. Several alternatives are now being considered. These include vaccination schemes that trigger adaptive immune responses and immunological memory in fish, phage therapy that uses lytic bacteriophages to selectively infect and kill bacterial pathogens, and quorum quenching strategies that target quorum-sensing pathways involved in virulence regulation. and the use of probiotics and prebiotics to enhance gut health and resistance to diseases. Other alternatives include plant-based therapies that have natural antimicrobial properties. Moreover, it is important to maintain high biosecurity levels. The use of “clean seed” or specific pathogen-free (SPF) stocks is a critical component in the prevention of disease introduction and spread, which forms the basis of a sustainable aquaculture system.

Conclusion

The emergence and spread of resistant bacteria can have severe implications not only for the productivity of aquaculture but also for human health, as resistant bacteria and antibiotics can enter the human food chain. Thus, it is important to use antibiotics judiciously, diagnose before treatment, implement biosecurity, and use alternative methods for the control of diseases to ensure sustainable aquaculture and combat the threat of antimicrobial resistance.

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