



## Antimicrobial Resistance (AMR) and Alternatives in Animal Practice

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Antibiotics are used for the prevention of growth and multiplication of bacteria, virus fungi and parasites which are responsible for derailment of human and animal health. Alexander Fleming invented Penicillin in the year of 1927 while working on *Staphylococcus aureus* culture at St. Mary's hospital, London and paved pathway for the subsequent inventions of other groups of antibiotics like Tetracyclines, Macrolides, Aminoglycosides, Fluoroquinolones etc., Antimicrobial agents are classified according to their mechanism of action as 'Bactericidal agents' which interfere the cell wall synthesis (or) DNA synthesis (or) RNA synthesis (or) interfering cell membrane function, and 'Bacteriostatic agents' which are capable of inhibiting growth and multiplication of bacteria by interfering protein synthesis (or) inhibition of metabolic pathways, etc. Meanwhile, bacteria may become resistant to these drugs by antibiotic inactivation, target modification, development of efflux pump and plasmidic efflux. AMR is defined as "unresponsiveness" of microorganism to antimicrobial agents after unscrupulous administration of antibiotics to the animals. During the process of developing of AMR by the microorganism which overwhelm the antagonistic effects of antimicrobial agent, for which they were previously susceptible, resulting in their resistance despite exposure to standard doses of antibiotic. As consequences of resistance microorganisms are slowly procuring one by one resistant gene incorporation into their genome may lead to development of multi drug resistant strain, extensively drug resistance (XDR) and pan resistance (PDR) strain those limit the therapeutic use of many conventional antibiotics.

AMR has now emerged into the global public health issues and threatening all kinds of creatures across the globe in terms of en-

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vironment, food production, poverty and health security. In view of the adverse or inverse health progress of animals and human being due to resistance bacteria and there is urgent requirement of new antibiotics invention, new alternative strategies may be incorporated to curtail spread and treat MDR, PDR and XDR strains.

Though antibiotic application in food producing animals are helped in maintaining good health and increasing in the production, besides that it has also a pivotal role in progression of development of unresponsiveness strains. Dairy farming and poultry industry are involved in the surplus use of antibiotics as prophylactic and growth promoting agents and when it was added to animal feed it turned out to be an excellent growth promoter as well. But bacteria defend themselves by developing resistance. A rapid spread of bacterial resistance to antimicrobial agents may limit the future progress of medicine and will pose a global problem. There are number of factors involved in development of AMR, and are indiscriminate use of antibiotics, selection of inappropriate antibiotics, lack of laboratory testing facilities, inadequate duration of therapy, environmental antibiotic selective pressure and diversified resistant gene get selected which are expected to result in a significant acceleration of the rate of microbial evolution.

### Alternative strategies

To overcome this AMR problem, there is dire need of alternative methods for alleviating microbial infections rather than the drugs. Efficient and laudable supervision programs at interdisciplinary level can overview about to better comprehension and to reduce the occurrence of emergence of resistance.

- Combination therapies: Combination prescribing two or more antimicrobial agents simultaneously for the potentiating or synergistic action posing more advantageous for treatment of different ailment. example  $\beta$ -lactam antibiotic combined with an aminoglycoside antibiotic, being widely used for the treatment of various Gram-negative bacterial infection while combination of  $\beta$  Lactamase inhibitors with  $\beta$  lactam resistant strain have offering potentiating activity of  $\beta$  lactam antibiotics example Of  $\beta$  lactamase inhibitors (such as clavulanic acid, salbactam and tazobactam) with  $\beta$ -lactam antibiotics helps restore the action of  $\beta$ -lactam antibiotics. antibiotic combination with  $\beta$ -Lactamase inhibitors example  $\beta$ -lactam antibiotic-resistant infections, the combination of  $\beta$ -lactamase inhibitors such as sulbactam, clavulanic acid, and tazobactam. Further, the coadministration of antimicrobial agents along with biocides like antiseptic, disinfectants and preservatives have been used for the treating pseudomonal infection.
- Use of medicinal plants and phytochemicals: Plants have different metabolites like primary metabolite, important in growth, energy and photosynthesis while secondary metabolites involved in protecting themselves from hostile environment, pathogens like microorganisms via natural phytochemicals. The medically important plant d derived substances (PDSs) which are poses the antimicrobial action due to presence of various secondary metabolites like phenolics, organ Sulphur, terpenes, alkaloids and coumarin and also organosulfur compounds are posing antimicrobial activity by interfering with sulfhydryl group of enzymes, replication of DNA, protein biosynthesis and genesis of ATP in gram positive and gram negative bacteria. Further, alkaloids also interfering with division of cell, protein formation, and DNA replication in *E. coli* [70] and also inhibiting enzyme ATP synthase in *Listeria*, *Bacillus*, and *Staphylococcus* spp.
- Use of probiotics an alternative to development of AMR. The administration of these live microorganism can confer antibiotics effects by competition at the desirable site. The strength of probiotics in the fight against AMR mainly relies upon competitively inhibiting through selective pressure by the probiotics on virulent organisms.
- (iv) Antimicrobial Peptides (AMP) from the bacteria and certain insects have been demonstrated antimicrobial activity
- Use of Lantibiotics (Lanthionine containing antibiotic). These are produced by using Gram positive bacteria which can exert antimicrobial activity against themselves. Bacteriocins are a type- A lantibiotic, that are proteinaceous or peptidic toxins produced by bacterium. These molecules can able to prevent the growth of similar strains of bacterium or unrelated bacteria but could not prevent the growth or kill the original bacteria due to presence of specific protein that are capable in strength immunity.
- RNA silencing: RNA silencing by different strategies for screening of natural and synthetic RNA silencing and its aptitude to offer new antimicrobial agents.
- Anti-persister drugs: Anti persister drugs are screened and therapeutically developed against persister cells. The disadvantage of bacterial persistence is to increasing intimidation of resistnace while curing the pesister cell as they are going to start recolonization and relapse post treatment of antimicrobial agent eventually lead to chronic resistant infections
- The quorum quencher are the agents which are capable of inhibiting quorum sensing of microbes that actually involved bacterial propagation, alter mechanical communication of bacteria, virulence, biofilm formation and adaptation of stress
- Production of monoclonal antibodies (mAbs): These are used to treat infections caused by nosocomial bacterial pathogens. Some of mAbs like Obiltoximab, Raxibacumab, Bezlotoxumab have been licenced for prevention or clinically to treat certain Gram positive bacteria *Bacillus anthracis* and *Clostridium difficile*.
- Screening of drugs molecules against biofilm formation by the bacteria in which antibiotics may not be cross and exerts its effect in the sessile communities. Biofilm breakers are another alternative to the AMR Dispersion Methods
- Nanoparticle Based Strategies: Presence of bulk metals are known to have antibacterial activity against pathogenic bacteria. They are believed to produce antimicrobial activity by oxidative stress, metal ion release, and non-oxidative mechanisms
- Bacteriophage therapy to individual pathogenic infection: Antimicrobial adjuvants therapy or the application of nanotechnology and plant based products development of antibiotic stewardship programmes are considered.
- Development of Vaccines in Combating AMR Pathogens: Hepatitis B virus and *Bordetella pertussis*.

Further, AMR problem in dairy farming involves surplus use of antimicrobial agents as prophylactic and growth promoting agents. This sub therapeutic dose of antimicrobial agents, dosage regimen and persistence of antimicrobial agents in the body (withdrawal period) should be review and documented, legitimate properly. A dairy animal also poses a serious risk of transmission of resistant strains to humans and environment thereby contaminating ecosystem. Hudicious use of antimicrobial agents to the food producing animals by the veterinarian and supporting staff can mitigate the AMR.