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Nanoparticle enabled combination therapy to overcome antimicrobial resistance in pathogenic bacteria isolated from swine farms

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Overuse and inappropriate use of antimicrobials in swine farms has majorly contributed to the emergence of antimicrobial resistant porcine pathogens. There has been an increased incidence in food borne infections related to multidrug resistant pathogens globally. We studied antimicrobial resistance characteristics, its mechanisms (such as efflux pumps, beta lactamase production) and virulence characteristics (such as biofilm formation, hemolysis and heavy metal resistance) in bacteria isolated from swine farms in Quebec. Bacterial isolates identified as *Staphylococcus aureus, Staphylococcus hyicus, Salmonella* Dublin, *Salmonella* Choleraesuis and *Salmonella* Typhimurium were included in this study. AMR profiling (included 24 antibiotics) showed that *Salmonella* Typhimurium to be resistant to most of the antibiotics followed by *Staphylococcus aureus* M12 and *Salmonella* Dublin. This reflects the prevalence of resistance amongst bacterial pathogens found in swine farms. Beta-lactamase production and active efflux were involved in overcoming the action of antimicrobials in most pathogens. Some

bacteria also showed virulence factors such as strong biofilm formation, hemolysis, and heavy metal resistance. Combinations of antibiotics (ampicillin, tetracycline, trimethoprim, and chloramphenicol) with adjuvant molecules (chlorpromazine, tazobactam, thymol, cinnamon essential oil and oregano essential oil) were tested against *Salmonella* Typhimurium and *Staphylococcus aureus* M12. Out of the tested combinations, ampicillin-tazobactam, ampicillin-cinnamon essential oil, and chloramphenicol-thymol showed synergistic effect in *Staphylococcus aureus* M12 and ampicillin-tazobactam showed synergistic effect in *Salmonella* Typhimurium. All in all, these studies showed the prevalence of AMR in swine pathogens and the possibility of nanoparticle-based combination therapy in eliminating drug resistant bacteria as it has been observed previously that nano material mediated co-delivery of antibiotic and adjuvant show better antimicrobial activity.