

Title: Towards controlling antimicrobial resistance in swine production systems: harnessing the paradoxical effects of micro-minerals and feed-grade antimicrobials on resistance in enteric bacteria - **NPB # 10-121.**

Revised

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Scientific Abstract:

Copper sulfate is often used as a growth promoter in swine production. Earlier work from our lab (Amachawadi et al., 2011) has illustrated the presence of the transferable copper resistance (*tcrB*) gene among swine enterococci and its co-location with *erm(B)* and *tet(M)* genes, coding for macrolide and tetracycline resistance, respectively, on the same transferable plasmid. The present study was undertaken to determine the effects of single or multiple feed grade antimicrobials on selection and co-selection of *tcrB*-positive enterococci in piglets. The study consisted of 240 weaned piglets, housed in groups of 5 animals per pen (n=48 pens). The pens were randomly allocated to six treatments (8 pens per treatment), arranged as an incomplete factorial design, comprising basal diets supplemented with none (control), copper (Cu), chlortetracycline (CTC), tylosin (Tyl), copper and tylosin (CuTyl), or copper and chlortetracycline (CuCTC). No combinations included both CTC and Tyl since this was not an FDA-approved combination. The treatment phase was for 4 weeks followed by a washout phase for two weeks. Fecal samples were collected on days 0, 7, 14, 21, 28, and 35. All the enterococcal isolates were tested for the presence of *tcrB* gene by PCR. An equal number of *tcrB*-positive and matched-negative isolates (by pen, date, and treatment) were also tested for both *erm(B)* and *tet(M)* genes. A total of 372 enterococcal isolates were positive for the *tcrB* gene with an overall prevalence of 14.4%. The prevalence of *tcrB*-positive enterococci in each treatment group was: control (47/432; 10.8%), Cu (52/432; 12.0%), CTC (79/432; 18.3%), Tyl (51/432; 11.8%), CuCTC (75/432; 17.4%), and CuTyl (68/432; 15.7%). The *tcrB*-positive isolates had a mean copper MIC of 17.8 mM, compared to *tcrB*-negative isolates with an average MIC of 6.6 mM. Non-parametric analysis (log-rank test) of median and 90th percentile MIC values revealed a similar conclusion. All the *tcrB*-positive and matched-negative isolates also carried both *erm(B)* and *tet(M)* genes (conferring phenotypic resistance to erythromycin and tetracycline, respectively). The supplementation of additional antimicrobials had an additive effect beyond what would have been expected as a simple substitution and resulted in higher prevalence of the *tcrB* gene when compared to copper supplementation alone. Further studies are being undertaken to study both the phenotypic and genotypic differences among other enterococcal and *E. coli* isolates derived from the present study.

These research results were submitted in fulfillment of checkoff-funded research projects. This report is published directly as submitted by the project's principal investigator. This report has not been peer-reviewed.

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