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## Antibacterial activities of aditoprim against pathogenic bacteria from pigs, chickens, calves, sheep and fish

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A ditoprim (ADP) is an antibacterial dihydrofolate reductase inhibitor. However, the antibacterial activities and spectrum of ADP and its metabolites have not been systematically studied yet. Here, the *in vitro* antibacterial activities of ADP and its main metabolites (ADP<sub>1</sub>, ADP<sub>2</sub> and ADP<sub>3</sub>) were assayed against common animal pathogens. It was shown that *Salmonella* and *Streptococcus* from swine, *Escherichia coli* and *Salmonella* from chickens, *E. coli*, *Streptococcus*, *Mannheimia*, *Pasteurella* from calves, *Pasteurella* and *Mannheimia* from sheep, and *E. coli*, Flavobacterium columnare, and Yersinia ruckeri from fish were highly susceptible to ADP (MIC or MIC50≤4 µg/mL). Haemophilus parasuis from swine, *Staphylococcus aureus*, *Aeromonas punctate*, *Mycobacterium tuberculosis*, *Streptococcus agalactiae* from fish, and Klebsiella from calves and sheep showed moderate susceptibility to ADP (MIC or MIC50=8~16 µg/mL), whereas *E. coli*, *Actinobacillus pleuropneumonia*, *Pasteurella*, *S. aureus*, *Clostridium perfringens* from swine, *S. aureus*, *C. perfringens* from chickens, and *S. aureus* from calves were resistant to ADP. ADP<sub>1</sub> and ADP<sub>2</sub> showed equal activities to those of their parent compound, while ADP3 exhibited no antibacterial activity. The killing effect of ADP against *Streptococcus suis* CVCC607 (MIC=2 µg/mL, MPC=12.8 µg/mL) is concentration-dependent. The post-antibiotic-effect (PAE) of ADP exhibited a positive correlation with the concentration and exposure time of ADP to *S. suis* CVCC607, and elongated in combination use with sulfamethoxazole. This study firstly showed that ADP had strong and broad spectrum antibacterial activity and had potential to be used in the treatment of streptococcosis in swine.

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