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Pharmacokinetics study and efficacy evaluation of Ceftriaxone and Tazobactam combination in ESBL *E. coli* infected diarrhoeic poultry birds

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The infections caused by ESBL strains of *E. coli* were often associated with diarrhea in poultry birds. The present research work was undertaken to study the pharmacokinetic profile of Ceftriaxone and Tazobactam in healthy and ESBL *E. Coli* infected diarrheic birds (Broiler, Rhode Island Red, Haringhata Black) following single intramuscular dosing of Ceftriaxone Tazobactam combination (8:1) at 28.125 mg kg^{-1}. Efficacy of Ceftriaxone Tazobactam combination was evaluated for ESBL producing *E. coli* infection in birds (Broiler, Rhode Island Red, Haringhata Black) at pre-determined dosage regimen based on pharmacokinetic study. For induction of infection in the experimental Broiler, Rhode Island Red and Haringhata Black birds, 56×108 CFU/ml of the bacterial culture was inoculated orally. Broilers birds showed severe diarrhea on 7th day following oral inoculation of 1 ml of ESBL producing *E. coli* whereas moderate diarrhoea was manifested in Rhode Island Red birds from the same day. Due to failure of initial challenge, Haringhata Black birds were again inoculated orally with a higher second dose (112×108 CFU/ml sub culture) after 21 days of first oral inoculation. Ultimately moderate diarrhoea was induced in Haringhata Black birds on 8th day after 2nd inoculation. A single dose of Ceftriaxone Tazobactam combination (8:1) at 28.125 mg kg^{-1} was administered intramuscularly to healthy and diarrhoeic Broilers, Rhode Island Red and Haringhata Black birds in six groups (Gr BCT & BCT-D, RCT & RCT-D, HCT & HCT-D) each containing six birds and blood samples were collected at pre-determined time intervals. Ceftriaxone and Tazobactam concentrations from plasma were analysed by HPLC to evaluate pharmacokinetic profile. Following induction of diarrhea Ceftriaxone-Tazobactam combination was given two times daily (at 12 hours interval) for three days at 28.125 mg kg^{-1} intramuscularly. In diarrheic birds of all the three breeds, Ceftriaxone persisted up to 8 hours in presence of Tazobactam and highest plasma concentration was recorded at 0.08 hours. Tazobactam also persisted up to 8 hours while the peak plasma concentration was recorded at 0.25 hour. Longer elimination half-life (t½ β: 3.72±0.24 hours) associated with higher levels of Tazobactam were evident at 2, 4, 6 and 8 hours in diarrheic Broiler birds in presence of Ceftriaxone. Significantly increased body clearance (ClB: 12.34±0.58 L kg^{-1} h^{-1}) of Ceftriaxone in healthy Haringhata Black birds in presence of Tazobactam compared to a mean ClB value of 10.19±0.57 L kg^{-1} h^{-1} in diarrhoeic birds was observed. It was also observed that Tazobactam undergoes rapid absorption in diseased Haringhta Black birds (Ka: 18.77±1.73 h^{-1}) compared to healthy birds (Ka: 11.91±1.39 h^{-1}) in presence of Ceftriaxone. Diarrhea began to subside on 2nd day of treatment in all the birds of three groups and a complete recovery was noticed on 3rd day of treatment.

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