Depletion of ABZ & Metabolites

Background

• Albendazole (ABZ) is a broad-spectrum benzimidazole anthelmintic, currently approved for use in cattle and sheep. After oral treatment, it is readily absorbed from the gut and converted into a number of metabolites, e.g., albendazole sulfone (ABZ-SO), albendazole sulfoxide (ABZ-SO2) and albendazole aminosulfone (ABZ-2-NH2SO2). The US Code of Federal Regulations lists ABZ-2-NH2SO2 metabolite as the marker residue (MR) in cattle and sheep with a tolerance of 50 µg/kg (ppb) in the muscle tissue.

• Previously, we reported the comparative metabolism and residue depletion of ABZ in muscle tissue of rainbow trout, Atlantic salmon, tilapia and channel catfish (2,3). All species were able to bio-transform ABZ into two of its metabolites, ABZ-SO, ABZ-SO2. However, only rainbow trout, Atlantic salmon and tilapia had detectable levels of a third metabolite ABZ-2-NH2SO2.

• In continuation of our efforts to study metabolic profiles of ABZ in a multiple finfish species to determine a potential MR, we report here the residue depletion of albendazole and its major metabolites in the muscle tissues of two additional species, hybrid striped bass (HSB) and largemouth bass (LMB).

Animal experiment

• Large mouth bass (Micropterus salmoides) and hybrid striped bass (Morone chrysops x saxatilis) were housed in 60 L flow-through glass tanks containing fresh water at temperature of 20±2 ºC and pH of 7.5±0.5.

• Both species were dosed with albendazole at 10 mg/kg body weight in gel capsule via intra-gastric tube with manual restraint.

• Six fish were used at each time point and necropsy was performed at post dose 8, 16, 24, 48, 72, 96 and 120 hours. Muscle fillets were collected and blended to fine tissue powder in dry ice.

Analytical methods

• Extraction: weigh 1g tissue in pp centrifuge tubes and add 0.1 mL 4M potassium carbonate (pH 11), 0.5 mL dimethyl sulfoxide, 0.4 mL 4M sodium metabisulfite and 5 mL ethylacetate.

• Vortex mix and shake for 10 minutes. Centrifuge and remove supernatant into another 15 mL tube. Add 5 mL ethylacetate to the pellet, vortex mix, centrifuge and combine the supernatant extracts.

• The extract was further purified using sodium sulfate, ethanol-0.2 M HCl and iso-octane as reported previously (1).

• HPLC analysis: column, Phenomenex Luna C18 (2) 150x4.6 mm, 5 micron at 30 ºC; mobile phase, ACN/MeOH/CH3COONH4 with ratio of 30:15:55 for ABZ and 12:8:80 for ABZ metabolites, flow rate 1 mL/minute; detector, fluorescence exc. 290 nm, em, 330 nm.

Results

• The parent drug, albendazole, was metabolized quickly in both species. It was detectable until 8 h (6.7 ºD) in HSB and 48 h (40 ºD) in LMB. It was also detectable in one HSB at 24 h post dose.

• Albendazole sulfone, a pharmacologically active metabolite of albendazole, was also rapidly depleted, in both species, by 48 h (40 °D) in HSB and 96 h (80 °D) in LMB. Again, LMB metabolized ABZ-SO slightly slower than HSB.

• Similarly, the inactive metabolite ABZ-SO2 was present until 72 h (60 ºD) in HSB and 96 h (80 ºD) in LMB.

• The other inactive metabolite, ABZ-2-NH2SO2 was present in LMB at all sampling times but was either absent or below the limit of detection in HSB, similar to the catfish studies previously.

• Comparing our previous results with the current study, we find that the parent drug ABZ was also quickly metabolized in other species and remained detectable until 8 h (8.3 °D) in catfish, 12 h in both tilapia (12.5 °D) and rainbow trout (6 °D), 24 h (15 °D) in Atlantic salmon.

• Among the six species studied, LMB depleted ABZ the slowest 48 h (40 °D).

Conclusions

• The results of the current study demonstrate that LMB bio-transforms ABZ into three of its major metabolites, ABZ-SO, ABZ-SO2 and ABZ-2-NH2SO2. This is similar to tilapia, rainbow trout and Atlantic salmon as reported by us previously (2).

• However, the metabolism of HSB is more similar to channel catfish (3), where parent drug ABZ is metabolized more rapidly, ABZ-SO2 is the most persistent metabolite and ABZ-2-NH2SO2 is generally lacking.

• This study infers that ABZ-2-NH2SO2 could potentially serve as a marker residue for four fish species, i.e., tilapia, rainbow trout, Atlantic salmon and large mouth bass; whereas, ABZ-SO2 would serve as potential marker residue for channel catfish and hybrid striped bass.

References