GLYCINE PROTECTS RENAL FUNCTION IN WINTER FLOUNDER (*PSEUDOPLEURONECTES AMERICANUS*)

J. Larry Renfro[1], Cristina Zeien[2], Alice R. Villalobos[1] and Jason Joseph[1]
[1]Department of Physiology and Neurobiology, University of Connecticut, Storrs, CT, 06269,
[2]Department of Pharmacology and Therapeutics, University of Florida, Gainesville, FL 32610

Lytic cell injury is prevented in the renal proximal tubule by millimolar levels of glycine (*see* Brezis, M., *Kidney Int'l.* 42:523-539, 1992). Accumulated evidence supports a ligand-receptor mechanism involving a glycine-gated anion channel (Heyman, S. et al., *Kidney Int'l.* 42:41-45, 1992). The latter phenomenon was the basis for our recent experiments showing glycine protection and enhancement of organic anion secretion by the teleost renal proximal tubule (Miller, D.S. et al., *Bull MDIBL* 36:73-74, 1997; Miller, D.S. et al., *Bull MDIBL* 37:95-96, 1998). This information, together with new information that dietary glycine supplementation prevents drug-induced nephrotoxicity in mammals (Thurman, R.G. et al., *Transplantation* 63:1661-1667, 1997), has prompted us to ask if treatment of flounder with glycine may provide *in vivo* renal protection from gentamicin, a nephrotoxic antibiotic commonly used by aquarists to treat bacterial infections in teleosts.

The renal clearances of inorganic phosphate, sulfate and inulin were determined in flounder (250-350g) following anesthetization with MS-222 (1:2000, w/v), surgical catheterization of the urinary bladder and cannulation of the caudal hemal vein. Following a 24 h recovery period, animals were given intramuscular injections of *i.)* glycine (261 mg/kg), *ii.)* gentamicin (3.5 mg/kg), or *iii.)* glycine (261 mg/kg) and gentamicin (3.5 mg/kg). Injections were repeated 24 h later. Glomerular filtration rate (GFR) was determined from the clearance of inulin given by i.m. injection immediately after surgery. Inulin was assayed by the indole acetic acid method, and anions were measured by anion chromatography (Dionex).

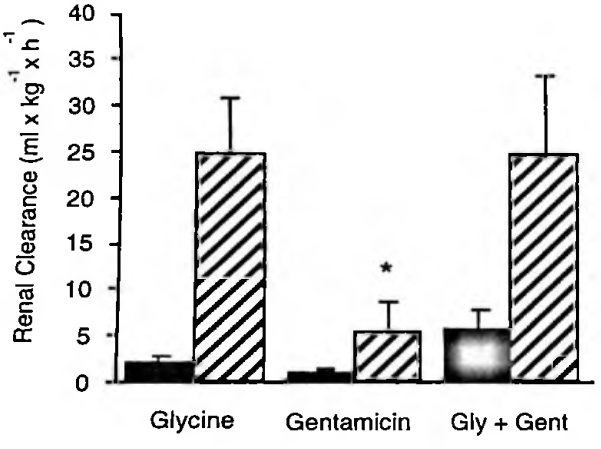

Figure 1. Effect of glycine and gentamicin on renal clearances of phosphate (solid bars) and sulfate (hatched bars) during 48 h of treatment. Average renal clearances are shown for the second 24 h treatment period. Values shown are means ± SEM for n = 3 fish in each group. *Significantly different from glycine treatment ($P < 0.05$).

No treatment significantly altered renal phosphate clearance, urine flow rate, or GFR. Given alone, gentamicin reduced sulfate clearance to 20% of that in glycine-treated animals (Figure 1). However, co-administration of glycine with gentamicin prevented the decrease in sulfate clearance. Sulfate secretion is an active, vital renal function in marine teleosts. These preliminary data indicate that increased levels of tissue glycine provide protection of this important renal function in fish.

Supported by NSF IBN 9604070 (JLR) and NIEHS P30-ES 3828 (Center for Membrane Toxicology Studies). J.L. Renfro was supported by a Salsbury Cove Research Fund Senior Fellowship. Ms. Zeien was supported by a University of Florida Summer Fellowship.