about 9. We found significant (T/M > 1), but substantially reduced, PAH accumulation after 24 hr preincubations. Reduction of the preincubation temperature to 10° or 4° dramatically improved tissue viability. These data indicate that, in contrast to mammalian tissue, the teleost renal preparation may be useful for testing drugs with long time courses of action.

Preincubation of tubules with 1 mM cisPt caused some initial stimulation of PAH transport, and maximal inhibition after 6 hr; with 5 mM cisPt, the stimulatory phase was not observed. Table 1 shows 6 hr I_{50} values (drug concentration causing 50% inhibition of transport) for 11 platinates. Chloroplatinic acid ($PtCl_3$), a potent nephrotoxin with no antitumor activity, was the strongest inhibitor and three compounds (NSC 247, 541, 256, 927 and 267, 583) were less toxic than the parent drug (cisPt). Comparison of the present results with available whole animal toxicity data shows the same rank order for drug-induced elevation of plasma BUN, renal histopathology and inhibition of flounder tubule PAH transport (Guarino et al., in preparation).

In the search for mechanisms of platinate nephrotoxicity, one must consider heavy metal sensitive sites within the proximal tubular epithelial cell, i.e.: 1) apical or basal lateral membrane organic acid carriers, 2) ATPases, which maintain essential gradients for cations, and/or 3) cytoplasmic or mitochondrial enzymes which are involved in metabolic processes. Our initial experiments have focused on the enzyme, Na,K-ATPase, since inhibitors of this enzyme, e.g., ouabain and heavy metals, also reduce PAH transport (Miller, unpublished data). As shown in Table 1, all platinates tested are flounder kidney Na,K-ATPase inhibitors. Comparison of these data with those for the rat kidney enzyme, shows that although the mammalian enzyme is less sensitive, the relative inhibitory potency of the drugs tested is similar (Table 1). The rat enzyme is also less sensitive to ouabain, since I_{50} values for rat and flounder are 1 mM and 1 μM, respectively. We have thus far tested only one of several possible sites of drug action using whole tissue homogenates. One, therefore, might not expect to see a perfect correlation between inhibition of enzyme activity and organic acid transport. Nevertheless, our data do show that the most potent inhibitors of transport are indeed the strongest inhibitors of flounder kidney, Na,K-ATPase. Supported by USPHS Grant ES 01678.

ION TRANSPORT PROPERTIES OF THE ISOLATED OPERCULAR EPITHELIUM OF *Fundulus grandis*

Edward Krasny Jr. and J. A. Zadunaisky, Department of Biology, University of Miami, Coral Gables, Florida and Department of Physiology and Biophysics, New York University Medical Center, New York, New York

The opercular epithelium of the killifish (*Fundulus heteroclitus*) has been used as an in vitro preparation for the study of ion transport and osmoregulation in teleosts fishes (Karnaky et al. Science 195:203, 1977). In search for other species of teleosts with similar characteristics we have determined the electrical properties, chloride fluxes and the actions of some drugs on isolated operculi of *Fundulus grandis*. This teleost is native to the warm seawaters of the Gulf of Mexico and easily available in the State of Florida. It is a larger form of *Fundulus*, and offers a larger surface area of opercular epithelium to be placed as a membrane in Ussing type chambers and study its transport characteristics. The methods utilized were previously described (Degnan et al. J. Physiol. 271:155, 1977).

The results, shown in Table 1 indicate that the opercular epithelium of *Fundulus grandis* exhibits an electrical potential difference comparable to the one of operculi from *Fundulus heteroclitus*, but the short circuit current is substantially lower than in the latter. The average electrical resistance was higher in *Fundulus grandis*. The fluxes of chloride (Table 2) determined with ^{36}Cl indicated that an active transport of this anion from the serosal to the mucosal side exists in operculi of *Fundulus grandis* which is responsible for most of the electrically measured short circuited current.

TABLE 1

Electrical properties of isolated operculi of *Fundulus heteroclitus* and *Fundulus grandis*

	N	I_{SCC} $\mu Am/cm^2$	P.D. mV	R cm^2
F. heteroclitus	(16)	108.7 ± 18.8*	15.1 ± 1.5	179.0 ± 21.8
F. grandis	(16)	52.1 ± 5.7	11.5 ± 0.6	256.8 ± 30.2

*Mean ± SEM

TABLE 2

Chloride fluxes across the isolated opercular epithelium of *Fundulus grandis*

	J_{SM} $\mu Eq.h^{-1}.cm^{-2}$	J_{MS} $\mu Eq.h^{-1}.cm^{-2}$	J_{Net} $\mu Eq.h^{-1}.cm^{-2}$		SCC $\mu Eq.h^{-1}.cm^{-2}$
Control (6)	1.77 ± 0.22*	0.66 ± 0.09	1.12 ± 0.19	30.0 ± 5.0	27.3 ± 6.1

*Mean ± SEM

TABLE 3

Action of some drugs on the electrical properties of the isolated opercular epithelium of *Fundulus grandis*

	I_{SE} $\mu A/cm$	P.D. mV	R $\Omega\ cm^2$
Control (8)	39.2 ± 10.1	8.6 ± 1.3	292.5 ± 53.6
Isoproterenol 10^{-5} M	28.6 ± 10.3	9.1 ± 1.3	306.4 ± 55.1
% change	1.5	5.8	4.8
Control (6)	57.4 ± 14.4	9.1 ± 1.1	195.4 ± 38.5
Theophylline 10^{-4} M	62.3 ± 16.4	9.6 ± 0.9	194.6 ± 41.8
% Change	8.5	5.5	0.4
Control (5)	65.3 ± 19.4	9.7 ± 0.9	186.0 ± 44.0
Adrenalin 13 x 10^{-6} M	0.7 ± 0.5	0.1 ± 0.1	176.8 ± 66.7
% Change	98.9	99.0	5.5
Control (6)	55.6 ± 8.7	9.8 ± 0.4	218.9 ± 66.9
Ouabain 10^{-5} M	2.9 ± 0.4	0.6 ± 0.1	259.9 ± 98.5
% Change	94.8	93.9	18.7
Control (6)	62.3 ± 10.3	10.9 ± 0.6	213.9 ± 64.7
Furosemide 10^{-3} M	10.8 ± 2.1	1.8 ± 0.3	198.9 ± 58.8
% Change	82.7	83.5	7.0

The easily dissected, larger area of opercular epithelium of *Fundulus grandis* offers a methodological advantage over the same tissue preparation obtained from *Fundulus heteroclitus*. In both species chloride ions are transported toward the mucosal side. The data in Table 3 demonstrate that isoproterenol and theophylline had less of a stimulatory effect on the short circuit current in *Fundulus grandis* than in *Fundulus heteroclitus*. Adrenaline, ouabain and furosemide had potent inhibitory effects on the isolated operculum of *Fundulus grandis* which were essentially similar to those previously reported for preparations obtained from *Fundulus heteroclitus* (Karnaky et al. Science 195:203, 1977). This work was supported by NIH Research Grants EY 01340 and GM 25002.