disrupting the normal Na^+ and K^+ distribution across the membrane, to inhibit the active chloride transport.

A number of features makes this tissue suitable for the study of transepithelial salt transport with the short-circuit current technique: the ready availability of the killifish; the ample surface area of the killifish opercular epithelium; the durability of the tissue in vitro; and the presence of large numbers of chloride-secreting cells in the tissue (*2*). The gill respiratory lamellae (*17*) present unsurmountable difficulties in studies of short-circuited gill filaments, and gills have a relatively small proportion of chloride-secreting cells (*4*). This opercular epithelium preparation may also be useful for studying active chloride transport across single cell membranes, in the same way that the giant neuron of *Aplysia* (*18*) is used in such studies.

Fundulus heteroclitus will adapt to a wide range of salinities, from fresh water to 200 percent seawater (*4*), and thus the opercular epithelium preparation may serve as a model for studies of the comparative aspects of ion transport mechanisms associated with euryhalinity. Extrarenal ion-secretory tissues, such as the salt glands (*19*), are also complex and cannot be studied as flat, short-circuited sheets. The killifish opercular epithelium may therefore be used as a general model for ion transport mechanisms in a broad range of osmoregulatory epithelia.

KARL J. KARNAKY, JR.
Mt. Desert Island
Biological Laboratory,
Salsbury Cove, Maine 04672
KEVIN J. DEGNAN
JOSE A. ZADUNAISKY
Departments of Physiology
and *Ophthalmology,*
New York University Medical Center,
New York 10016

References and Notes

1. For a review, see J. Maetz and M. Bornancin, *Fortschr. Zool.* **23**, 321 (1975).
2. Since their initial description in 1932 [A. Keys and E. N. Willmer, *J. Physiol. London* **76**, 368 (1932)], chloride-secreting cells of the gill epithelium have been assumed to be the cellular basis for osmoregulatory sodium and chloride secretion in seawater teleosts. Chloride-secreting cells were originally described in *F. heteroclitus* opercular epithelium by J. Burns and D. E. Copeland [*Biol. Bull. Woods Hole Mass.* **99**, 381 (1950)]. For an estimate of the relative percentage of the cell types, the chloride-secreting cell density, and a description of the fine structure of the opercular epithelium of *F. heteroclitus* see Karnaky and Kinter (*3*). For gill ultrastructure see C. W. Philpott [*Protoplasma* **60**, 7 (1965)], J. D. Newstead [*Z. Zellforsch.* **116**, 1 (1971)], and Karnaky *et al.* (*4*).
3. K. J. Karnaky, Jr. and W. B. Kinter, in preparation.
4. ———, L. B. Kinter, C. E. Stirling, *J. Cell Biol.* **70**, 157 (1976).
5. Specimens of *F. heteroclitus* (6.0 to 14.0 g) were adapted for 2 to 5 weeks to 100 percent artificial seawater according to the technique described by Karnaky *et al.* (*4*). Each fish yielded two opercular epithelia, one from each operculum.
6. This small chamber has been described by J. A. Zadunaisky and K. J. Degnan [*Exp. Eye Res.* **23**, 191 (1976)] for small areas of ocular tissues. It consists of two hemidiscs between which the membrane is positioned across the aperture; the discs are then placed between the two halves of the chamber. The volume of each chamber half was 2.5 ml.
7. Modified Forster's medium [R. P. Forster, *Science* **108**, 65 (1948)]: NaCl, 135 m*M*; KCl, 2.5 m*M*; $CaCl_2$, 1.5 m*M*; $MgCl_2$, 1.0 m*M*; $NaHCO_3$, 16 m*M*; Trizma base, 20 m*M*. The *p*H was 8.25, and the solutions were gassed with 100 percent O_2 at 24° to 26°C.
8. T. J. Shuttleworth, W. T. W. Potts, J. N. Harris, *J. Comp. Physiol.* **94**, 321 (1974).
9. H. H. Ussing and K. Zerahn, *Acta Physiol. Scand.* **23**, 110 (1951); J. A. Zadunaisky, *Am. J. Physiol.* **211**, 506 (1966).
10. Least squares analysis of the pooled data of four experiments gave a mean slope of 28.3 ± 2.1 mv per tenfold change in chloride concentration. The correlation coefficient was 0.845.
11. J. Maetz and F. G. Romeu, *J. Gen. Physiol.* **47**, 1209 (1964); F. G. Romeu, A. Salibian, S. Pezzani-Hernandez, *J. Gen. Physiol.* **53**, 816 (1969); M. Field, D. Fromm, I. McColl, *Am. J. Physiol.* **220**, 1388 (1971).
12. A stock solution of Diamox (Lederle) was prepared by dissolving the powder in Ringer solution and readjusting the *p*H to 8.25 with HCl. In four experiments portions of this stock solution were added to both sides of the chamber; when diluted into 2.5 ml the solutions had a final concentration of 10^{-2} *M* Diamox. No inhibitory effects were observed up to 1 hour after the addition of the Diamox. Furosemide was obtained as Lasix ampules (Hoechst) and was used as supplied. The introduction of small volumes of this solution into the bathing solutions did not change the *p*H and there was no detectable precipitation.
13. M. Burg, L. Stoner, J. Cardinal, N. Green, *Am. J. Physiol.* **225**, 119 (1973).
14. O. Candia, *Biochim. Biophys. Acta.* **298**, 1011 (1973).
15. I. L. Cooperstein, *J. Gen. Physiol.* **42**, 1233 (1959); J. A. Zadunaisky, O. A. Candia, D. Chiarandini, *ibid.* **47**, 393 (1963); O. A. Candia, *Am. J. Physiol.* **223**, 1053 (1972); M. B. Burg and N Green, *ibid.* **224**, 659 (1973); A. S. Rocha and J. P. Kokko, *J. Clin. Invest.* **52**, 612 (1973).
16. R. P. Durbin, *J. Gen. Physiol.* **47**, 735 (1964); J. A. Zadunaisky, M. A. Lande, J. A. Hafner, *Am. J. Physiol.* **221**, 1832 (1971); F. H. Epstein, J. Maetz, G. deRenzis, *ibid.* **224**, 1295 (1973).
17. Gill filaments are the sites of osmoregulatory ion transport as well as of gas exchange, the latter being affected by the numerous respiratory leaflets protruding from the filaments. The application of the short-circuit current technique to this structurally complex gill has never been reported and should prove difficult with the techniques presently available.
18. J. M. Russell and A. M. Brown, *J. Gen. Physiol.* **60**, 499 (1972).
19. These salt glands are found in elasmobranchs, marine turtles and snakes, desert lizards, and birds.
20. This work was supported by NIH research grants AM 15973 (to W. B. Kinter) and EY 01340 (to J.A.Z.), and research fellowships GM 57244 (to K.J.K.) and EY 05059 (to K.J.D.).

13 July 1976; revised 8 September 1976

Diabetic Cataracts and Flavonoids

Abstract. *Oral administration of quercitrin, an inhibitor of aldose reductase, leads to a significant decrease in the accumulation of sorbitol in the lens of diabetic* Octodon degus. *The onset of cataract is effectively delayed when quercitrin is continuously administered. Thus in these diabetic animals, as in galactosemic rats, the use of an effective aldose reductase inhibitor impedes the course of cataract development. These observations support the hypothesis that in diabetes, as in galactosemia, aldose reductase plays a key role in initiating the formation of lens opacity.*

Aldose reductase has been implicated in the etiology of cataracts in diabetic and galactosemic animals (*1*, *2*). This enzyme catalyzes the reduction of glucose and galactose to their respective polyols, sorbitol and galactitol, by the reaction: Aldose + NADPH → Polyol + NADP [NADPH, reduced form of nicotinamide adenine dinucleotide phosphate (NADP)]. In diabetes and galactosemia these polyols attain a strikingly high level in the lens, leading to an osmotic overhydration of the tissue. This osmotic change initiates a series of physicochemical events that ultimately lead to the formation of mature cataracts. Thus, according to this theory, aldose reductase plays a key role in the cataractous process. The most convincing evidence in support of this hypothesis comes from in vivo experiments involving the inhibitors of aldose reductase. In galactosemic rats, systemic administration of an aldose reductase inhibitor effectively delays the onset of the cataractous process (*3*). In the diabetic situation, however, the support of this thesis comes mainly from the in vitro lens culture studies (*4*). Validation of the hypothesis from experiments with the intact diabetic animal has not been obtained because the rat develops a nuclear opacity after a long period of 3 to 4 months following the establishment of experimental diabetes. Under these circumstances it is difficult to establish the effectiveness of an in-

Table 1. Effect of quercitrin on the concentrations of sugars and polyols in the lenses of diabetic degus. Average blood glucose of animals was 465 ± 20 mg/100 ml; period of diabetes was 2 days. Experimental details have been described in the text. Number of analyses in each group was six. Results are expressed as micromoles per gram wet weight of the tissue ± standard deviation. Lenses were analyzed for the sugars and polyols by gas-liquid chromatographic technique described previously (*7*).

Animals	Glucose	Fructose	Sorbitol	Inositol
Treated	1.5 ± 0.1	4.1 ± 0.4	9.4 ± 1.1	1.5 ± 0.8
Nontreated	1.7 ± 0.1	8.4 ± 1.5	18.7 ± 1.9	1.1 ± 0.4

hibitor in delaying the onset of diabetic cataracts. Besides the long experimental period required for cataract development, the time of appearance of the opacity varies considerably from animal to animal. We discovered that the degu (*Octodon degus*), a rodent native to the Andes of South America, develops nuclear opacity in 10 to 12 days after induction of diabetes. The rapid development of cataract appears to be related to a high aldose reductase activity in the lens of this animal. The enzyme activity in the degu lens was observed to be three to four times higher than that in the rat lens. Degus thus appeared to provide a more suitable model for testing the role of aldose reductase in the formation of diabetic cataracts. This report describes the effect of quercitrin treatment on the course of cataract development in experimentally diabetic degus. We recently reported that quercitrin, a flavonoid, is the most potent inhibitor of lens aldose reductase (*5*).

Degus weighing 90 to 100 g were used in this study, and before induction of diabetes they were segregated into two groups. One group received regular lab chow powder; the other group received the lab chow mixed with quercitrin (25 mg per gram of lab chow). In addition, the latter group was given orally a single dose of 70 mg per day of quercitrin in aqueous suspension. After 3 days on the above schedule both groups of degus were given streptozotocin intraperitoneally (dose, 10 mg per 100 g of body weight). On the third day after streptozotocin administration some animals were killed for determination of lens sugars and polyols; others were maintained longer for ophthalmoscopic examination. The data summarized in Table 1 show that the flavonoids are effective as aldose reductase inhibitors in vivo. Levels of sorbitol as well as of fructose, the two metabolites of the polyol pathway, were about 50 percent lower in the lenses of diabetic degus receiving quercitrin than in the lenses of controls. Glucose concentrations were approximately the same in lenses of the two groups, which probably is a reflection of the fact that blood sugar concentrations were similar.

The next phase of the study was to determine whether quercitrin could in fact delay the onset of cataracts. The control diabetic degus not receiving quercitrin developed a nuclear opacity by about the tenth day after the onset of hyperglycemia (Fig. 1). In contrast, the degus treated with quercitrin, although having a blood sugar concentration similar to that of the control group (approximately

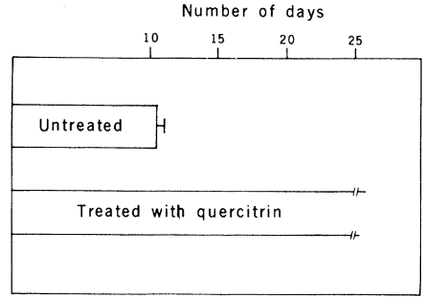

Fig. 1. The appearance of nuclear opacity in diabetic degus. There were 13 animals in each group. The average blood glucose of all animals was 385 ± 20 mg/100 ml. Experimental details have been described in the text.

380 mg/100 ml) did not develop cataracts even 25 days after the onset of diabetes, the time at which the experiment was terminated. The effect of quercitrin should, however, be viewed as a delay and not a prevention of cataract formation, since the lenses of the treated degus, although clear, did show vacuoles.

Results provide strong support of the hypothesis that aldose reductase initiates the formation of cataracts in diabetes. This study reveals for the first time that inhibition of aldose reductase not only leads to a decrease in the sorbitol accumulation in the lens but also impedes the cataractous process. The cataract formation in diabetes may thus be at least delayed, if not prevented, by the in vivo use of an aldose reductase inhibitor. We have also examined other flavonoids for their ability to inhibit aldose reductase activity in the hope of finding even more potent derivatives than quercitrin (*6*). Possibly other flavonoids are effective in still lower doses and are more suitable therapeutically against the diabetic manifestations initiated by polyols.

S. D. VARMA
A. MIZUNO, J. H. KINOSHITA
Laboratory of Vision Research, National Eye Institute, Bethesda, Maryland 20014

References and Notes

1. R. Van Heyningen, *Nature (London)* **184**, 194 (1959).
2. J. H. Kinoshita, *Invest. Ophthalmol.* **13**, 713 (1974).
3. D. Dvornik, N. Simmard-Duquesne, M. Krami, K. Sestanj, K. H. Gabbay, J. H. Kinoshita, S. D. Varma, L. O. Merola, *Science* **182**, 1146 (1973).
4. L. T. Chylak and J. H. Kinoshita, *Invest. Ophthalmol.* **8**, 401 (1969).
5. S. D. Varma, I. Mikuni, J. H. Kinoshita, *Science* **188**, 1215 (1975).
6. S. D. Varma and J. H. Kinoshita, *Biochem. Pharmacol.*, in press.
7. ———, *Biochim. Biophys. Acta* **338**, 632 (1974).
8. Quercitrin was kindly supplied by Alcon Laboratories, Fort Worth, Texas. Animals used in the experiments were obtained from Dr. D. K. Boraker of the University of Vermont.

13 July 1976; revised 25 August 1976

Ocean Thermal Gradients—A Practical Source of Energy?

In "Ocean thermal gradient hydraulic power plant," Beck (*1*) describes a scheme for extracting power from the ocean thermal gradients, a very important subject. He suggests introducing warm surface water through a restriction in the lower end of a vertical pipe, which leads to a closed, direct-contact spray condenser, cooled by water from lower ocean depths. Cavitation would occur in the restriction and steam bubbles would be formed, which would then travel up the vertical pipe, carrying water with them (as in the well-known air-lift pump) to a height of hundreds of feet.

There are a number of fallacies in this concept. Ignoring the energy required to pump the low-temperature subsurface water up to the condenser, the inefficiencies of direct-contact spray condensers, the energy required to remove air from the condenser, and the energy required to move water through the restriction, it should be noted that any vapor bubbles formed in the restriction would collapse immediately after entering the high-pressure zone just above the restriction, near the bottom of the vertical pipe. Vapor bubbles are, therefore, simply not available to provide pumping action as in the air-lift pump. Vapor bubbles would be created by boiling near the top of the vertical pipe as the warm water enters the condenser. These vapor bubbles would be available to lift the water, but then only a few inches, assuming reasonable driving temperatures such as 80°F for surface water and 40°F for subsurface water. This few inches of water, rather than a few hundred feet, is the only head available to drive a turbine to extract the energy.

One might suggest that entrained or absorbed air would be separated from the warm surface water by the cavitating restriction, and that it would provide the bubbles needed for an air-lift pump. Ignoring the fact that not enough air could be provided by this means, it should be noted that any air entering the system must be pumped from the condenser to maintain its pressure near that corresponding to the condensing steam temperature. The energy required to remove this air from the condenser is more than the potential energy stored in the water raised by the air-lift pump. Therefore,