

Table 1. Evidence of diabetes mellitus in sand rats (*Psammomys obesus*).

Sex	Age (mo)	Wt. (g)	Glucose (mg/100 ml)		Age when cataracts observed (mo)	Pancreas		Glycogen nephrosis
			Plasma	Urine		Beta-cell degranul.	Vacuoles	
Diet: Laboratory chow and vegetables								
♀	6	221.5	565	12,700	2	++++	+++	+++
♀	7	219.0	560	20,700	4	++++	+++	+++
♀	6	218.0	498	15,600	3	++++	+++	+++
♂	7	258.3	489	9,700	3	++++	+++	+++
♂	7	223.0	466	9,030	2	++++	+++	+++
♂	7	317.5	386	9,320	2	++++	+++++	+++
♂	6	238.0	268	3,880	3	++++	0	0
♀	7	310.5	192	38	4	+++	0	0
♀	7	291.8	140	84	—	++++	0	0
♂	7	274.0	140	2.5	4	++++	+	0
♀	6	217.0	110	65	5	+++	0	0
♀	7	225.0	70	122	4	0	0	0
Diet: Vegetables								
♀	9	141.5	117	84	—	0	0	0
♂	9	169.0	94	59	—	0	0	0
♀	9	128.0	94	8.1	—	0	0	0
♀	7	93.5	62	3.1	—	0	0	0
♂	9	152.9	59	0.8	—	0	0	0

flected a high incidence of naturally occurring diabetes in this species.

In order to evaluate this latter possibility, animals freshly trapped in Egypt were examined immediately. In 40 animals the mean plasma glucose concentration was 97.8 ± 7.35 mg/100 ml (S.E.), and in 36 animals the mean urine glucose concentration was 15.1 ± 1.90 mg/100 ml. In all these animals the pancreas was histologically normal and contained well-developed islet structures with normal beta-cells. Thus, diabetes does not seem to occur in sand rats in the wild state.

The hypothesis that the diabetes was caused by the diet provided in the laboratory was tested by keeping female sand rats with their newborn young on two different diets and then raising the young on these diets after weaning. One group (12 young) received Purina Laboratory Chow (49.4 percent digestible carbohydrate, 23.4 percent protein, and 3.8 percent fat) as desired, supplemented with fresh mixed vegetables (carrots, beets, beet greens, and spinach); the other group (10 young) received fresh mixed vegetables only, as desired. Five of the ten animals fed vegetables were killed for histological examination. Water was available to all the animals. Samples of blood and urine were collected and analyzed for glucose at monthly intervals from the time of birth until the experiment was terminated.

The 12 animals feeding on laboratory chow began to develop cataracts and elevated urine sugar at the age of 2 months, and when the experiment was terminated at 6 to 7 months 11 of these

animals had cataracts (Table 1). The beta-cells of the islets of Langerhans showed marked degranulation in sections stained with aldehyde-fuchsin. The only animal in this group with normal beta-cell granulation also had a normal concentration of plasma glucose. The six animals with the highest concentration of glucose in urine and plasma showed marked vacuolar changes of the islet cells and glycogen nephrosis. The five animals fed on vegetables only were carried to an age of 9 months to permit time for development of any incipient diabetes (one died of pneumonia at seven months). However, none of this group had cataracts, all had normal pancreatic islets, the plasma glucose was in a normal range, and although glucose was occasionally found in the urine it was always relatively low. The animals feeding on laboratory chow were quite obese (body weight, 251.1 ± 11.0 g

S.E.) while those on vegetables (148.0 ± 8.6 g) were in the range of animals trapped in nature (141.4 ± 10.7 g).

The only rodent in which spontaneous diabetes mellitus has been reported is an inbred strain of the Chinese hamster (3). The diabetes mellitus that occurs in the Egyptian sand rat is of particular interest since in many respects it resembles the clinical and pathologic picture of human diabetes. Because the onset of the disease in the sand rat can be strictly controlled by the type of diet fed, this animal should be an excellent experimental model with which to study the interrelations of such factors as diet, obesity, and early metabolic and pathologic changes.

At the present time the cause of the diabetes that occurs in the sand rat is not known, although it may be due to an excessive caloric intake, or to a carbohydrate intake that is greater than that occurring in the natural diet.

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4. The original stock of sand rats was generously provided by H. Hoogstraal, U.S. Naval Medical Research Unit No. 3, Cairo, Egypt. This work was supported by NIH grant HE-02228 and was done during the tenures of a NIH postdoctoral fellowship No. GPD-14,316-C1 to one of us (H.B.H.), and a U.S. Public Health Service Career Research Award to another (D.B.H.).

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Water Transport across Root Cell Membranes:

Effect of Alkenylsuccinic Acids

Abstract. *Alkenylsuccinic acids increase permeability of cells to water by incorporation of the molecules into the lipid layer of the cytoplasmic membrane, thereby changing the membrane from a phase characterized by a high activation energy for water transport to a phase where only the effect of the viscosity of water is observable.*

Currier (1) observed a sudden increase in permeability of plant cells exposed to benzene vapor, which he ascribed to the destruction of the lipid-rich plasma membrane. Similar effects

of ether and chloroform have been described by Chibnall (2). Van Overbeek and Blondeau (3) concluded from their experiments that phytotoxic hydrocarbons are taken up by the cell membrane

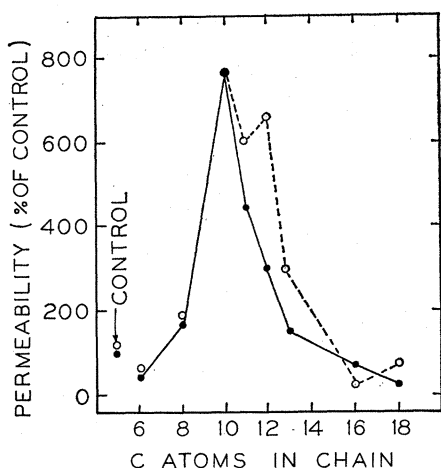


Fig. 1. Effect of alkenylsuccinic acids of different hydrocarbon chain length on permeability of bean roots to water. Closed circles, $10^{-3}M$ solution in aerated water. Open circles, same but in 1 percent ethyl alcohol.

of the plant and induce separation of the lipid layers. Consequently, these substances increased the permeability of the membrane. Hydrocarbons of small molecular weight disrupt the plasma membrane more than hydrocarbons of larger molecular weight.

It is clear, from studies on monolayers on water surfaces, that the strong resistance to evaporation of a compressed monolayer of saturated fatty acids can be greatly reduced by contamination of the film with small amounts of unsaturated fatty acids, such as oleic acid (4). The effect of temperature on the evaporation resistance of such a film depends on the amount of oleic acid added. One may expect that incorporation of molecules with unsaturated hydrocarbon chains into the lipid layers of the cytoplasmic membranes should greatly increase the permeability of the cells to water, while the effect of temperature on water transfer across the membrane should also change (5).

For this reason the effect of several alkenylsuccinic acids of the type $CH_3-(CH_2)_n-CH=CH-CH_2-CH(COOH)-CH_2-COOH$ on water uptake of bean roots was studied (6). A constant suction tension of 60 cm-Hg was applied to the stem. Cytoplasmic membranes of the meristematic cells of the root tip and of the endodermis of the upper root zone account for the main resistance to water transport (5, 7). Exposing the roots to a $10^{-3}M$ solution of decenylsuccinic acid ($n = 6$) resulted in a gradual increase in water uptake amounting to nearly 800 percent of the

original value after 2 hours. This value could not be raised with stronger solutions. Even when the resistance to water transport offered by the conducting xylem vessels—roughly 10 percent of the total resistance—is taken into account, the cytoplasmic membrane resistance has become very small.

By comparison, in an experiment with the analogous saturated compound, decylsuccinic acid, a reduction in water uptake of 55 percent was obtained after 2 hours. This comparison shows that the double bond in the hydrocarbon chain is essential for the increase in water permeability. The effect probably depends on an increase in the London repulsive force between the incorporated molecule and its neighboring lipids in the cytoplasmic membrane (8).

Alkenylsuccinic acids with hydrocarbon chain lengths of from 6 to 18 carbon atoms ($n = 2$ to 14) were compared (Fig. 1). Although the C_6 -succinic acid derivative itself diminished water permeability, an increase in permeability with increasing number of CH_2 -groups was observed. The C_{10} -succinic acid was the most effective. The occurrence of an optimal chain length can probably be ascribed to the van der Waal's attraction between the CH_2 groups of the incorporated molecule and those of neighboring molecules in the lipid layers of the cytoplasmic membrane, a force which retains the alkenylsuccinic acid molecule within the membrane.

The succinic acids of higher molecular weight were less soluble in water and consequently less effective. Adding ethyl alcohol to the root environment increased both solubility of the C_{11} -, C_{12} -, and C_{13} -succinic acids and its effect on water permeability of the root cells. The C_{16} - and C_{18} -succinic acids could be tested only as suspensions.

Water uptake of bean roots is greatly affected by root temperature (7). In one experiment the activation energy amounted to about 25,000 calories per mole, corresponding to a Q_{10} value of 3.8 (Fig. 2). Two hours after application of a $5 \times 10^{-4}M$ solution of decenylsuccinic acid ($n = 6$) to the environment of the root, only a small effect of temperature on water uptake was observed. The activation energy was about 3200 calories per mole, and the Q_{10} value dropped to 1.18. The experiment gives additional evidence that decenylsuccinic acid is incorporated into the lipid layers of the cytoplasmic mem-

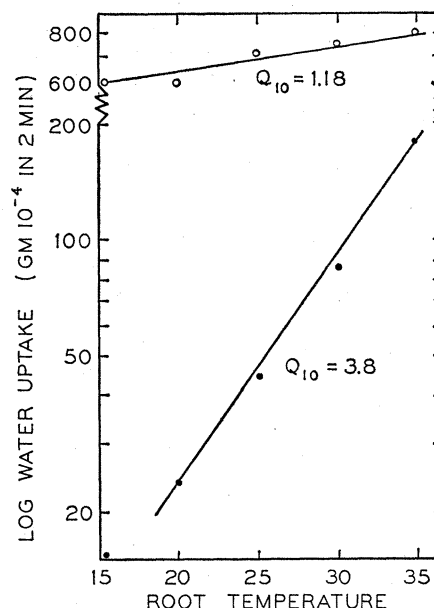


Fig. 2. Effect of temperature on water uptake of bean roots in aerated water (closed circles) and after 2 hours' exposure to a $5 \times 10^{-4}M$ solution of decenylsuccinic acid (open circles).

branes and changes the membrane from a phase, characterized by a high potential energy barrier for water transport ("liquid condensed" phase), to a phase in which only the effect of the viscosity of water is observable ("gaseous" phase). Alkenylsuccinic acids may also be useful in other instances where it is desired to raise the permeability of cell membranes to water irrespective of the temperature conditions of the experiment. These compounds may control the stomata of leaves by a similar mechanism as reported by Zelitch (9).

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