Rectification of Water Flow across Frog Skin

Dear Sir:

It was recently proposed in this *Journal* (1) that the net influx of water across isolated frog skin in the absence of osmotic and hydrostatic pressure gradients occurs as a direct consequence of the permeation of NaCl across the outer epithelial cell membranes and of KCl across the inner membranes. This model of water absorption is essentially identical with the theory developed by Patlak, Goldstein, and Hoffman (2). Their asymmetrical double-membrane system had several additional properties. In particular, such a system should exhibit rectification of solvent flow and, further, the absorbate should be hypertonic when the system is bathed by very dilute media and *vice versa.*

Osmotic experiments (1) performed on normal and poisoned skins bathed in NaCl-Ringer's solutions containing certain concentrations of sucrose were considered to be described mathematically by:

Normal:

$$J_v = (J_v)_0 + L_p RT(C_s^i - C_s^0)$$

Poisoned:

$$J_v = L_p RT(C_s^i - C_s^0)$$

where J_v is the net water influx (cm^3 cm^{-2} second^{-1}); C_s^i and C_s^o, the concentrations (mole cm^{-3}) of sucrose in the internal and external media; R, the gas constant; T, the absolute temperature; L_p, the hydraulic conductivity (cm second^{-1} atm^{-1}) of frog skin, and $(J_v)_o$ is the rate of fluid transport between identical Ringer's in cm^3 cm^{-2} second^{-1}. A thorough statistical examination of these data, however, proves that neither of these curves is perfectly linear and that they can be fitted more satisfactorily by orthogonal polynomials. The main disturbance ($P \leqq 0.01$) from linearity in these cases occurs in the cubic term; *i.e.*, $(C_s^i - C_s^o)^3$. It can be simply concluded from this sigmoidal relation between J_v and $(C_s^i - C_s^o)$ that normal and poisoned skins bathed in NaCl-Ringer's show rectification of water flow in the presence of osmotic gradients.

Dainty and House (3) have performed similar osmotic experiments on normal skins bathed in Na_2SO_4-Ringer's containing sucrose at various concentrations, and after using the same statistical analysis they have found a completely linear relationship between J_v and $(C_s^i - C_s^o)$; in this case, the quadratic, cubic, and higher terms in the analyses of variance were comparable ($P \doteqdot 0.10$) with error. The absence of rectification of solvent flow in these circumstances is also completely compatible with the asymmetrical double-membrane picture of frog skin since this phenomenon can only occur in the presence of some permeating solute and the skin can be considered practically impermeable to Na_2SO_4.

Further indirect support for the double-membrane effect in frog skin lies in the observation (4) that the absorbate becomes considerably hypertonic when the skin is bathed in diluted Ringer's. To thoroughly substantiate this view, however, direct measurements must be made of reflection coefficients of the outer and inner membranes for NaCl and KCl, *cf.* Whittembury (5); in particular, his work indicates that the reflection coefficient of the outer membrane for NaCl is significantly less than unity.

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