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Aqueous pores in lipid bilayers and red cell membranes

A.K. SOLOMON and C.M. GARY-BOBO★
Biophysical Laboratory, Harvard Medical School, Boston, Mass. 02215 (U.S.A.)
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SUMMARY

There are striking similarities between the properties of the aqueous channels induced in lipid bilayers by the polyene antibiotics nystatin and amphotericin B, and the equivalent pores in human red cell membranes. The equivalent pore radius in the human red cell membrane, calculated from the ratio of the hydraulic conductivity to the water permeability coefficient is 4.5 Å, whereas that for the lipid bilayers, calculated by the same method, is 4.6 Å for the nystatin-treated membrane and 4.3 Å for the amphotericin B-treated membrane. Reflection coefficients for urea, ethylene glycol and glycerol in lipid bilayers are in agreement with those for human red cell membranes. Permeability coefficients for small hydrophilic non-electrolytes are exponentially dependent upon molar volume in both systems and all the data fall on the same curve. The properties of the aqueous channels in these two systems appear to be virtually identical as measured by each of these three independent criteria.

There are remarkable similarities between the aqueous diffusion channels created in lipid bilayers by polyene antibiotics and the equivalent pores in human red cell membranes. Andreoli *et al.*[1] and Cass *et al.*[2] have studied the characteristics of the pathways induced in lipid bilayers by the antibiotics amphotericin B and nystatin, and Holz and Finkelstein[3] have determined the permeability coefficients of small hydrophilic non-electrolytes through these induced pores. It is illuminating to compare their results with those of Sha'afi *et al.*[4] who have measured the permeability of aqueous pathways in the human red cell to hydrophilic non-electrolytes.

Holz and Finkelstein[3] have pointed out that the ratio of the hydraulic con-

★ Laboratoire de Physiologie, Collège de France, 11 Place Marcella Berthelot, Paris V^e, France.

ductivity to the diffusion permeability coefficient for water in the antibiotic-treated lipid bilayers is very similar to the ratio in human red cells. Solomon[5] gives the equivalent pore radius of human red cells as 4.3–4.5Å. When the equations used by Solomon[5] are applied to the data given by Holz and Finkelstein[3], the calculated equivalent pore radius is 4.6 Å for the nystatin-treated membrane and 4.3 Å for the amphotericin B-treated membrane.

An independent method of characterizing the discrimination of a porous membrane between solute and solvent is given by the reflection coefficient, σ. Goldstein and Solomon[6] have measured the reflection coefficient for a number of hydrophilic non-electrolytes in the human red cell membrane and have used these data to compute an equivalent pore radius of 4.3 Å. Holz and Finkelstein[3] have measured σ for the nystatin-treated membranes and compared their results with human red cell data. Comparisons were made for urea ($\sigma_{nystatin}$: $\sigma_{red\ cell}$, 0.55:0.66), ethylene glycol (0.67:0.63) and glycerol (0.78:0.88). The close relation between these coefficients supports the view that the equivalent pore radius of the nystatin-treated membrane is not far different from 4.3 Å.

Horowitz and Fenichel[7] pointed out that the diffusion coefficients of small

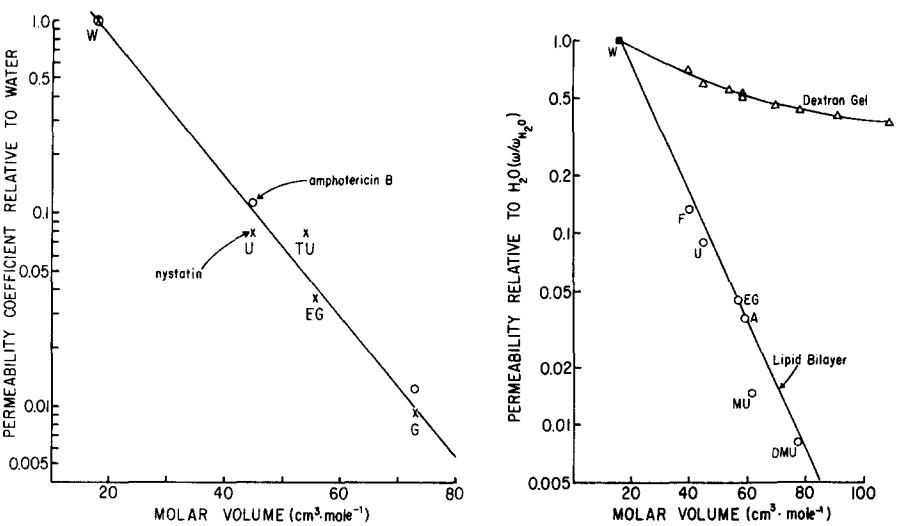

Fig. 1. Permeability of thin lipid membranes to hydrophilic solutes. Permeability coefficients determined by Holz and Finkelstein[3] plotted as a function of molar volume. O, lipid bilayers treated with amphotericin B; X, lipid bilayers treated with nystatin. W, water; U, urea; TU, thiourea; EG, ethylene glycol; and G, glycerol.

Fig. 2. Relative permeability to hydrophilic solutes. Permeability coefficients, relative to water, of dextran gels, human red cell membranes and lipid bilayers. The dextran gel data[7] include: the ureas (urea and thiourea), the amides (formamide, acetamide and propionamide) and the alcohols (the homologous series of 1-ols from methanol to 1-pentanol). O, red cell membrane data[4]. MU, methylurea; DMU, dimethylurea; F, formamide; and A, acetamide. The line is that for the aqueous pores in the lipid bilayer taken from Fig. 1.

non-electrolytes in water-swollen dextran gels is a smooth function of the molar volume. Sha'afi *et al.*[4] have shown the permeability coefficients of small hydrophilic non-electrolytes in human red cells to be exponentially dependent on molar volume. Holz and Finkelstein[3] have measured the permeability coefficient of a number of similar small hydrophilic non-electrolytes in both nystatin- and amphotericin B-treated membranes. We have plotted their data in Fig. 1, which shows the bilayer permeability to be an exponential function of the molar volume of the solutes.

Solute diffusion in these diverse systems may be compared by expressing permeability coefficients relative to that of water, as has been done in Fig. 2. It can be seen that the relative permeability coefficients of both lipid bilayers and red cells fall well below the data in the water-swollen gels. This is a reflection of the steric hindrance offered by the aqueous pathways in the membrane systems. The permeability coefficients in the dextran gels have been compared with water diffusion coefficients determined by Longsworth[8] for many of the same molecules. The ratio of the permeability coefficients, for the five molecules that fall in both series is 0.67 ± 0.01 (gel/bulk water) which means that the apertures in the gels do not offer any steric hindrance to solute molecules of this size, and that the gel diffusion data in Fig. 2 are equivalent to diffusion in bulk water. The most striking conclusion from Fig. 2 is the finding that a single line describes the steric hindrance offered by equivalent pores in the human red cell membrane and by the aqueous channels induced in lipid bilayers by amphotericin B or nystatin. We conclude that the properties of the aqueous pathways of these two systems are virtually identical as measured by each of the three independent criteria employed.

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