Proton Permeability of Renal Membranes: Influence of Amphotericin B

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Dear Sir,

One essential role of the renal system is the maintenance of physiologic acid-base balance. An important parameter in this control is the proton permeability of the brush border membranes on the luminal side of the renal proximal tubule [1]. This report examines the relative permeability of renal membranes to ions and protons. The influence of amphotericin B on these observations was examined due to its strong effects on renal membrane function. Renal brush border membrane vesicles were prepared from rabbit kidney cortex using a method of homogenation, differential centrifugation and Ca^{2+} precipitation [2, 3]. The potential sensitive dye, 3,3-dipropyl-1-thiodicarbocyanine iodide [diS-C₃-(5)] was used to measure the membrane potential. The relative ion permeabilities were derived from the observed membrane potential and the ionic concentrations in the buffer solutions using the constant field equation [2]. Vesicles were equilibrated in solutions of choline and gluconate salts buffered to pHs of 5.5-8.5. Diffusion potentials were measured with extravesicular solutions with varying pHs. These proton-driven membrane voltages were calibrated using known Na^{+} -ETH 1097 and K^{+} -valinomycin diffusion potentials. In the absence of permeable ions, the proton diffusion potentials were nernstian as one would expect when a single species contributes to the membrane voltage. In the presence of permeable cations such as Na^{+} and K^{+} , the proton-induced potentials were less than nernstian.

In the absence of amphotericin B the permeability ratios of ions relative to Cl^{-} (P_{γ}/P_{Cr}) were Cho^{+} (0.08 ± 0.02) < Glu^{-}

(0.15 ± 0.03) < Na^{+} (0.34 ± 0.06) < F^{-} (0.54 ± 0.04) < Ch^{-} (1.00 ± 0.06) < K^{+} (1.6 ± 0.2) < Li^{+} (1.9 ± 0.2) < NH_4^{+} (2.2 ± 0.2) < Br^{-} (4.8 ± 0.4) < I^{-} (43 ± 7) < H^{+} ($1.4 \times 10^7 \pm 0.6 \times 10^7$). In the presence of $2.0 \mu\text{g/ml}$ the permeability ratios were changed significantly to Cho^{+} (0.10 ± 0.02) < Na^{+} (0.47 ± 0.06) < Glu^{-} (0.9 ± 0.1) < NH_4^{+} (2.5 ± 0.4) < Li^{+} (3.8 ± 0.5) < K^{+} (4.0 ± 0.4) < P^{-} (4.9 ± 0.3) < Cl^{-} (7.2 ± 0.8) < Br^{-} (26 ± 3) < I^{-} (200 ± 40) < W^{+} ($1.2 \times 10^7 \pm 0.4 \times 10^7$). The effects of amphotericin B can be best illustrated by the ratios of permeability in the presence and absence of drug ($\text{P-Amp}/\text{P-Amp}^{\beta}$). For the cations, the ratios were Cho^{+} (1.3), Na^{+} (1.4), K^{+} (2.5), Li^{+} (2.0), NH_4^{+} (1.1) and H^{+} (0.9) while those for anions were Ghr (6.0), F^{-} (9.1), Cl^{-} (7.2), Br^{-} (5.4) and 1^{-} (4.6). From these observations it appears that amphotericin B-induced selectivity increased the ion permeability of all anions over that observed for cations. In addition amphotericin B demonstrates specific ionic selectivity within both the anion and cation groups. Amphotericin B had little effect on proton

permeability H^+ (1.4×10^7 vs. 1.2×10^7). In both the presence and absence of amphotericin B, the proton conductance (G_H) of the renal membrane would be in the range expected for Na^+ and K^+ . From these changes in ion permeability, it can be predicted that amphotericin B would significantly hyperpolarize the renal tubular membranes as well as alter intra- and extracellular ion concentrations in spite of little effects on proton permeation.

References

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