Passive Sugar Flux Across Frog Jejunum in vitro* **

K. LOESCHKE, D. HARE, and T. Z. CSÁKY

Department of Pharmacology, College of Medicine, University of Kentucky, Lexington, Kentucky 40506, U.S.A.; and Departments of Medicine and Biophysics, State University of New York at Buffalo, Buffalo, New York 14203, U.S.A.

Received February 25, 1971

Summary. Transmural diffusion of 3-O-methylglucose (3-MG) shows symmetry in bullfrog jejunum perfused in vitro. In both the mucosal to serosal (M to S) and serosal to mucosal (S to M) direction, the permeability coefficient is 1–2 $\times 10^{-6}$ cm/sec as measured in isosmotic Na$_2$SO$_4$ Ringer’s solution containing phlorizin, or K$_2$SO$_4$ Ringer’s. The coefficient—both from M to S and S to M—increases several fold when osmotic water flow is induced from M to S. This is believed to be due to the opening of intercellular spaces. Furthermore, M to S osmotic flow exerts a solvent drag effect on 3-MG. With S to M osmotic flow which is smaller for the same osmotic driving force and induces no space opening, no permeability change is observed and no significant solvent drag effect. The data, along with measurements of mucosal cell and submucosal tissue concentrations during stationary 3-MG diffusion, indicate that the main resistance to sugar diffusion resides in the mucosal cells, especially in their luminal border. By some isosmotic non-electrolyte Ringer’s solutions and moderately hyperosmotic media, the epithelium is progressively destroyed, leading to a time-dependant increase of sugar permeability and a rapid loss of active transport capacity.


Introduction

Transport of non-electrolytes across biological membranes may occur by diffusion, convective flux, active transport or a combination of these mechanisms. For intestinal glucose absorption, the quantitative significance of active transport is unquestioned. As a consequence, the study of passive glucose transfer has been neglected although it has become increasingly clear during the past years that, in composite membranes...
like epithelia, passive molecular movement does not necessarily follow the classical pattern observed in simpler membranes. For instance, osmotic water flow is asymmetric in frog jejunum [28] and toad bladder [37], a feature probably related to the anatomical polarity of the cell. For sugar, a directional difference of convective flux was recently demonstrated in the dog jejunum [26]. Extended knowledge of passive sugar fluxes in the intestine seems, therefore, desirable, if only to further clarify their contribution to overall transport in various experimental situations. In addition, the role played by individual cell barriers involved in transmucosal sugar transport may be elucidated by such work.

In this paper, we describe the influence of two factors on passive sugar flux across jejunum in vitro: of various incubation media and of net water flow.

In many studies, sodium has been replaced by non-electrolytes in isosmotic solutions assuming that sugar diffusion was not affected. Yet the experiments reported here show that some isosmotic non-electrolyte media as well as hyperosmotic solutions markedly change sugar permeability.

To examine a possible relation between passive sugar flux and net water flow, the frog jejunum was thought to be especially interesting since here rectification of osmotic water flow is observed in vitro: osmotic water permeability is much higher in the mucosal to serosal direction than vice versa, for the same pair of solutions [28]. Sugar diffusion was found to be increased during mucosal to serosal osmotic flow but unaffected when flow direction was reversed. Furthermore, a convective flux component was clearly demonstrable only in the mucosal to serosal direction, similar to results obtained in dog jejunum in vivo [26].

Methods

Bullfrogs (R. catesbeiana) of 250–400 g body weight were obtained commercially during May to August and kept unfed in frequently changed tap water of 4°C for 1–8 weeks until experimental use. A 10 cm piece of isolated jejunum was mounted in the in vitro system described by Csáky and Thale [10] and perfused at room temperature. Essentially, this design provides for a recirculating perfusion of the lumen while the serosal fluid is kept in a lucite chamber and mixed by a to and fro motion pump. Both fluid compartments initially contained 13 ml of fluid.

A variety of bathing media was used, the compositions of which are listed in Table 1. Isosmotic solutions were 290 mOsm [16]. Except when stated otherwise, the media contained either 10⁻⁴ M phlorizin or were sodium free, so that carrier-mediated sugar transport was inhibited. In most experiments, sulfate was used as the principal anion for sodium thus eliminating solute-coupled water flow [8], and Table 3). When transmural osmotic water flow was induced, isosmotic and hyposmotic Na₂SO₄ media were paired. In solution pair A₁/A₂, the electrolyte composition of both fluids was identical while the osmolar concentration difference (170 mOsm)