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LITHIUM TRANSPORT AND FACTORS AFFECTING THE MOVEMENT OF LITHIUM IN ISOLATED JEJUNAL MUCOSA OF GUINEA PIG

Lithium carbonate is widely used in the prophylactic treatment of manic-depressive psychoses [1] and is always administered orally. Lithium (Li^+) absorption from small intestine (Mucosal to Serosal) is passive both *in vitro* [2-4], and *in vivo* [5]. It is not affected by temperature, substrate depletion and metabolic inhibitors [6]. One criticism of these earlier studies is that a multicompartiment system with muscle and connective tissue is present and we now report studies in a three compartment system and also in isolated epithelial cells. Isolated jejunal mucosa of guinea pig was prepared and mounted to occlude a «porthole» separating two flux chambers [7]. Both sides were exposed to oxygenated Krebs-Tris buffer at 37°C.

Lithium replaced sodium, total $\text{Na}^+ + \text{Li}^+$ concentration being 106 mM.

Viability was tested by observation of active transport, potential difference, ^3H -PEG900 permeation and histological integrity. Bi-directional transfer of Li^+ across the epithelium was measured using stable isotopes ^6Li and ^7Li [8]. Lithium was determined using either an IL Video 22 or IL 357 atomic absorption spectrometer. Bi-directional fluxes of ^6Li and ^7Li showed no asymetry suggesting that there was no active component involved. Luminal and basolateral surfaces handled Li^+ isotopes similarly. Li^+ movement was independent of glucose transport and there appears to be no significant interaction between Li^+ and either Ca^{2+} or Mg^{2+} .

Acidification of the serosal side alone (pH 5.4) stimulated Li^+ absorption ($P < 0.01$) whereas mucosal acidification alone had no effect on transport. Neither treatment affected tissue uptake. Lithium, therefore, might be substituting for Na^+ in the Na^+/H^+ exchanger [9]. The pH gradient dependent increase in absorption was abolished by 1 mM Amiloride ($P < 0.0004$).

In further studies using ^3H -PEG900 as a measure of paracellular permeation, permeation of lithium correlated with that of PEG suggesting that movement of lithium in either direction occurred via the same PEG permeable, extracellular pathway. Confirmation for this route was obtained using solutions of high osmolarity, which collapsed the tight junctions [10]: lithium absorption was reduced ($P < 0.02$).

The transmucosal fluxes and tissue uptake of lithium in the absorptive (M to S) and secretory (S to M) directions were linearly related to the lithium concentration. Furthermore, the uni-directional fluxes both in the absorptive and secretory direction were similar. Total lithium transport after 45 minutes into serosal or mucosal compartments was 3-4 times greater than that found in the tissue. The plasma membrane of epithelial cells offers greater resistance to the movement of lithium than intact epithelium which suggests that the majority of ions pass via «pores» in the epithelium.

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PREPARATION, CHARACTERIZATION AND ANTI-INFLAMMATORY ACTIVITY OF IMIDO GOLD(I) TRIETHYLPHOSPHINE COMPLEXES

The orally-administered gold(I) compound auranofin ("Ridaura", Smith Kline and French Laboratories) [(2,3,4,6-tetra-*O*-acetyl-1-thio- β -D-glucopyranosato-S)(triethylphosphine)gold] exhibits anti-inflammatory activity in animal models and is currently undergoing Phase IV clinical testing [1]. Structure-activity correlations with the series of complexes $R_3P-Au-SR'$ (where SR' is a sugar thiolate) have shown optimum activity when the phosphine is PEt_3 [2]. We report here the preparation, characterization and biological testing of a series of new imido complexes of triethylphosphine gold(I).

There have been very few previous reports of Au(I) complexes with nitrogen ligands. Gold(I)-N bonds are usually considered to be relatively weak. Five complexes of general formula $Et_3PAu(imide)$ containing the imido ligands shown in the Figure were prepared in good yield and gave satisfactory elemental analyses. The structure of one of them $Et_3P-Au-(phthalimide)$ was determined by X-ray crystallography and