INTERACTION BETWEEN PREDNISOLONE AND PREDNISONE FOR BINDING SITES ON PLASMA PROTEINS

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The commonly prescribed corticosteroids, prednisolone and prednisone, bind to corticosteroid binding globulin (CBG) and albumin in plasma. CBG is a high affinity but low capacity protein and is readily saturated at therapeutic concentration of these steroids; albumin has a low affinity but high capacity and is not saturated (Lewis et al 1971). The binding of prednisolone alone has been studied, but as prednisone and prednisolone are interconverted in vivo (Jenkins and Sampson 1967) the possibility of competitive displacement exists.

We explored this possibility of an interaction using rabbit plasma, stripped of its endogenous corticosteroid, by the method of equilibrium dialysis at $37^{\circ}C$ using tracer markers. Eight concentrations of each steroid were used (range 0-500ng/ml , and the binding of each steroid was determined at all combinations of these concentratons. The fraction unbound of prednisone varied from 0.07 to 0.29 and that of prednisolone from 0.05 to 0.15. A definite interaction was observed.

The following model (Eq. 1 and 2) was fitted to the data by non-linear least-squares regression.

$$C_{PN} = Cu,_{PN} + \frac{Cu,_{PN} \cdot K_{T,PN} \cdot n_T \cdot C_T}{1+Cu,_{PN} \cdot K_{T,PN} + Cu,_{PNL} \cdot K_{T,PNL}} + Cu,_{PN} \cdot K_{A,PN} \cdot n_A \cdot C_A \qquad (1)$$

$$C_{PNL} = Cu,_{PNL} + \frac{Cu,_{PNL} \cdot K_{T,PNL} \cdot n_T \cdot C_T}{1+Cu,_{PN} \cdot K_{T,PN} + Cu,_{PNL} \cdot K_{T,PNL}} + Cu,_{PNL} \cdot K_{A,PNL} \cdot n_A \cdot C_A \qquad (2)$$

where C_x represents the total concentration of x , refering to either prednisone (PN), prednisolone (PNL), CBG(T), or albumin (A) ; $Cu,_{PN} Cu,_{PNL}$ represent the unbound concentration of prednisone and prednisolone respectively, n_T, n_A represent the number of binding sites on CBG and albumin respectively, and $K_{T,x}, K_{A,x}$ represent the binding affinity constants of x for CBG(T) and albumin (A), where x refers to either prednisone or prednisolone.
The final parameter estimates were:

$K_{T,PN} = 3.25.10^7 \text{ M}^{-1}$, $K_{T,PNL} = 4.44.10^7 \text{ M}^{-1}$, $n_T \cdot C_T = 3.42.10^{-7}$ M,

$n_A \cdot K_{A,PN} = 2.59.10^3 \text{ M}^{-1}$, $n_A \cdot K_{A,PNL} = 6.66.10^3$ M-1.
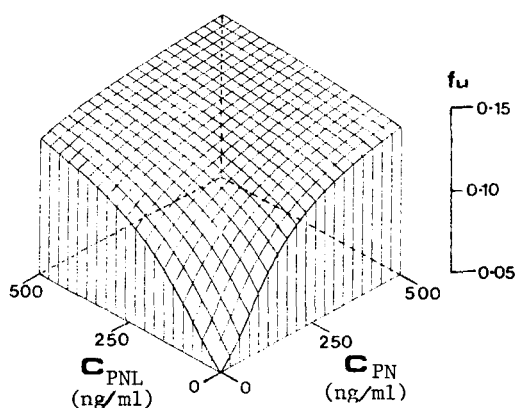

Fig.1 shows the dependence of fraction of prednisolone unbound (fu) on the concentration of both prednisolone (PNL) and prednisone (PN). A similar shaped binding surface exists for prednisone.

Jenkins, J.S., Sampson, P.A. (1967) Brit. Med. J. 2: 205-207
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