DEMONSTRATIONS

Effect of chlorpromazine on hexose penetration in the human erythrocyte

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It has been previously shown that chlorpromazine both accelerates and inhibits glucose exit from erythrocytes pre-loaded with glucose at 36° C depending upon the drug concentration (Baker & Rogers, 1972). The entry of sorbose, a hexose which obeys diffusion kinetics when penetrating the erythrocyte but which in fact is transported on the hexose system for which it has a very low affinity (Widdas, 1954) has been studied using the Ørskov photoelectric technique. Chlorpromazine produces a similar biphasic type of inhibition in the case of this sugar but, unlike glucose exit, sorbose entry is not accelerated. Glucose exit flux measured by optical techniques at 17° C resembles that seen at 36° C but glucose exchange flux determined by isotopic methods at this temperature does not show a biphasic response. The exchange flux is only minimally decreased over the concentration range which produces a two-fold inhibition of exit rate. At drug concentrations corresponding to the second phase of exit inhibition some small decrease in the rate of exchange is seen but this is not comparable in magnitude with the change in exit rate. This suggests a fundamental difference between these two processes and places limitations upon the kinetic models which may attempt to describe such fluxes. Simple carrier models (Widdas, 1954) or the more complex conformational models (Lieb & Stein, 1972) which do not contain separate terms in their kinetics for net and exchange fluxes cannot meet this criterion. Any model to describe these phenomena adequately must contain an exchange rate term which is separate from the net rate. These effects of chlorpromazine may be contrasted with the smooth acceleration of ethylidene glucose (4,6-0-ethylidene glucopyranose) entry, a sugar entering the cell by diffusion, which has been previously described (Baker & Rogers, 1972). It is concluded that changes produced by chlorpromazine on glucose permeation are effective upon the carrier itself rather than a generalized membrane effect.

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Use of the guinea-pig foetal placenta, perfused *in situ*, as a model to study the placental transfer of pharmacological substances

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Perfusion of the placenta *in situ*, via the umbilical arteries with the foetus removed, was introduced by Money & Dancis (1960) using the guinea-pig. The method has been used to study the placental transfer of metabolites and hormones (Dancis, 1971); the transfer of electrolytes has been investigated in the perfused rabbit placenta *in situ* (Faber, 1970; Tucker, 1970). The preparation which will be demonstrated, has not so far been used to study the placental transfer of pharmacological agents and their metabolites, or their effect on the transfer of physiological substances or other drugs.