USE OF GOLDFISH TURNOVER TIME IN PREDICTING GASTROINTESTINAL ABSORPTION

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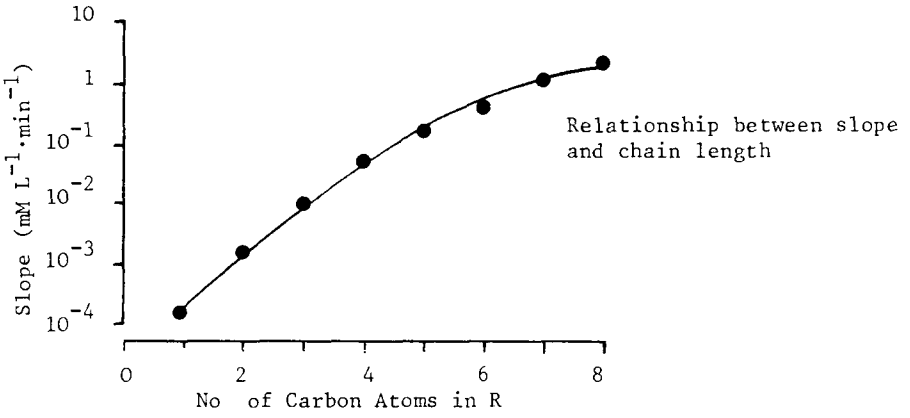
The use of goldfish as model membranes to assess gastrointestinal absorption phenomena is widespread. Mathematical models have been derived which relate drug-induced narcosis (the time taken for a fish to turnover (T) after being placed in drug solution of known concentration) in terms of the permeability properties of the drug (Yalkowsky & others, 1973 and references within). Little attempt has been made to relate the permeability parameters obtained from goldfish with those obtained in man or experimental mammals. The purpose of this investigation was to determine T-concentration relationships of a series of homologues and to compare the parameters obtained with previously published data (Houston & others, 1974) for gastrointestinal absorption of these compounds in the rat.

The compounds studied were a series of straight chain aliphatic carbamates of general structure $R\text{-}O\text{-}CO\text{-}NH_2$ where R ranges from methyl to octyl. For each homologue there was a positive linear relationship between I/T and the concentration of carbamate solution into which the fish was placed. The intercept on the concentration axis decreased regularly in a logarithmic fashion as the R group increased (approximately 0.5 log unit per methylene group). This intercept value may be regarded as the minimum effective concentration to produce T and reflects the potency of the homologue. The slope (S) of the I/T-concentration plot for each homologue increased with chain length. Regular logarithmic increments of approximately 0.8 were observed when R < C4 and when R > C4 the increments were smaller. This behaviour is indicative of a hyperbolic relationship between goldfish permeability and chain length for the carbamate homologues (see figure).



Linear regression analysis showed a strong (r^2 = 0.80) and highly significant (P < 0.005) relationship between S and the gastric absorption rate constants. However no significant relationship (r^2 = 0.32) was apparent using the intestinal absorption rate constants. Since the intestine is the major site of absorption in mammals, it is concluded that goldfish turnover data is of very limited use for predicting absorption rates in higher species.

Houston, J.B. & others (1974). J. Pharmac. Exp. Ther., 189, 244.
Yalkowsky, S.H. & others (1973). J. Pharm. Sci., 62, 1949.