THE INTERACTION OF PHENOTHIAZINE DRUGS WITH PHOSPHATIDYL CHOLINE LIPOSOMES

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The interaction of chlorpromazine with liposomal preparations of lipids from egg-yolk was analysed by Kovaleva & others (1975) using the reciprocal plot method of Klotz & others (1946). A more thorough investigation of the binding of this and other phenothiazine drugs to phospholipid liposomes is reported here.

The equilibrium binding of chlorpromazine, thioridazine, prochlorperazine and perphenazine to unsonicated liposomes formed from soy-bean phosphatidyl choline was studied at $25 \pm 1^{\circ}C$ in subdued artificial lighting. The binding was determined under these conditions by equilibrium dialysis using Visking tubing.

Binding data were analysed by both the linear method of Scatchard (1949) and the non-linear method of Thompson & Klotz (1971). Linear Scatchard plots indicated simple binding to identical sites for all the drugs, and gave values of k, the intrinsic association constant, and 1/n, the number of lipid molecules bound per molecule of drug (Table 1). These binding parameters for chlorpromazine are similar to those obtained by Kovaleva & others (1975), using a linear method of analysis. However, the more informative Thompson & Klotz analysis indicated a complex type of binding for all the drugs, except prochlorperazine. According to the Thompson & Klotz plots, this complex behaviour could be attributed to an interaction between binding sites, being mostly of the 'obstructive' type, although there was some evidence of 'co-operative' binding for low concentrations of chlorpromazine. Binding complexity is also reflected in the discrepancy between the binding parameters determined by the two methods (Table 1), and the failure to obtain values of these for chlorpromazine by the Thompson & Klotz method. Similar complex behaviour has been observed in the binding of these drugs to liposomes prepared from brain lipids.

Table 1

Drug	Scatchard		Thompson & Klotz	
	k ($10^4 M^{-1}$)	1/n	k ($10^4 M^{-1}$)	1/n
chlorpromazine	5.3	12.3	-	-
thioridazine	5.9	6.6	3.5	3.3
prochlorperazine	4.0	5.2	3.9	4.9
perphenazine	6.2	8.3	6.9	10.6

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