

The binding of benzyl alcohol to erythrocyte membranes

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Many studies of "non-specific" interactions of lipid soluble molecules with membranes have emphasized the correlation of biological activity (for example anaesthetic action) with oil/water partition coefficients. There is, however, considerable evidence that the orientation of an extraneous molecule in the membrane, its relation to the interface with the aqueous medium, and its distribution between the lipid and protein components, depends on both the structure of the small molecule and the precise organization of the membrane components.

We have found that the interaction of an anaesthetic, benzyl alcohol, with the erythrocyte membrane provides a simple illustration of the way in which interaction depends on the membrane structure. The partition coefficient for binding of benzyl alcohol to erythrocyte membranes is nearly constant at prelytic concentrations up to 80 mM, but shows a marked increase at higher concentrations in the lytic range. Pretreatment of the membranes with benzyl alcohol concentrations in the prelytic range has no effect on the partition coefficient and the interaction is reversible. However, pretreatment at the maximum concentration (300 mM) results in an irreversible increase in partition coefficient over the whole concentration range. The reason for this is quite clear when the binding to the separated membrane components is examined. The partition coefficient of the protein is approximately twice that of the membrane lipids; and the lipid value is itself greater than that of the intact membrane. The mean value of the separated components weighted according to the membrane composition is close to the value for membranes pretreated with 300 mM benzyl alcohol.

We conclude that in the intact membrane, the membrane structure itself restricts and modifies the interaction with benzyl alcohol. In the lytic range, the membrane progressively interacts as the sum of its separated components, and the major binding component is the membrane protein. It is also clear that these partition measurements on membrane preparations are more informative than partition coefficients measured in unrelated hydrophobic solvents.

Change from agonism to antagonism in the action of some oxytocin analogues: interpretation by a receptor model

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[2-O-Methyltyrosine]-oxytocin (methyloxycytocin) may act on the rat or rabbit uterus *in vitro* as a full agonist, partial agonist, or antagonist according to the experimental conditions (Krejčí, Poláček & Rudinger, 1967). Other analogues of oxytocin modified in sequence position 2 (Zhuze, Jošt, Kasářík & Rudinger, 1964) show similar properties to varying degrees and other tissues such as the isolated rat tail artery (Krejčí, Kupková & Vávra, unpublished results) react in a similar fashion.