Since it fails to show any effect at high compressions, it appears unlikely that the hydrophilic nucleic acid will contribute materially to the asymmetry potential across the film at any area. The form of the dipole moment-area curves therefore suggests that the nucleic acid, at areas greater than that representing close packing, causes a displacement in the orientation of the protein dipoles, in relation to that assumed normally at a water surface.

Since a precisely analogous effect is obtained when the haemoglobin is replaced by poly-DL-leucine (mean molecular weight $> 25{,}000$), the dipoles concerned are probably those associated with the peptide bonds. In other words, the whole polypeptide framework would seem to have undergone re-orientation in such a manner that the sum of the vertical components of the dipole moments is increased.

The predominance of hydrogen bonding between the protein and the nucleic acid is also suggested by the effect on poly-DL-leucine, and confirmed by the finding that the effect of RNA on haemoglobin is almost completely eliminated when urea is added to the substrate to a concentration of 2%.

Deoxyribonucleic acid from thymus gland has been found to give effects similar to those of RNA.

REFERENCES

1 D. F. CHEESMAN AND T. HULTIN, *Arkiv Kemi, Mineral., Geol.*, 24B (1946) No. 4.
2 F. HAUROWITZ, *Chemistry and Biology of Proteins*, New York, 1950, p. 333.
3 F. BINKLEY, *Nature*, 167 (1951) 888.
4 H. B. BULL, *Advances in Protein Chem.*, 3 (1947) 106.
5 W. T. ASTBURY, *Symposia Soc. Exptl. Biol.*, 1 (1947) 66.

Received April 15th, 1953

THE ACTIVE SURFACE OF PSEUDO-CHOLINESTERASE AND THE POSSIBLE ROLE OF THIS ENZYME IN CONDUCTION

by

FELIX BERGMANN AND MENACHEM WURZEL

Department of Pharmacology, The Hebrew University, Hadassah Medical School, Jerusalem (Israel)

Whereas the function of true cholinesterase in the conductive process is indicated by the specific localization of this enzyme[1], little success has so far attended all attempts to define the physiological function of pseudo-cholinesterase[2]. The affinity of this enzyme for choline esters is not yet sufficiently understood, since ADAMS AND WHITTAKER[3] on the basis of their experiments considered it doubtful whether "a negative, nitrogen-attracting group exists in the plasma enzyme".

We have now applied to the pseudo-cholinesterase of human plasma the same criteria that led us previously to a definition of the active surface of true cholinesterase and to a possible explanation of its role in the process of nerve conduction[4,5,6]. We find that quaternary ammonium ions form a typical series of inhibitors, in which—in analogy to their affinity for cation exchangers—the effect is proportional to chain length. However the "limiting" size of the ion appears to be much greater than for the true esterase. In Table I we compare the I_{50}-values for both enzymes. Our figures show clearly that the pseudo-esterase contains a negative site in the neighborhood of the esteratic site. This conclusion finds further support in the observation that the inhibitory effect of eserine, a tertiary base, shows a similar pH dependence as was found previously for the system eserine—true esterase[7].

It is especially noteworthy that hexamethonium, which does not reveal any effect towards the true esterase, is an effective inhibitor of the pseudo-esterase, in view of the fact that this enzyme is present in various parts of the nervous system[8]. The ganglionic blocking action of hexamethonium and other quaternary ammonium salts[9] may be related to the presence of pseudo-cholinesterase in ganglionic synapses, where the enzyme could play a similar role in conduction as does the true esterase in other parts of the nervous system[10]; but due to its smaller turnover number the pseudo-

TABLE I

CONCENTRATION OF QUATERNARY AMMONIUM SALTS TO PRODUCE 50% INHIBITION (I_{50})

Compound	I_{50} — value for	
	pseudo-cholinesterase (from human plasma)	*true cholinesterase (from electric eel)*
1. Tetramethylammonium iodide	$6 \cdot 10^{-2} M$	$1.5 \cdot 10^{-2} M$
2. Tetraethylammonium bromide	$4 \cdot 10^{-2}$	$3 \cdot 10^{-3}$
3. Tetra-*n*-propylammonium iodide	$5.5 \cdot 10^{-3}$	$1.5 \cdot 10^{-4}$
4. Tetra-*n*-butylammonium iodide	$2 \cdot 10^{-3}$	$3 \cdot 10^{-4}$
5. Choline chloride	$5.5 \cdot 10^{-2}$	$4 \cdot 10^{-3}$
6. Hexamethonium*	$1.6 \cdot 10^{-3}$	not measurable up to $10^{-1} M$
7. Decamethonium*	$6 \cdot 10^{-5}$	$2.5 \cdot 10^{-5}$

* Hexamethonium = N,N′-bis(trimethylammonium)hexane di-iodide
Decamethonium = N,N′-bis(trimethylammonium)decane di-iodide

esterase will produce a less rapid recovery of the resting potential. Our experiments thus furnish an enzymological basis for KOELLE's[10] claim—which was based on histochemical evidence—that "non-specific cholinesterase plays a role in synaptic transmission".

It appears possible that a genetic relation exists between the two types of cholinesterases and that in various parts of the nervous tissues mixtures of the two enzymes or esterases with intermediate degrees of specificity participate in the conductive process.

A detailed account of our experiments on substrate specificity, the relationship to inhibitors and the influence of pH changes on the activity of pseudo-cholinesterase will be published in this Journal.

REFERENCES

[1] D. NACHMANSOHN in PINCUS AND THIMANN, *The Hormones*, Academic Press, New York 1950, p. 520.
[2] C. J. EARL AND R. H. S. THOMPSON, *Brit. J. Pharmacol.*, 7 (1952) 685.
[3] D. H. ADAMS AND V. P. WHITTAKER, *Biochim. Biophys. Acta*, 4 (1950) 543.
[4] F. BERGMANN AND E. SHIMONI, *ibid.*, 8 (1952) 520.
[5] F. BERGMANN AND E. SHIMONI, *ibid.*, 9 (1952) 473.
[6] F. BERGMANN AND E. SHIMONI, *ibid.*, 10 (1953) 49.
[7] I. B. WILSON AND F. BERGMANN, *J. Biol. Chem.*, 185 (1950) 479.
[8] See e.g. M. G. ORD AND R. H. S. THOMPSON, *Biochem. J.*, 46 (1950) 346 for earlier references.
[9] W. D. M. PATON AND E. J. ZAIMIS, *Brit. J. Pharmacol.*, 6 (1951) 155.
[10] G. B. KOELLE, *J. Pharm. Exp. Ther.*, 100 (1950) 158.

Received May 11th, 1953