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The anticholinesterase activity of physostigmine

SIR,—When physostigmine in solution undergoes decomposition, its urethane grouping is first lost and a colourless compound termed eseroline is formed; subsequent oxidation leads to rubreserine, a red quinone, which is later converted to eserine blue or eserine brown (Ellis, 1943). We have now investigated the anticholinesterase activities of these degradation products.

Samples of eseroline, rubreserine, eserine blue and eserine brown were kindly supplied by Mr. G. Smith, Department of Pharmacy, Heriot-Watt University. They were dissolved in freshly distilled water and stored at 4° until required. The anticholinesterase activities of the different solutions were compared with that of physostigmine.

In the first experiments, comparisons were made using horse serum as the source of pseudocholinesterase and acetylcholine as the substrate. Both the Warburg manometric technique and the biological method which involves measuring the residual acetylcholine on a piece of isolated tissue (rat colon, rat uterus, guinea-pig ileum) were used. All the degradation products of physostigmine were less active than the parent compound; eserine blue, the most potent, was 100–500 times less active whilst eseroline and rubreserine were 10 times less active than eserine blue. When the comparisons were made using both serum and red blood cells of rabbit, horse and man as the sources of enzyme and acetylcholine as the substrate, all of the degradation products were more active against the pseudocholinesterases than against the true enzymes; on the other hand, physostigmine at a very much lower concentration was equally active against both enzymes.

Finally, tests using the chromodacryorrhoea response in rats (Burgen, 1949) showed that eserine blue, rubreserine and eseroline were about 1,000 times less active than physostigmine in potentiating the *in vivo* action of acetylcholine.

The results are of relevance in that ophthalmic solutions of the British Pharmaceutical Codex are now required to be sterile, and physostigmine eye-drops B.P.C. (Supplement, 1966) may be sterilized by heat. Hydrolysis may occur during the heating process, resulting in the formation of an inactive colourless compound, eseroline, before the appearance of the pink oxidation product, rubreserine. Thus solutions of physostigmine may be colourless but relatively inactive.

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Book Review

PRINCIPLES OF PHYSICAL CHEMISTRY FOR BIOLOGY AND PHARMACY. By L. Saunders. Pp. ix + 438 (including Index). Oxford University Press, London, 1966. 63s. U.K. only.

As this book is aimed at students of biology and pharmacy, it might be as well to emphasize at the start that it is an undergraduate textbook of physical chemistry, not of physical pharmacy or physical biochemistry. To achieve orientation and brevity, special criteria have been applied in selecting material and the result is an unusual but interesting balance between depths and shallows. Some topics have been skimmed over, others extensively treated and developed mathematically step-by-step to give a basis in the physics of chemical processes, particularly those of chemical kinetics, thermodynamics, electrochemistry, chromatography and physical methods of determining molecular size and shape, "topics . . . which are of greater interest in pharmacy and biology." The treatments are relatively simple and for students having a foundation in logarithms, series, differential and integral calculus, most of the steps should be recognizable. However, there are some situations in wave mechanics, entropy, distribution of energies, multiple partition and diffusion, in which more than the usual thin knowledge of mathematics is required and many will grope through these proofs and skip parts of them. Two appendices, on the mechanics of rotors and the distribution of molecular energies, are of more value to the good than the bad mathematician and will not help the laggards and gropers.

Thermodynamics is given as a general background throughout the text rather than as a separate entity and this is a praiseworthy feature. Usually the foundation is built upon energy interconversion and the first law, but here these topics are in the first chapter, in company with rather bald definitions of units and constants, and a 50 page interval deprives the section on work of expansion of gases of its appropriate antepast; some recapitulation would be valuable to condition the student to the thermodynamic approach and need not disrupt the otherwise excellent unity between kinetic theory and internal energy of gases.

A major problem is the assimilation of new and difficult concepts, such as entropy, free energy and chemical potential. They are better described here than in most textbooks, and a real attempt is made to give them meaning.