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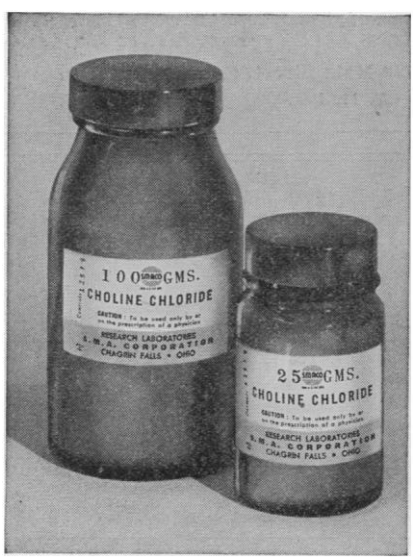

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THE GOLDEN AGE OF BOTANY[1]

By Dr. EDGAR N. TRANSEAU

THE OHIO STATE UNIVERSITY

THOSE of us who were so fortunate as to enter the field of botany about the beginning of the century have witnessed the period of its greatest growth and differentiation. In no other country and at no other time have there been so many undergraduate students of botany, so many graduate students and so many botanists employed in educational and research institutions. We vividly recall that this 40-year period began just after the Spanish-American war when America took over the Philippine Islands. We have likewise had a part in all the educational phenomena before, during and after the first World War. The period closes as World War II is thrust upon us.

This time the war is not "to make the world safe for democracy," but to keep democracy from being crushed against the wall at its back. After the first world war came the collapse of European credits and subsequently a variety of social revolutions that have ended in ruthless dictatorships. The state-supported Continental universities were first impoverished, then regulated and finally regimented or liquidated. Because of declining financial aid, teaching and research in botany have been possible only to men of independent means, and in many of the Continental

[1] Address of the retiring president of the Botanical Society of America, delivered at Dallas, Texas, on December 29, 1941.

BINDING OF SULFONAMIDES BY PLASMA PROTEINS

CEREBROSPINAL fluid concentrations of sulfathiazole which occur during treatment of meningitis do not generally exceed 25 per cent. of the plasma concentrations; values for sulfanilamide in the cerebrospinal fluid may reach 100 per cent. of the plasma concentrations, whereas the values for sulfapyridine and sulfadiazine are intermediate. These differences in concentration have been ascribed to differences in the diffusibility of the drugs into the spinal fluid. An alternative explanation would be the existence of part of the drug in combination with plasma protein. Schonholzer[1] has demonstrated binding of the azo-dye of sulfanilamide, Prontosil, to serum albumin in electrophoresis experiments, but this technique does not furnish quantitative data for partial binding. The experiments reported in the present paper support the view that the sulfonamide drugs are bound to plasma proteins in varying proportions, the relative concentration of drug attained in the spinal fluid depending upon the extent to which the drug is bound in the blood.

Normal human plasma was dialyzed in Cellophane bags against 0.15 N. NaCl, buffered at pH 7.4 by the addition of 0.01 M. phosphate, with varying additions of a sulfonamide. At equilibrium the drug concentration was found to be higher in the plasma than in the buffer. While this distribution coefficient is not direct evidence of binding to protein, the data fit the Freundlich adsorption isotherm, as is the case with phenol red,[2] for which direct evidence of chemical binding has been furnished by absorption spectrophotometry.[3] Whether the phenomenon be due to adsorption, coordination, or simply depression of the activity coefficient by the protein is of less biological than chemical interest, for in any case, it is the value of the distribution coefficient which determines the distribution in the body. The binding (using the term in a very general sense) is due to albumin but not to globulin; lipid-free plasma behaves similarly. In normal plasma containing 7 per cent. protein, with drug concentrations of 10 mg per cent., the proportion of "free" (unacetylated) drug which is bound to protein is as follows:

Sulfanilamide	20 per cent.
Sulfapyridine	40 per cent.
Sulfadiazine	55 per cent.
Sulfathiazole	75 per cent.

These data can explain the observed distribution in body fluids and the greater solubility in plasma than in saline.

[1] G. Schonholzer, *Klin. Wchnschr.*, 19: 790, 1940.
[2] A. Grollman, *Jour. Biol. Chem.*, 64: 141, 1925.
[3] H. W. Robinson and C. G. Hogden, *Jour. Biol. Chem.*, 137: 239, 1941.

Preliminary bacteriostatic experiments were carried out with *B. coli* in a synthetic medium, with and without added albumin.[4] The results suggest that the concentration of unbound drug determines the level of bacteriostatic activity, the bound drug being apparently inactive. It was also noted that the order of increasing tendency to be bound to plasma albumin was identical with the order of increasing bacteriostatic effectiveness for the four sulfonamides studied.[5] This latter relationship may be of theoretical significance and is being studied further.

It has been demonstrated that the sulfonamide drugs behave as though bound in varying degree to plasma albumin or some fraction thereof, and it appears that the bound drug is not bacteriostatically effective. The effective level of the sulfonamides in the cerebrospinal fluid may therefore be as great as that in the blood stream, and the apparent level compared with the blood should not be used as a guide to the choice of a drug. Inasmuch as excellent therapeutic results have been reported with the use of sulfathiazole in meningococcic meningitis[6] it may be preferable to the more toxic sulfanilamide and sulfapyridine, which have often been favored because of the higher concentrations attained in the cerebrospinal fluid.

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[4] We are indebted to Dr. W. Barry Wood for assistance in the bacteriological work.
[5] (a) W. B. Wood, personal communication. (b) H. J. White, T. T. Litchfield, Jr., and E. K. Marshall, Jr., *Jour. Pharm. and Exp. Therap.*, 73: 104, 1941.
[6] (a) M. Finland and J. H. Dingle, *New Eng. Jour. Med.*, 225: 825, 1941. (b) H. S. Banks, *Lancet*, 1: 104, 1941.

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HUREWICZ, WITOLD and HENRY WALLMAN. *Dimension Theory*. Volume 7 in Princeton Mathematical Series, MARSTON MORSE, H. P. ROBERTSON and A. W. TUCKER, editors. Pp. 165. Princeton University Press. $3.00.

JOHNSTONE, RUTHERFORD T. *Occupational Diseases*. Illustrated. Pp. x + 558. Saunders.

KNIGHT, HARRY H. *The Plant Bugs, or Miridae, of Illinois*. Bulletin of the Illinois Natural History Survey, Volume 22, Article 1. Illustrated. Pp. 234. State of Illinois.

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