the amount of PD^- that is formed, and recent work[4] indicates that sulfonamide potency is a direct function of its protein-combining capacity, then in a series of drugs of various pK's acting in a solution at pH near 7, for example, those of intermediate pK should be most effective. For if the drug is a very weak acid, the number of D^- ions is very small, even though most of them may combine with the acid P to form PD^-. On the other hand, if the drug is a very strong acid, the number of D^- ions would be quite large in a solution of pH 7, but since D^- is weakly basic, little PD^- would be formed. The maximum PD^- concentration, for equal additions of sulfonamide, would be formed by a drug with some intermediate value of pK.

The same considerations apply when one considers a basic sulfonamide such as sulfaguanidine, except that in this case the neutral molecule D can combine directly with the acid P to form PD. For basic sulfonamides the same correlation should exist between pK and potency, except that pK now refers to the equilibrium $HD^+ = H^+ + D$.

This qualitative description is supported fully by a detailed, quantitative consideration of the equilibria involved. Complete details of this treatment will be given in a forthcoming publication. For the present it will be sufficient to point out that the equations finally reduce to the following condition relating the pK of the sulfonamide of maximum activity to the pH of the solution:

$$pK_{HD} = pH - \log \frac{1-f}{f} \qquad (1)$$

where

$$f = \frac{d \ln K_{PD}}{d \ln K_{HD}}, \qquad (2)$$

K_{PD} being the dissociation constant of the enzyme-sulfonamide complex. When f is determined for a given bacterial system, pK_{HD} can be predicted immediately.

Unfortunately we can not make a direct test of this prediction at present, because data for the direct evaluation of f for bacteria are unavailable. Nevertheless, we can evaluate f indirectly for *E. coli* and compare the value so obtained with that derivable from work[4] on the combination of serum albumin with sulfonamides.

Bell and Roblin[1] have found that in a solution of pH 7, maximum bacteriostasis of *E. coli* was obtained with a sulfonamide with a pK of about 6.7. Substituting the appropriate values in (1) we find f is 0.3. Such a value of f is apparently very reasonable if we may compare it with the approximate value derived for serum albumin. From the work of Davis and Wood[4] one can calculate relative values of K_{PD}, for sulfonamides of various K_{HD}'s. A plot of log K_{PD} vs. log (K_{HD}) fits a straight line fairly well and the slope of this line is f. For serum albumin f turns out to be 0.5.

The inhibition of sulfa action by p-aminobenzoic acid is also amenable to the type of treatment described above. In this case we assume that when the ratio of PA^- (the p.a.b.-enzyme combination) to PD^- reaches some fixed value, inhibition sets in. The mass law treatment then predicts that the ratio of the total amount of p-aminobenzoic acid necessary to cause inhibition, to the total amount of sulfonamide present, will be a maximum for the sulfa compound of greatest potency. This is in agreement with the data of Rose and Fox.[5]

Thus, the law of mass action, as applied to a system consisting of a sulfonamide and an enzyme in a buffer solution, predicts the existence and acid dissociation constant of a drug of maximum potency, correlates the effectiveness of basic as well as acid sulfa compounds with their acid ionization constants, and accounts quantitatively for the inhibitory effect of p-aminobenzoic acid.

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CORRECTION

IN a revision of the proof a serious omission was made in the inadvertent dropping of "and 1 ml. of 0.1% $CuSO_4 \cdot 5H_2O$ solution" after "Aliquots of 2.0 ml are mixed with 6 ml of clear 12.5 per cent Na_2CO_3 solution" on p. 405. Addition of copper is essential in enhancing the sensitivity of the Folin reagent, as already noted by others.

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SCIENTIFIC BOOKS

PHYSIOLOGICAL CHEMISTRY

The Dynamic State of Body Constituents. By R. SCHOENHEIMER. Harvard University Monograph in Medicine and Public Health No. 3. 79 pp. Harvard University Press. 1942. $1.75.

THE nineteenth century, which ended about 1914, was the callow age of the physiological chemist. Rudolph Schoenheimer's "The Dynamic State of Body Constituents" marks the transition to a humbler, more realistic and more mature state of mind.

Until recently, the physiological chemist described

[4] Davis, SCIENCE, 95: 78, 1942; Davis and Wood, *Proc. Soc. Exptl. Biol. Med.*, 51: 283, 1942.

[5] Rose and Fox, SCIENCE, 95: 412, 1942.