of the structural requirements of the cystine peptide substrates, it is suggested that the enzyme responsible for reaction I be designated "exocystine desulfurase." It may be that the exocystine desulfurase-dehydropeptidase system is involved in a detoxification mechanism. Free cystine in excess is known to produce hepatic and renal damage.[8] Peptides of cystine are more soluble than the free amino acid, and it may be advantageous for the tissues to destroy the cystine while it is in susceptible peptide form before it can accumulate to the free, largely insoluble and certainly toxic amino acid.[9]

FLORENCE M. LEUTHARDT
JESSE P. GREENSTEIN
NATIONAL CANCER INSTITUTE,
NATIONAL INSTITUTE OF HEALTH,
BETHESDA, MD.

THE DIFFUSION CONSTANT OF PENICILLIN

USING the sintered glass membrane technique, the diffusion constant of penicillin has been measured over the pH range 4.0–8.0. To minimize errors due to the decomposition of the active material, the experiments were conducted at 0.5° C. Preliminary experiments indicated that at low temperatures the rate of decomposition of penicillin was not significantly affected by concentration at pH 7; this fact has been verified for the entire pH range covered.

The diffusion cells were similar to those described by Mouquin and Cathcart.[1] They were calibrated with 2.0M sodium chloride solutions, the value 1.27 cm² per day being taken for the diffusion constant of this substance at 25.0°.[2] Lederle penicillin (sodium salt, potency 250–300 Oxford units per mg) was employed. At pH 4.0 and 5.0, Na_2HPO_4-citric acid buffer was the solvent; for the other experiments KH_2PO_4-Na_2HPO_4 mixtures were used. The diffusion constants were calculated by means of the equation:

$$D = \frac{V_2 C_2}{tKC_1}$$

where V_2 is the volume of the cell compartment into which diffusion occurs, K is the cell constant, and C_2 and C_1 are the penicillin concentrations on the "low" and "high" sides of the membrane, respectively, at the end of time t. For experiments of short duration ($C_2 < 0.02\ C_1$) this calculation gives results nearly identical with those obtained using the more elaborate expression derived from the integration of Fick's first law.

Penicillin concentrations were estimated by a turbidimetric microbiological assay procedure, using *Staphylococcus aureus* as the test organism. This method will be described in detail in a subsequent publication.

The experimental results are summarized in Table 1. Included are the values of C_1; essentially, this figure represents the concentration difference across the membrane throughout the run. Each value for D presented is the average of at least two determinations made with different cells. The average deviation was about 2 per cent.

TABLE 1

pH	C_1 (Oxford units per ml.)	$D_{0.5°}$ (Cm² per day)
4.0	50	0.192
5.0	59	0.165
6.0	46	0.180
7.0	45	0.176
8.0	38	0.178
7.0	608	0.165

The change in D observed as the pH is decreased is probably a reflection of the conversion of the salt to the acid form. Abraham and Chain[3] have reported that penicillin appears to be a dibasic acid, characterized by "titration constants" of 2.43 and 3.5.

The last value in Table 1 is the result of an experiment performed to observe the effect of concentration upon the diffusion constant. The significance of this datum as compared with the corresponding one at lower concentration is uncertain.

Friedman and Carpenter[4] have demonstrated that the Stokes-Einstein equation (relating D to molecular radius) is valid for molecules as small as the hexoses. Applying this equation to the data at pH 7 results in the value 5.37 Å for the radius of the penicillin molecule. Assuming the density to be 1.25, the calculated molecular weight is 490. This figure is consistent with the value 510 suggested by Abraham and Chain.[3]

EDWARD H. FRIEDEN
DEPARTMENT OF BIOLOGICAL CHEMISTRY,
THE UNIVERSITY OF TEXAS SCHOOL OF MEDICINE

to whether dehydropeptides might not also be derived under natural conditions from peptides of serine. This possibility must be borne in mind, although there is as yet no enzymatic evidence relating to the possible degradation of serine peptides. We have confirmed Smythe's findings that free serine, unlike free cystine, is not enzymatically attacked in rat liver extracts.[5]

[8] A. C. Curtis and L. H. Newburgh, *Arch. Int. Med.*, 39: 828, 1927; D. P. Earle and J. Victor, *Jour. Exp. Med.*, 73: 161, 1941; P. György and H. Goldblatt, *Jour. Exp. Med.*, 75: 355, 1942.

[9] Since this communication was submitted for publication, Dr. Max Bergmann died, untimely, at the height of his productivity and usefulness. It is my hope that this brief note may serve, even if inadequately, as a tribute to the memory of a man who was a great chemist, an unassuming personality and a warmhearted friend.—J.P.G.

[1] H. Mouquin and W. H. Cathcart, *Jour. Amer. Chem. Soc.*, 57: 1791, 1935.

[2] M. L. Anson and J. H. Northrop, *Jour. Gen. Physiol.*, 20: 575, 1937.

[3] E. P. Abraham and E. Chain, *Brit. Jour. Exp. Path.*, 23: 103, 1942.

[4] L. Friedman and P. G. Carpenter, *Jour. Am. Chem. Soc.*, 61: 1745, 1939.