results indicating satisfactory comparability with rubber-latex treated papers but with somewhat less tensile strength.

PATHFINDERS OF PROGRESS IN PLASTICS

The institute's plasticians have maintained their master researchmanship on twenty-four diverse fellowships. Growing attention to cyclopentadiene in the synthetic plastic and organic chemical fields has greatly stimulated research on methods for its utilization. In action is a study of the electrolytic preparation of certain organic compounds of relevance in the manufacture of synthetic resins, rubbers and fibers. A completed two-year investigation has yielded a new curable liner for container closures. Continued research on resin-pulp products has led to further applications for pre-formed materials. The use of new vulcanizable elastomers and low-temperature curing resins has likewise brought advances in the field of cellulosic molding. Organic salts of hydrous aluminum silicates have been studied with reference to their employment as plastics. The development of military and industrial applications of leather-like plastics, announced a year ago, has been extended. Artificial filaments of various types are receiving long-range research. The synthesis of morpholinomethyl derivatives of ureas has been published. New techniques have been introduced for the preparation of vinyl-resin coating compositions; ketones have been described as solvents for those resins.

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(To be concluded)

SPECIAL ARTICLES

THE RELATOINSHIP OF LYSOZYME TO AVIDIN[1,2]

FROM hen's eggwhite two seemingly unrelated biological principles have been obtained, lysozyme and avidin. Lysozyme is a basic protein[3,4] which lyses susceptible microorganisms like *Micrococcus lysodeikticus* or *Sarcina lutea* by depolymerizing and hydrolyzing a mucoid contained in the bacterial membrane[5,6]; while avidin is said to be a basic protein[7] which combines stoichiometrically with biotin, thus depriving the test microorganisms[8] or the animal[9] of this essential vitamin. Some of the reported chemical properties of avidin were so similar to those of lysozyme that we undertook the study of their relationship, although Woolley and Longsworth[7] reported their avidin preparation free of lysozyme activity.

Seven avidin preparations[10] were tested for lysozyme activity against *M. lysodeikticus* and two strains of *S. lutea*. Avidin activity, varying from 60 to 5,200 units per gm, was proportional to lysozyme activity, varying from 4 to 160 units per mg.

The action of biotin[11] on the lytic action of lysozyme was then tested. In these tests acetone dried *M. lysodeikticus* were used, suspended in M/15 KH_2PO_4, corresponding to a density of a No. 10 $BaSO_4$ standard. With live organisms in 0.9 per cent. NaCl the activity is about double. It is known (see review[12]) that the organisms do not dissolve in acid solution, although lysozyme activity is optimal at an acid pH. To demonstrate visible lysis a drop of N NaOH is added at the end of the experiment (usually 1 hour at 37° C.) to stop enzyme activity and to observe clearing of the suspension. The controls without lysozyme are not affected by this treatment.

It can be seen from Table 1 that addition of 10 γ of biotin increases the activity of lysozyme, both against live and acetone-ether killed and extracted organisms, from 8 to 250 times. The effect of 10 γ of biotin is even more marked if incomplete lysis

TABLE 1

Lysozyme preparations	Lysozyme units per mg		*M. lysodeikticus*
	Without biotin	With 10 γ biotin	
Avidin (5200 units/gm)	640	2,600	Living
85 B	2,600	164,000	Living
85 C	1,300	164,000	Living
85 C	640	164,000	Acetone dried
85 C	16	2,000	Acid acetone extracted
85 C	640	164,000	Acetone dried
97 C	1,300	20,500	Acetone dried
97 D	640	5,000	Acetone dried

[1] From the Department of Ophthalmology, College of Physicians and Surgeons, Columbia University, and the Institute of Ophthalmology, Presbyterian Hospital, New York.

[2] The author is greatly indebted to William L. Laurence for suggesting experiments on the relationship of avidin to lysozyme, and to Miss Anita Steinberg for assistance in this work.

[3] K. Meyer, R. Thompson, J. W. Palmer and D. Khorazo, *Jour. Biol. Chem.*, 113: 303, 1936.

[4] E. P. Abraham, *Biochem. Jour.*, 33: 622, 1939.

[5] K. Meyer, J. W. Palmer, R. Thompson and D. Khorazo, *Jour. Biol. Chem.*, 113: 479, 1936.

[6] L. A. Epstein and E. Chain, *Brit. Jour. Exper. Path.*, 21: 339, 1940.

[7] D. W. Woolley and L. G. Longsworth, *Jour. Biol. Chem.*, 142: 285, 1942.

[8] R. E. Eakin, E. E. Snell and R. J. Williams, *Jour. Biol. Chem.*, 136: 801, 1940.

[9] P. György, C. S. Rose, R. E. Eakin, E. E. Snell and R. J. Williams, SCIENCE, 93: 477, 1941.

[10] We are indebted to Dr. Vincent du Vigneaud, of Cornell University Medical College, and to Dr. H. M. Wuest, of Hoffmann-La Roche for the samples of avidin.

[11] The generous gift of synthetic crystalline biotin by Dr. D. F. Robertson, of Merck and Co., is gratefully acknowledged.

[12] R. Thompson, *Arch. Path.*, 30: 1096, 1940.

(+++) is taken as the endpoint. The activity then increases, for example, from 20,500 to 10,500,000, that is over 500 times.

In Table 2 the influence of increasing biotin concentration on the lysis of acetone dried *M. lysodeikticus* is shown.

TABLE 2

Biotin concentration in micrograms	Lysozyme units per mg
0	640
0.01	640
0.1	2,600
1.0	5,000
2.0	5,000
4.0	10,000
6.0	41,000
8.0	82,000
10.0	164,000

The data reported here can not be explained with certainty at the present time. In analogy with many other enzyme systems, biotin might be considered as the prosthetic group of a protein carrier. This protein carrier would bind biotin, while the biotin-avidin complex would have lysozyme activity. In accordance with this hypothesis is the fact that avidin contains both free avidin and an avidin-biotin complex.[13]

However, all attempts to dissociate lysozyme into carrier and prosthetic group have failed so far. These attempts included dialysis in acid and alkaline solutions and electrophoresis. The preparation migrated cathodically at pH 7.80 with a sharp boundary ($u = +6.75 \times 10^{-5}$, Dr. D. Moore). It had an activity greater than 1,000 units per mg. The increasing activation of lysozyme with increasing biotin concentration may contraindicate a simple coenzyme effect of biotin, since the concentration of biotin is far greater than that of lysozyme. The biotin effect, however, apparently is not due to action on the test organisms, since it varies in extent with different preparations of lysozyme.

Aside from any hypothesis, however, the experiments reported in this paper definitely link biotin with lysozyme, a mucolytic enzyme concerned with defense against bacterial invasion. It remains to be seen whether a similar relationship holds true for other enzymes of this important group. It might be pointed out further that an enzyme with the bacteriological specificity of eggwhite lysozyme occurs in many if not in all lysozyme susceptible organisms.[5,12] Similar enzymes with other specificities have been demonstrated in many microorganisms. Such enzymes, which in high concentration partly or completely lyse the organisms from which they are derived, are probably concerned with bacterial multiplication.

KARL MEYER

[13] P. György and C. S. Rose, SCIENCE, 94: 261, 1941.

ON THE POSSIBLE IDENTITY OF "AVIDIN"[1] AND EGGWHITE LYSOZYME

COMPARATIVE studies on "avidin"[2,3] and eggwhite lysozyme[4] bring to light a number of common physical and chemical characteristics. Both seem to be present in the same fraction of raw eggwhite in the same relative abundance. Both have been concentrated by similar chemical procedures. The more similar procedures, *i.e.*, those of Meyer *et al.* for eggwhite lysozyme[4] and of Woolley and Longsworth for "avidin,"[3] have also yielded concentrates of qualitatively similar chemical elements, while the quantitative differences could be accounted for by the seeming differences in the degree of purification. Furthermore, the concept of "avidin" as "antibiotin" makes it difficult to reconcile the fact that whereas biotin is found in so many divergent organisms and tissues, "avidin" has hitherto been found only in whites of eggs or in the oviduct of certain species of frogs and fowl.[5] Moreover, the history of biotin, which was found to be identical with coenzyme R and vitamin H, further suggested that "avidin" may also be a more widely distributed substance.

These considerations led to a series of experimental procedures in which (A) a sample of known eggwhite lysozyme, prepared by Dr. Karl Meyer in October, 1937,[6] was subjected to the standard yeast test[7] for "avidin" activity, and (B) samples of "avidin" of known varying potencies,[8] prepared by Hoffmann-La Roche, Inc., were tested for lysozyme activity.[9]

All tests for both (A) and (B) proved strongly positive, and, furthermore, showed that the "avidin" activity in each "avidin" concentrate closely paralleled its lysozyme activity. The results in the (A) series of tests are shown in Table 1.

[1] The term "avidin" as used here refers to concentrates containing both "free avidin" and avidin-biotin complex.

[2] R. E. Eakin, E. E. Snell and R. J. Williams, *Jour. Biol. Chem.*, 140: 535, 1941.

[3] D. W. Woolley and L. G. Longsworth, *Jour. Biol. Chem.*, 142: 285, 1942.

[4] K. Meyer, R. Thompson, J. W. Palmer, and D. Khorazo, SCIENCE, 79: 61, 1934; *Jour. Biol. Chem.*, 113: 303, 1936; *ibid.*, 113: 479, 1936.

[5] R. Hertz and W. H. Sebrell, SCIENCE, 96: 257, 1942.

[6] The author is deeply indebted to Dr. Meyer for supplying him with this sample.

[7] E. E. Snell, R. E. Eakin and R. J. Williams, *Jour. Am. Chem. Soc.*, 62: 175, 1940.

[8] Supplied through the courtesy of Dr. H. M. Wuest, of Hoffmann-La Roche, Inc., and Dr. Ira I. Kaplan, of Bellevue Hospital, New York City. The initial sample tested had a potency of 2,000 units per gm.

[9] The author hereby wishes to acknowledge his debt to Dr. Gustav J. Martin, of the Warner Institute for Therapeutic Research, New York City, for his invaluable assistance in carrying out the experimental work on the "avidin" activity of lysozyme, and to Dr. Meyer, who carried out the tests on the lysozyme activity of "avidin." Dr. Meyer will present his data on these tests, as well as on further tests initiated by himself, in a separate communication.