PANTOTHENIC ACID STUDIES. V. REVERSAL OF 2-CHLORO-4-AMINOBENZOIC ACID INHIBITION IN *E. coli*. BY PANTOTHENIC ACID[1]

Sir:

Wyss, Rubin and Strandskov[2] and Shive and Roberts[3] have demonstrated that the growth inhibition which takes place when *E. coli* cells are incubated with 2-chloro-4-aminobenzoic acid (CAB), can be reversed by either *p*-aminobenzoic acid (PAB) or methionine. From an analysis of the inhibition data, the latter authors concluded that CAB interfered with the synthesis of methionine, which was normally formed through the action of a PAB-containing enzyme system.

We have found that CAB inhibition of *E. coli* can also be reversed by pantothenic acid (PA). This vitamin is even more effective than PAB, as may be seen from the accompanying table. The growth medium used contained glucose and minerals, including ammonium chloride. Sterilization was accomplished by autoclaving except for the CAB solutions, which were filtered and added aseptically. Cultures were incubated for nineteen hours at 37°.

At high levels of CAB, reversal was more nearly complete when combinations of methionine and PA or methionine and PAB were employed. No growth depression was produced by 10 mg. of CAB per tube in the presence of 100 γ of methionine and 2 γ of PA or PAB. The pantothenic acid conjugate recently described in this laboratory[4] is at least as active as PA in effecting reversal of CAB inhibition. However, folic acid, which is normally synthesized from PAB, has no reversing power.

TABLE I

REVERSAL OF 2-CHLORO-4-AMINOBENZOIC ACID (CAB) INHIBITION BY PANTOTHENIC ACID (PA), *p*-AMINOBENZOIC ACID (PAB) AND METHIONINE IN *E. coli*.

	PA				PAB			Methionine		
	γ per 10 ml. of culture									
CAB, mg. per 10 ml.	0	0.02	0.2	2.0	0.02	0.2	2.0	10	100	1000
	Optical density (2-log G)									
0.0	0.465	0.465	0.455	0.470	0.475	0.460	0.470	0.460	0.455	0.475
0.3	.050	.270	.450	.470	.230	.240	.420	.460	.450	.470
1.0	.010	.210	.410	.440	.140	.180		.420	.460	.470
3.0	.020	.100	.270	.380	.075	.160		.400	.460	.470
10.0	.015	.010	.080	.290	.020	.070	.125	.280	.350	.360

On the basis of the present findings, it would appear that an interrelationship exists between methionine and pantothenic acid in *E. coli*. Further experiments are in progress to determine their relative positions, as well as the possible relationship between this system and PAB.

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(2) O. Wyss, M. Rubin and F. B. Strandskov, *Proc. Soc. Expll. Biol. Med.*, **52**, 155 (1943).

(3) W. Shive and E. C. Roberts, *J. Biol. Chem.*, **162**, 463 (1946).

(4) T. E. King, L. M. Locher and V. H. Cheldelin, *Arch. Biochem.*, **17**, 483 (1948); T. E. King, I. G. Fels and V. H. Cheldelin, THIS JOURNAL, in press.

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NEW BOOKS

Detoxication Mechanisms. The Metabolism of Drugs and Allied Organic Compounds. By R. TECWYN WILLIAMS, Ph.D. (Wales). D.Sc. (Birmingham). Senior Lecturer in Biochemistry, University of Liverpool. John Wiley and Sons, Inc., 440 Fourth Ave., New York, N. Y., 1947. viii + 288 pp. 14 × 22.5 cm. Price, $5.50.

In this excellent reference text, the author has collected and organized most of the available information on detoxication mechanisms published before 1945 and much of that published in 1945 and 1946. The subject is treated broadly as being concerned primarily with qualitative and quantitative studies of the metabolism of foreign organic compounds. The necessity of obtaining quantitative information for any critical analysis of the pathways of metabolism has been justifiably stressed. In the first chapter there is given a general survey of oxidative and reductive changes and processes of conjugation. The following twelve chapters present details of the metabolism of aliphatic compounds, cyclohexane derivatives, aromatic hydrocarbons, derivatives of aliphatic and aromatic hydrocarbons, terpenes, camphor, heterocyclic compounds and organic compounds of arsenic. The collection of data is compiled in such a way that it will be useful as a basis for predicting the metabolic fate of compounds similar to those listed. The author indicates that in addition to the use of such analogies, predictions will be aided by an increased knowledge of the specificity of enzyme systems in the animal under study. The bibliography and index are well prepared. Some errors and certain omissions, such as the use of spectrophotometric procedures, are inevitable in a first edition. Considering the difficulties in collecting

and assaying the significance of the mass of information on the subject, there can be no doubt of the great value of the contribution to biochemistry and organic chemistry that Dr. Williams has made in writing the text.

HUGH J. CREECH

Theory of the Stability of Lyophobic Colloids. The Interaction of Sol Particles Having an Electric Double Layer. By E. J. W. VERWEY AND J. TH. G. OVERBEEK. Natuurkundig Laboratorium N.V. Philips' Gloeilampenfabrieken, Eindhoven (Netherlands). With the collaboration of K. Van Nes. Elsevier Publishing Company, Inc., 215 Fourth Avenue, New York 3, N.Y., 1948. xi + 205 pp., 54 figs. 16.5 × 24 cm. Price, $4.50.

The purpose of the book is to develop a quantitative theory of the stability of lyophobic colloids and suspensions based on modern theories of the diffuse electric double layer, supplemented by the theory of van der Waals forces. The core of the book is a survey of partly unpublished theoretical work carried out by the authors with the help of H. B. G. Casimir during the war years. The detailed development of the theory is preceded by a general discussion of the problems of stability of lyophobic colloids. Earlier work in the field is critically reviewed.

As in earlier treatments, the theory is based upon a calculation of the curve of potential of mean force between two colloidal particles. The rate of coagulation is related to the curve of potential of mean force by means of the Smoluchowski theory of coagulation and extensions of this theory by later workers. The authors make a rigorous calculation of the electrostatic interaction of flat plates and spherical particles on the basis of the assumptions of the Gouy–Chapman and Debye–Hückel theories of the diffuse electric double layer. They find that the interaction of two colloidal particles due to the interpenetration of their diffuse double layers always gives rise to a repulsive force between them. They convincingly demonstrate the correctness of this conclusion, and analyze the errors that have led other workers to the opposite conclusion. They attribute the attractive force which must be superimposed upon the electrostatic repulsion in order to account for the facts to van der Waals interaction. They make an approximate calculation of the van der Waals interaction by means of the London theory. It is pointed out that at large distances of separation between the particles the London theory must be replaced by the quantum electrodynamic theory of Casimir which leads to a more rapid decrease of the potential with distance than the inverse sixth power.

Applications of the theory are discussed and its predictions are shown to be in good accord with the facts of colloid chemistry. The influence of electrolytes upon the stability of suspensions and emulsions is reliably predicted by the theory and it also leads to a qualitative understanding of the phenomena of thixotropy and tactoid formation.

The authors are to be congratulated on a thorough and sound treatment of the subject within the scope of theoretical methods at present available. However, in the reviewer's opinion it must not be concluded that the last word has been said on the interaction of colloidal particles, particularly in regard to long-range electrostatic interactions. Although the authors correctly calculate that electrostatic interaction between colloidal particles of the same sign is always one of repulsion on the basis of the Gouy–Chapman and Debye–Hückel theories of the double layer, it is not certain that these theories will lead to correct conclusions under all conditions. One of the defects of both theories is the neglect of the size of the ions constituting the diffuse part of the double layer. When the size of the ions is taken into account the possibility exists, under certain conditions, that an ordered distribution of gegenions between two spherical colloidal particles of the same charge would give rise to an attraction between them. It is also not certain that van der Waals interaction will always give rise to an attraction between two colloidal particles, if the van der Waals potential between one of the particles and the solvent displaced by the other is greater in absolute magnitude than the van der Waals potential of the particles themselves.

JOHN G. KIRKWOOD

BOOKS RECEIVED

September 10, 1948–October 10, 1948

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