AN Factor Identified As Biotin L-Sulfoxide

Experimental evidence for a new oxidative cycle in carbohydrate metabolism disclosed

AUSTIN, TEXAS.—AN factor, isolated by a complicated fractionation procedure from some 20,000 liters of *Aspergillus niger* filtrate, has been positively identified as biotin L-sulfoxide, says L. D. Wright, of Sharp and Dohme. This fundamental fact, expected to assist scientists in efforts to improve the health of humans and lower animals, was announced at the Symposium on B-Vitamins sponsored here by the Biochemical Institute of the University of Texas and the Clayton Foundation for Research Dec. 3 and 5.

According to L. D. Wright, the biotin L-sulfoxide arises enzymatically and is a normal intermediate (perhaps the first sulfur-containing compound) formed in the biosynthesis of biotin or biosytin. Experiments by L. D. Wright and E. L. Cresson, Sharp & Dohme Division of Merck & Co., and also John Valient, D. E. Wolf, and Karl Folkers, of the Chemical Division, produced biotin L-sulfoxide but no biotin D-sulfoxide during mold growth under conditions which should have yielded biotin D-sulfoxide. The mechanism by which divalent sulfur gets into a number of important biological compounds, lipoic acid for example, is unknown. If there is any analogy with biotin, it is suggested that the sulfur enters in the partially oxidized form, such as the sulfoxide, which is in turn reduced. Sulfur-containing compounds are significant in a number of biochemical systems.

Vitamin B_{13}. S. M. Hauge, Purdue University, seems convinced that one of the principle handicaps in fundamental animal nutrition research is the lack of a source of proteins free from all vitamins and unidentified growth factors. If such a protein could be made available, it would open up not only many new avenues of research, but make possible more precise determination of vitamin requirements. In the Purdue laboratory, he says, B. J. Brandwein is working on the devitaminization of casein. Although able to reduce the vitamin content to a fraction of that contained in the so-called "vitamin-free casein," Brandwein has concluded the problem needs further study.

Discussing his own problems with vitamin B_{13}, Dr. Hauge explained that it has been isolated in a high degree of purity from distillers' dried solubles, whey, and liver concentrate. Since vitamin B_{13} and orotic acid have absorption spectra which are very similar, this suggests that vitamin B_{13} may be related to orotic acid. Studies involving the growth responses of rats show that orotic acid may be a decomposition product of vitamin B_{13}. Other equally important data indicate vitamin B_{12}, vitamin B_{13}, and orotic acid are all involved in some phase of a common metabolic process, one possibility being the synthesis of nucleic acids. There appears to be some interrelationship between vitamin B_{13} and orotic acid in their ability to stimulate growth in rats and certain microorganisms such as *L. bulgaricus-Hanson*, but further studies are needed to prove the presence or absence of orotic acid in the B_{13} molecule.

Roger Williams, University of Texas and director of the Biochemical Institute, explains how biochemistry has been moving toward better human understanding

Carbohydrate Metabolism. B. L. Horecker, National Institutes of Health, presented experimental evidence for a new oxidative cycle in carbohydrate metabolism. This cycle involves phosphate esters of sugars containing from three to seven carbon atoms, and begins with the oxidation of glucose-6-phosphate to pentose phosphate. He discussed two new enzymes which catalyze the conversion of pentose phosphate to a seven-carbon sugar, sedoheptulose-7-phosphate, followed by the conversion of heptulose phosphate to fructose-6-phosphate and an unidentified tetrose phosphate. The first of these enzymes, transketylase, contains thiamin (vitamin B) pyrophosphate and appears to involve an activated glycolaldehyde which can react to form several products including the heptulose ester.

This new function for thiamin pyrophosphate was disclosed in which a decarboxylation is not necessarily involved; and active glycolaldehyde, rather than the commonly-known product, active acetaldehyde, is formed. It is apparent that thiamin pyrophosphate plays a larger role in carbohydrate metabolism than previously suspected, claims Dr. Horecker.

The other new enzyme, transaldolase, appears to catalyze a transfer of a C_3 group from acetoheptulose phosphate to triose phosphate, with the resultant formation of hexose and tetrose phosphates, according to Dr. Horecker. This cycle may be of importance in several biological processes, including the oxidation of carbohydrates for energy utilization, the synthesis of pentose for nucleic acid production, and also in the photosynthesis of carbohydrates.

Human Understanding. In the decades to come, there will be a new era in human understanding. Biochemistry will play an important role, says Roger Williams, director of the Biochemical Institute. Biochemistry has always been moving toward better human understanding.

Let us take a look at the so-called man. What is he like biochemically? The current opinion more often tacitly accepted rather than emphasized or even expressed is that the normal human being has normal biochemical values, that in all the hundreds of ways he can be measured biochemically, he is always within the normal range. This view, in the opinion of Dr. Williams, is utterly fallacious. It overlooks the laws of probability which operate. This fallacious point of view is of particular interest to Dr. Williams in considerations of human nutrition. Suppose 20 independent nutritional requirements are set at levels such that in each case 80% of the population would be without deficiency. The probability, cites Dr. Williams, is that only 1% of the population would be free from deficiency with respect to all 20 items.

We need the scientific method more than we have ever needed it before, says Dr. Williams. The trouble with human science according to Dr. Williams, has been the formulation of too wide and sweeping generalizations on the basis of too little fundamental data. Most important, he asserted, is the problem of biochemical individuality and the possible contributions which can be made in this area. An understanding of human variability is absolutely indispensable.