is an excellent lesson in hormone detection and isolation. It is full of examples of disappointments, difficulties, cooperative, national and international, give and take attitude and final success and independent confirmation. Dr. Corner also delights in "endocrine arithmetic," as he calls it. As a result he presents some truly astronomical values on the rate of formation and utilization of progesterone.

Laymen, physicists, chemists, biochemists and biologists alike will find this book exceptionally interesting and valuable.

F. C. KOCH

REPORTS

WARTIME ACTIVITIES OF MELLON INSTITUTE, 1942–43

DURING Mellon Institute's fiscal year ended February 28, 1943, the industrial research staff of the organization has been enlarged to 208 fellows and 187 fellowship assistants—a total increase of 40 for the year. These scientists and engineers have been employed on the 97 industrial fellowships in operation. Forty-four chemically trained women are doing capable work in fellowship laboratory investigations, primarily helping key men. The research demands of the war have indeed given rise to a general expansion of the institute's work.

The donors and members of the institute are exerting every effort to assist the armed forces, federal government agencies and American science and technology in this period of stress. A large number of fellowships are giving their full time to pressing problems induced by warfare. All other fellowships irrespective of name or field have direct or indirect contributory parts in the war effort. Many fellows are serving the nation on emergency advisory or research committees or are participating in field studies of wartime value. Constant technical aid is being furnished to the War Production Board, the Rubber Reserve Company, the National Defense Research Committee and the War Metallurgy Committee of the National Academy of Sciences. In consequence silence must be maintained during war regarding the nature, scope and results of most of the institute's industrial research programs. During the fiscal year—March 1, 1942, to March 1, 1943—the institute has expended $1,520,333 in conductng its various pure and applied science projects. These facts are set forth in the thirtieth annual report of the director, Dr. E. R. Weidlein, to the trustees of the institution.

The interest of the institute's department of research in pure chemistry in cinchona alkaloids has naturally led to investigations relating to synthetic anti-malarials. Apart from any socio-economic significance attached to the normal prevalence of malaria —an estimated one third of the population of the world is subjected to this disease—the gravity of the problem of coping with the malady in many military campaigns renders urgent the discovery of more effectual measures of control. Occupation by the Japanese of those regions in the Far East normally producing the bulk of the world's supply of quinine has made it even more imperative that research on synthetic antimalarials be extended. The department is carrying on a program comprehending various series of compounds for appraisal in malaria therapy. These studies involve in part simple heterocyclic nuclei structurally akin to the cinchona alkaloids and also compounds not so related. Certain Guatemalan plants esteemed locally in the treatment of malaria are being investigated chemically and pharmacologically.

In concluding for the time being researches on the cinchona alkaloids a number of ethers of hydroxyethylapocupreine have been prepared for comparison of their chemical and pharmacological properties with the qualities of the corresponding ethers of 6′-(β-thiolethyl) apocupreine. An innovation in building up certain members of the series of polyhydroxyalkyl ethers of apocupreine, and of other phenolic substances, was the use (as alkylating agents) of the monotosyl esters of the poly-isopropylidene acetals of suitable sugar alcohols. One method for the preparation of hydroxyethylapocupreine has been the hydrolysis of the benzyl group from benzyl-oxyethylapocupreine. It is now known that under the same conditions its homolog, α-phenyl-ethoxyethylapocupreine, is completely hydrolyzed to hydroxyethylapocupreine in approximately one sixth the time with consequent diminution of decomposition to a negligible amount of isolation of very pure hydroxyethylapocupreine in practically quantitative yield.

The statistical study of the use of hydroxyethylapocupreine in the clinical treatment of pneumonia has been suspended in order that the stock of this drug on hand may be utilized for antimalarial investigations. During the past year, however, medical collaborators of the department reported that, after three years of comparing pneumococcic pneumonia cases treated with sulfapyridine, sulfathiazole, sulfadiazine and hydroxyethylapocupreine, the percentage mortality with the latter was nearly the same as with the sulfonamides. Moreover, in contrast with the cases in which sulfa drugs were employed, no toxicity was observed under treatment with hydroxyethylapocupreine. The latter has been shown to be efficacious in the treatment of pneumococcic and staphylococcic infections of the eye.

The pharmacopoeial studies during the year have fallen into three classes. First, have been those quests for facts which inevitably come immediately after the end of a revision period, in consequence of complaints that new standards are too drastic or that new tests or assay procedures are inapplicable to certain lines of manufacture. In general, protests of this nature are usually cared for through easy adjustments of testing methods. Secondly, the national emergency has brought two new sets of problems to the attention of the pharmacopoeial committee of revision occasioned by the failure of foreign sources of supply of important drugs and the need for adjustments in the conservation of sucrose and glycerol. Thirdly, the war has stimulated medical research with particular reference to the requirements in the armed forces for the treatment of burns and traumatic wounds. The laboratory in the institute is also assisting in the revision of the "National Formulary" and the "Pharmaceutical Recipe Book."

The investigations pursued in the Western Pennsylvania Hospital, under subsidy of Mellon Institute, have pertained to burns and wound healing, the mode of action of sulfonamides and the prevention of the common cold. In the work on the treatment of burns attention has been focused on certain polysulfide solutions, one objective being to elucidate the biochemical mechanisms that might explain the improved healing, without infection, characterizing the recovery of several hundred clinical burns already reported. Research on the action of sulfonamide compounds has made use of the colon bacillus. More precise knowledge of the rôle of p-aminobenzoic acid is being sought. The project has involved the mathematical analysis of the growth curves of *B. coli* on a suitable synthetic medium. So far the indications are that a chemical factor (possibly of enzymatic nature) normally originating in bacteria is directly or indirectly responsible for the fission of the cells, that the synthesis of this factor is markedly inhibited by sulfonamides, and that, in the presence of p-aminobenzoic acid, it is possible for the production of this factor to occur. The basic findings of the past six years on the effect of large doses of ascorbic acid on the prevention of the common cold are being subjected to a controlled mass clinical test. The results to date support the original thesis that large doses of this vitamin have an antishocking pharmacological effect, which is quite in contrast to its action where given to correct a nutritional deficiency.

Collaborating with the U. S. Public Health Service, Industrial Hygiene Foundation, whose headquarters are at Mellon Institute, and a group of its member companies are carrying forward a study to assist in reducing sick absenteeism in the industries. The foundation has conducted more plant hygiene surveys than in any previous year; these investigations check on the possible existence of health hazards in the workplaces. If hazards are detected, effectual measures are prescribed for their correction. Besides fostering healthful working conditions, the foundation's plant surveys are proving to be increasingly helpful in advancing harmonious labor relations. The introduction of unfamiliar and new chemicals into manufacturing processes, some with little known effects, is demanding ever greater attention to plant hygiene measures. Meanwhile the dermatoses continue to be the most common of all occupational diseases. The foundation is urging the industries to consult with its specialists regarding the procural of basic information of pertinence and the definition of proper protective measures respecting novel chemical products.

The foundation continued to sustain medical and preventive engineering researches in industrial health by grants to The Saranac Laboratory and the University of Pennsylvania. But studies at the latter institution, as well as at the Harvard School of Public Health, have lately been interrupted by the war. The results of researches in roentgenography at the University of Pennsylvania and on magnesium at The Saranac Laboratory have been published. Another investigation at the University of Pennsylvania pertained to industrial exhaust ventilation.

The foundation's seventh annual meeting, held at the institute on November 10 and 11, was attended by more than 500 industrial executives, health specialists and governmental representatives. There were panels on "Fatigue in Wartime Industry—Hours of Work and Rotation of Shifts," on "More Manpower through the Reduction of Absences" and on "Putting Women, Older Men, and Physically Handicapped to Work." It was reported that the use of aluminum dust in the treatment of silicosis appears to be followed by beneficial results in a significant proportion of cases, chiefly in the amelioration of symptoms and in the increased capacity to work. The campaign to promote proper nutrition for war workers, with emphasis on "pack a lunch that packs a punch," has been stressed as never before and promises to accomplish lasting good. There are now 246 company and association members in the foundation, practically all of which are directly engaged in war production and employ between 2 and 3 million workers.

The number of different industrial fellowships in various fields at the institute are as follows: building technology, 4; ceramics, 7; chemical technology, 31; foods, 8; fuels, 2; hygiene, 4; metallurgy, 7; mineral technology, 4; paper, 2; petroleum, 3; plastics, 12; textiles, 10; miscellaneous, 3. It is timely to point out that investigations of 17 fellowships have related wholly or in part, in one way or another, to synthetic rubbers or rubber replacers of diverse kinds and that

70 research staff members have been carrying on this specific work. Ten fellowships began operation during the year: alumina, cellulosic molding, chemical storage, coal products analysis, coke-plant physical technology, molasses technology, nickel, pencil technology, special lubricants and synthetic rubber hygiene. Four other new fellowships will start soon. During 1942–43 ten fellowships concluded their activities: Cotton Research Foundation, dielectrics, ethanol, Gartex, iodine, meat merchandising, oil cleaner, plate glass, powder metallurgy and special plastics. The Gartex project has been assigned temporarily to the mineral products fellowship; the iodine researches have been intermitted owing to the emergency; the fellowship on powder metallurgy and the multiple industrial fellowship on chain and welding technology have been consolidated with an increase in the personnel.

The investigations on cotton, 1937–43, have left a prominent record of achievement in the field and have opened the door to the future of an important American crop. The research findings have been incorporated in more than fifty publications, including patents. During the past year the multiple fellowship on plate glass technology finished an important study to determine the effect of bomb explosions on glass and other glazing materials. Much information of value in the design, use and protection of windows has been developed and made available to the services and the civilian defense organizations.

During the calendar year 1942, 2 books, 14 bulletins, 33 research papers and 43 other articles appeared from the institute. Twenty-nine United States patents and 17 foreign patents on fellowship inventions were issued. In 1942 investigational results were contributed to the literature by the following fellowships: chemical hygiene, chemical storage, cigaret technology, Cotton Research Foundation, ethanol, food varieties, gas purification, industrial hygiene, meat merchandising, meter, protected metals, Raolin, refractories, tar distillation and tar synthetics. The department of research in pure chemistry also has several papers to its credit during the past year. *Nutritional Observatory,* a quarterly periodical edited by the staff of the multiple fellowship on food varieties, has entered its fourth volume; this journal has a complimentary mailing list of 26,450.

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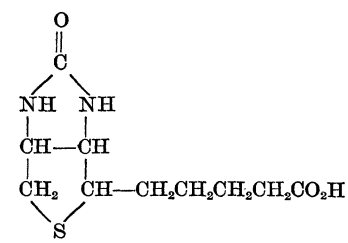
SPECIAL ARTICLES

SYNTHETIC BIOTIN

BIOTIN has been obtained by a total synthesis in this laboratory, and it has been found to be identical with the natural product. This verifies the structure assigned to biotin.

The isolation of biotin as the methyl ester from egg yolk[1] and vitamin H from liver[2] has been described, and the identity of vitamin H and coenzyme R with biotin has been established.[3]

Results of chemical structure investigations in Europe[4] and in this country[5] gave evidence for a carboxylic acid containing a cyclic urea structure and sulfur in a thioether linkage. Further work in this country,[5, 6, 7] showed biotin to consist of a five-membered urea ring fused to a five-membered cyclic thioether having a normal valeric acid side chain. The essential evidence for the five-membered urea ring in biotin was obtained by hydrolysis to a diamine, which gave a dibenzoquinoxaline derivative and which was reconverted quantitatively to biotin by treatment with phosgene.[5] The essential evidence for the ring containing sulfur and having the side chain was furnished by oxidation of the diamine to adipic acid,[5] by the degradation of biotin to desthiobiotin by hydrogenolysis[6] and by degradation to thiophene valeric acid through a modified Hofmann reaction.[7] The structures of the last two compounds were proved by syntheses involving conventional reactions. Barring molecular rearrangements or other obscure reactions during the degradations, these results justified the conclusion drawn by du Vigneaud and collaborators[6, 7] that biotin has Structure I.



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[1] Kögl and Tönnis, *Zeits. physiol. Chem.*, 242: 43, 1936.
[2] du Vigneaud, Hofmann, Melville and György, *Jour. Biol. Chem.*, 140: 643, 1941.
[3] György, Melville, Burk and du Vigneaud, SCIENCE, 91: 243, 1940; du Vigneaud, Melville, György and Rose, *ibid.*, 92: 62, 1940; György, Rose, Hofmann, Melville and du Vigneaud, *ibid.*, 92: 609, 1940.
[4] Kögl and Pons, *Zeits. physiol. Chem.*, 269: 61, 1941; Kögl and deMan, *ibid.*, 269: 81, 1941; Kögl, Erxleben and Verbeek, *ibid.*, 276: 63, 1942.
[5] Refer to review papers by du Vigneaud (SCIENCE, 96: 455, 1942), and Hofmann ("Advances in Enzymology," Vol. 3, p. 289, 1943. Interscience Publishers, Inc., New York).
[6] du Vigneaud, Melville, Folkers, Wolf, Mozingo, Keresztesy and Harris, *Jour. Biol. Chem.*, 146: 475, 1942.
[7] Melville, Moyer, Hofmann and du Vigneaud, *ibid.*, 146: 487, 1942.