TECHNICAL PAPERS

Chemotherapeutic Investigations of Cyanine Dyes

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Although extensive investigations have been carried out on the chemotherapeutic properties of the cyanine, styryl, and related dyes by Prof. Browning and his collaborators at the University of Glasgow (*1*), the chief use of these dyes has remained in the field of photography, where they are indispensable as color sensitizers. Because of their significance in this connection, a very large number of new dyes of these classes has been prepared during the past 20 years in the Research Laboratories of the Eastman Kodak Company, in the department of one of us (L. B.) who, prompted by the earlier work of Browning, was eager to see the pharmacological investigations extended and the newer cyanine dye types in particular given adequate chemotherapeutic testing. An arrangement was reached whereby certain representative compounds were prepared[1] in a suitably soluble form and submitted for extensive testing.

Some of the dyes were supplied to the National Research Council Chemotherapy Center for Tropical Diseases for testing against the organisms of such diseases. The most striking fact to emerge from the investigations which ensued was the pronounced antifilarial and anthelmintic activities of many of the cyanine types.[2] Many of the dyes also showed antimalarial activity, but not such as to equal that of drugs already available. The antimalarial results have been reported (*2*).

Another extremely interesting activity was noted in our laboratories when (1-amyl-2,5-dimethyl-3-pyrrole) (1,6-dimethyl-2-quinoline) dimethinecyanine chloride was tested *in vitro* against the lactic acid-producing bacilli.[3] This cyanine dye completely inhibited the growth of *Lactobacillus casei* at 2×10^{-6} M. *L. arabinosus* was inhibited by a concentration of 2×10^{-6} M, *Streptococcus faecalis* by 4×10^{-6} M, and *Escherichia coli* by 3×10^{-6} M. The inhibition of *E. coli* by 3×10^{-6} M concentration of cyanine dye was partially reversed by 100 mg./100 cc. of vitamins B_1 and B_2, nicotinic acid, and pantothenic acid. The reversal by crude yeast and liver extracts was even greater than indicated by their vitamin content. Vitamin B_6 and p-aminobenzoic acid were without effect on the inhibitory action of the dye.

In order to determine the nature of the bacterial inhibition, the effect of the cyanines on various enzyme systems was studied. There was no appreciable effect on the d-amino acid oxidase, cytochrome oxidase-cytochrome C, succinic dehydrogenase, glucose dehydrogenase, lactic dehydrogenase, and liver glyoxalase enzyme systems.

Representative dyes were also tested *in vivo* for activity against *Str. hemolyticus, Str. viridans, Staph. aureus, Diplococcus pneumoniae I, Trypanosoma equiperdum, Treponema pallidum*, St. Louis encephalitis, influenza, typhus, and other viruses, and a group of intestinal parasites; also *in vitro* against *Endamoeba histolytica*.[3] While an occasional compound showed some demonstrable activity against these organisms, the order of activity was not sufficiently great to be therapeutically significant.

A summary of the cyanine, styryl, and related dyes studied will be supplied on request.

References

1. BROWNING, C. H. *Edinb. med. J.*, 1937, N.S. 44, 497.
2. WISELOGLE, F. Y. (Ed.) *A survey of antimalarial drugs*. Ann Arbor, Mich.: Edwards Bros., 1947.

[1] The dye syntheses were carried out by E. Van Lare, R. H. Sprague, F. L. White, G. H. Keyes, and Miss G. VanZandt, to whom the authors acknowledge their indebtedness.

[2] These investigations will be reported at the May meeting of the Federated Biological Societies in Chicago by R. N. Bieter and A. D. Welch and their associates.

[3] The authors acknowledge the work of F. D. Stimpert, O. M. Gruhzit, O. D. Bird, and G. Rodney, of the Research Laboratories, Parke, Davis & Company, under whose supervision many of these tests were performed.

Hereditary Obesity and Efficient Food Utilization in Mice[1]

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Energy costs of transferring food materials into body tissues constitute a recurrent problem of genetics, nutrition, and physiology. The specific problem of inherited fatness in relation to efficiency of food utilization came to our immediate attention in a study of rate and economy of gain and carcass composition of swine (*3*). It was found that the hereditary influences which reduced the food required per pound of gain also increased the proportion of the gain that was fatty tissue. These results were at variance with the supposition that food requirements would be larger for deposition of fatty tissue, because of its higher energy content, compared with nonfatty tissue. This supposition apparently holds for the

[1] Journal paper No. J-1422 of the Iowa Agricultural Experiment Station, Ames, Iowa; Project No. 252.

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