13335

Bis-para-aminobenzoyl-l-cystine.

EDWIN J. FELLOWS AND RAYMOND W. CUNNINGHAM.

From the Department of Pharmacology, Temple University School of Medicine, Philadelphia, Pa.

Abel and Geiling[1] concluded unstable sulfur was an essential part of the insulin molecule. Du Vigneaud[2] stated insulin probably was a derivative of cystine and later it was reported[3] that while the disulfide linkage *per se* was not responsible it was nevertheless necessary for the insulin action. The importance of sulfur in the insulin molecule has prompted many investigators to test a number of relatively simple miscellaneous organic sulfur compounds, sulfur-containing guanidine derivatives, certain cystinyl peptides and cystine itself for hypoglycemic activity.[4] None of the compounds investigated exhibits or approximates the physiological behavior of insulin.[4]

The present experiments were carried out to test a cystine derivative, bis-para-aminobenzoyl-l-cystine,* for possible hypoglycemic properties.

These studies† were made on rats fasted 15-18 hours. After amputation of a thin segment of the tail, blood was milked into an oxalated glass capsule and blood sugar determined by the Shaffer-Hartman Somogyi method[5] on filtrates prepared by the zinc hydroxide precipitation procedure of Somogyi.[6] Blood was withdrawn before subcutaneous administration of the sodium salt of the cystine compound and ½, 1, 2, 3, and 5 hours thereafter. In Fig. 1 are shown the results of a typical experiment and it is to be noted that blood sugar values for the animals receiving the cystine compound closely approximate those obtained for the control group, whereas the rats receiving 1.5 units of insulin per kg show a well defined hypoglycemia. Almost identical results were obtained in

1 Abel, J. J., and Geiling, E. M. K., *J. Pharm. and Exp. Therap.*, 1925, **25**, 423.

2 du Vigneaud, V., *J. Biol. Chem.*, 1927, **75**, 393.

3 du Vigneaud, V., Fitch, A., Pekarek, E., and Lockwood, W. W., *J. Biol. Chem.*, 1931, **94**, 233.

4 Braun, C. E., Mason, M. B., and Brown, C. L., *J. Chem. Educ.*, 1938, **15**, 261.

* This compound was made available to us through the courtesy of Dr. R. L. Shriner of the Department of Organic Chemistry, University of Illinois.

† This investigation was supported in part by the D. J. McCarthy Foundation and by the Smith, Kline and French Laboratories Fellowship Fund.

5 Shaffer, P. A., and Somogyi, M., *J. Biol. Chem.*, 1933, **100**, 695.

6 Somogyi, M., *J. Biol. Chem.*, 1930, **86**, 655.

20 other rats using doses of from 50-200 mg/kg of the cystine compound. In Fig. 2 are shown the results obtained in 9 Wistar rats after injection of 3.5 g/kg of glucose (10% solution) intraperitoneally and it is to be noted that the glucose tolerance curve of the rats receiving the cystine compound is similar in all respects to that of the control animals.

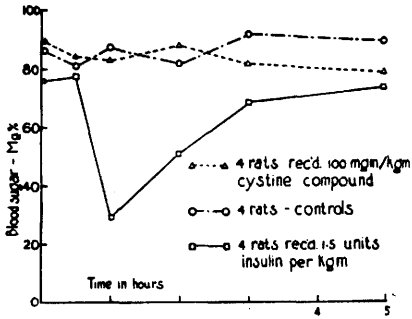

FIG. 1.

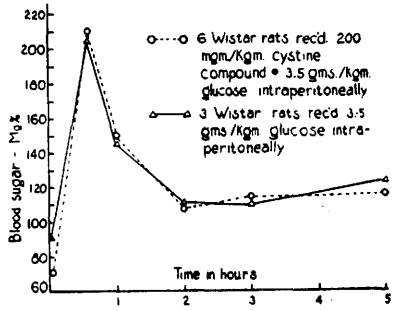

FIG. 2.

FIG. 1. Comparative effectiveness of bis-p-aminobenzoyl-l-cystine and insulin on blood sugar of rats.

FIG. 2. Glucose tolerance studies on Wistar rats.

Summary. Bis-p-aminobenzoyl-l-cystine was found to be devoid of hypoglycemic properties in normal rats. This compound also did not affect the glucose tolerance curves of Wistar rats.

13336 P

Increase in Blood Lipids of Fasted Mice.

P. L. MACLACHLAN. (Introduced by E. J. Van Liere.)

From the Department of Biochemistry, School of Medicine, West Virginia University, Morgantown.

The observations of Entenman, Changus, Gibbs and Chaikoff[1] on adult dogs fail to confirm the claim that fasting produces a lipemia. Since fasting mice promptly show a marked degree of fatty infiltration into the liver[2] it was considered of interest to determine whether a lipemia accompanies fasting in this species.

1 Entenman, C., Changus, G. W., Gibbs, G. E., and Chaikoff, I. L., *J. Biol. Chem.*, 1940, **134**, 59.

2 Hodge, H. C., MacLachlan, P. L., Bloor, W. R., Stoneburg, C. A., Oleson, M. C., and Whitehead, R., *J. Biol. Chem.*, 1941, **139**, 897.