possible that the antifibrinolysin activity of plasma is derived from the platelets.

References

1. GUEST, M. M., WARE, A. G., and SEEGERS, W. H. *Am. J. Physiol.*, **150**, 661 (1947).
2. RATNOFF, O. D. *Bull. Johns Hopkins Hosp.*, **88**, 304 (1951).
3. SEEGERS, W. H., and LOOMIS, E. C. *Science*, **104**, 461 (1946).
4. PERMIN, P. M. Ph.D. thesis. Copenhagen: Store Nordiske Videnskabsboghandel (1949).
5. SHULMAN, N. R. *J. Exptl. Med.*, **95**, 571 (1952).
6. LEWIS, J. H., and FERGUSON, J. H. *J. Clin. Invest.*, **29**, 1059 (1950).
7. GUEST, M. M., *et al. Ibid.*, **27**, 785 (1948).
8. LOOMIS, E. C., GEORGE, C., JR., and RYDER, A. *Arch. Biochem.*, **12**, 1 (1947).
9. SEEGERS, W. H., MCCLAUGHRY, R. I., and FAHEY, J. L. *Blood*, **5**, 421 (1950).
10. WARE, A. G., FAHEY, J. L., and SEEGERS, W. H. *Am. J. Physiol.*, **154**, 140 (1948).

Manuscript received July 25, 1952.

Protection Against Alloxan Diabetes by Mannose and Fructose

Gangagobinda Bhattacharya[1]

Department of Physiology,
University College of Science and Technology,
Calcutta, India

In a previous communication (*1*) from this laboratory, it was reported that glucose, given prior to the injection of diabetogenic doses of alloxan, prevented diabetes in rats.[2] The present communication reports the results of similar experiments done with the other physiologically important hexoses—namely, mannose, fructose, and galactose.

Rats fasted overnight were given diabetogenic doses (40 mg/kg) of alloxan intravenously at different intervals of time after intravenous administration of varying doses of the above sugars. Blood sugar values of the rats were then determined daily for 7 days. The urine was also tested daily for the presence of sugar during the experimental period. A blood sugar value over 180 mg% for 2 consecutive days and the presence of sugar in the urine for a similar period of time were considered to indicate a diabetic condition in the animals. The results are given in Table 1.

Thus mannose and fructose, given prior to the injection of diabetogenic doses of alloxan, prevented diabetes in rats. Galactose had no such preventive action. The present results, considered together with those given in the previous communication (*1*), show that the preventive abilities of glucose and mannose are practically of the same order. Mannose is possibly slightly less effective than glucose. Fructose, however, is obviously much less effective.

Inhibition of essential sulfhydryl enzymes of the β-cells has been suggested as the cause of the diabetogenic action of alloxan (*2*). Reversal of the action of alloxan by sulfhydryl compounds (*3*) has added strength to this hypothesis. Mammalian hexokinase is a sulfhydryl enzyme, being inactivated by alloxan and reactivated by cysteine (*4*). There is considerable evidence (*5, 6*) that this enzyme is fundamentally related to the condition of diabetes in animals—the activity of the enzyme being inhibited in diabetes. Hexokinase is a nonspecific enzyme acting on glucose, mannose, or fructose. The affinity of fructose for the enzyme is, however, low compared to that of glucose or mannose for it (*7*). In addition to the above nonspecific hexokinase, mammalian tissues may contain a specific fructokinase, which does not act on glucose or mannose (*7*). Galactose is attacked by another specific enzyme, galactokinase (*8*). The ordinary hexokinase is presumably present in the β-cells; for, like all other cells, the β-cells must also ordinarily obtain energy from the oxidation of glucose, the first step in the process being catalyzed by the above enzyme.

The results obtained show that the relative abilities of the hexoses to prevent the diabetogenic action of alloxan are directly comparable to their affinities for hexokinase.[3] They also show a close similarity with the results obtained on the protection of yeast hexokinase against inactivation by proteolytic enzymes by the above sugars (*7*). One therefore wonders whether the protection against the diabetogenic action of alloxan by glucose, mannose, and fructose is due to a protection of the hexokinase in the β-cells against alloxan poisoning and whether inhibition of β-cell hexokinase is the primary cause of the diabetogenic action of alloxan. It is also interesting to speculate whether the results reported here offer any clue to the understanding of the selectivity of alloxan for the

TABLE 1

EFFECT OF PREVIOUS ADMINISTRATION OF MANNOSE, FRUCTOSE, AND GALACTOSE ON THE PREVENTION OF DIABETES CAUSED BY INTRAVENOUS ALLOXAN (40 MG/KG) IN RATS

Sugar injected	Dose of sugar injected (g/kg)	Interval between injection of sugar and alloxan (min)	No. rats used	No. diabetic rats
Mannose	1	5	6	0
	1	10	6	5
	2	5	5	0
	2	10	6	0
	2	15	6	6
Fructose	2	5	5	5
	5	5	6	0
Galactose	2	5	5	5
	5	5	5	5

[1] I am greatly indebted to P. B. Sen for advice and criticism and for the grant of laboratory facilities. My thanks are due to the Lady Tata Memorial Trust, Bombay, for the grant of a research scholarship.

[2] Similar results (unpublished) have been obtained with rabbits.

[3] It may also be noted that the relative abilities of the hexoses to protect against alloxan diabetes are directly comparable to their effectiveness to alleviate hypoglycemia in animals.

β-cells. The β-cells synthesize and store insulin. It is therefore likely that the concentration of glucose in these cells will be lower than elsewhere in the body. A specifically low concentration of glucose in the β-cells may, in view of the above results, account for the selectivity of alloxan for these cells.

References

1. SEN, P. B., and BHATTACHARYA, G. *Indian J. Physiol. Allied Sci.*, **6**, 112 (1952).
2. LAZAROW, A. *Proc. Soc. Exptl. Biol. Med.*, **61**, 441 (1946).
3. SEN, P. B., and BHATTACHARYA, G. *Science*, **115**, 41 (1952).
4. GRIFFITHS, M. *Arch. Biochem.*, **20**, 451 (1949).
5. PRICE, W. H., CORI, C. F., and COLOWICK, S. P. *J. Biol. Chem.*, **160**, 633 (1945).
6. COLOWICK, S. P., CORI, G. T., and SLEIN, M. W. *Ibid.*, **168**, 583 (1947).
7. COLOWICK, S. P. In Sumner, J. B., and Myrbäck, K. (Eds.), *The Enzymes, Chemistry and Mechanism of Action*. New York: Academic Press, **2**, 114 (1951).
8. TRUCCO, R. E., *et al. Arch Biochem.*, **18**, 137 (1948).

Manuscript received July 28, 1952.

The Attempted Dehydrogenation of 3,4-Disubstituted Thiolanes[1]

Alvin I. Kosak[2] and Robert L. Holbrook[3]

The Department of Chemistry,
The University of Cincinnati, Cincinnati, Ohio

We have subjected 3,4-thiolanediol and its diester and diethyl ether derivatives to dehydrogenation procedures in an attempt to prepare the corresponding thiophene analogs. Thiolane itself has been dehydrogenated to thiophene in 32% yield, using platinized charcoal at 400°, and in 18% yield with nickel sulfide on alumina at 350° (*1*); in each case the remainder of the material was converted to hydrogen, hydrogen sulfide, olefins, and alkanes. Passage of thiolane vapors through a "red-hot" glass tube is reported to give traces of thiophene (*2*). The syntheses of thiophene and its homologs from hydrocarbons and sulfur probably involve thiolane intermediates which subsequently undergo dehydrogenation (*3*), and sulfur and thiolane under pressure do give small yields of thiophene (*4*).

DL-1,4-Dichloro-2,3-dihydroxybutane (*5*) was cyclized to 3,4-dihydroxythiolane (*6*) with sodium sulfide. The latter was converted to the diacetate and dibenzoate esters. The diacetate was also prepared by cyclizing DL-1,4-dichloro-2,3-diacetoxybutane (*5*). 3,4-Diethoxythiolane was prepared by a slight modification of the method of Patterson and Karabinos (*7*).

The four substituted thiolanes were heated with sulfur under dehydrogenating conditions with and without solvents. When short reaction times were employed, most of the starting material was recovered unchanged. Under more vigorous conditions decomposition occurred, with the concomitant evolution of hydrogen sulfide. Similar results were obtained using platinum on charcoal as the dehydrogenating agent. Neither of the diesters was attacked by chloranil.

In a series of vapor phase runs, solutions of sulfur and the dibenzoate or the ether were passed under nitrogen pressure through a tube packed with "non-catalytic" fused alumina balls[4] and maintained at temperatures varying from 450° to 525°. Decomposition occurred in every case. Attempts to split out two molecules of acid from the diester by pyrolysis in the absence of sulfur (*8*) were also unsuccessful.

We believe that dehydrogenation took place during these various experiments, and that the substituted thiophenes then decomposed. The instability of 3,4-dihydroxythiophene has been mentioned by Fager (*9*) and by Turnbull (*10*). The ethoxy, benzoxy, and acetoxy substituents would tend to increase the susceptibility of the thiophene nucleus to degradative attack because of their action in increasing the electron density in the ring.

References

1. JURJEW, Y. K., and BORISSOW, A. E. *Ber. deut. chem. Ges.*, **69**, 1395 (1936).
2. GRISCHKEWITSCH-TROCHIMOWSKI, E. *J. Russ. Phys. Chem. Soc.*, **48**, 901 (1916).
3. FRIEDMANN, W. *Refiner Natural Gasoline Mfr.*, **20**, 395 (1941); *J. Inst. Petroleum*, **37**, 325 (1951); *cf.* RASMUSSEN, H. E., HANSFORD, R. C., and SACHANEN, A. N. *Ind. Eng. Chem.*, **38**, 376 (1946).
4. FRIEDMANN, W. *J. Inst. Petroleum*, **37**, 239 (1951).
5. OWEN, L. N. *J. Chem. Soc.*, 241 (1949).
6. KILMER, G. W., *et al. J. Biol. Chem.*, **145**, 495 (1942).
7. PATTERSON, W. I., and KARABINOS, J. V. U. S. Pat. 2,400,436 (1946).
8. MORELL, S. A., GELLER, H. H., and LATHROP, E. C. *Ind. Eng. Chem.*, **37**, 877 (1945); SHLECHTER, N., OTHMER, D. F., and BRAND, R. *Ibid.*, **37**, 905 (1945).
9. FAGER, E. W. *J. Am. Chem. Soc.*, **67**, 2217 (1945).
10. TURNBULL, S. G. U. S. Pat. 2,453,103 (1948).

Manuscript received July 29, 1952.

[4] We wish to thank the Aluminum Company of America for the gift of this material.

The Response of Two Species of Pine to Various Levels of Nutrient Zinc[1]

Charles C. Wilson

Department of Botany,
University of Georgia, Athens

The effect of a lack of nutrient zinc on the growth of a number of forest tree species has been reported by several workers (*1–4*). In general, the symptoms of all the species studied have been quite similar, being subsumed under the heading of little-leaf or rosette disease. These names are quite descriptive, since the affected trees usually exhibit diminished bud growth, reduction of leaf size, and chlorosis of varying degrees of severity. The symptoms are also concordant with the known effect of a lack of zinc in reducing the auxin level of the deficient plants. Although naturally occurring zinc deficiencies have been

[1] This work has been assisted by a grant from the Tennessee Corp.

[1] Abstracted from the M. S. thesis of R. L. H., University of Cincinnati (Dec. 1951).

[2] Present address: Institute of Industrial Medicine, New York University–Bellevue Medical Center, 477 First Ave., New York 16.

[3] Present address: The Mathieson Chemical Corp., Niagara Falls, N. Y.