2. Weston, R. E., Grossman, J., Jr., Edelman, J. S., Escher, D. J. W., Leiter, L., Hellman, L., *Fed. Proc.*, 1949, v8, 164 (abst.).

3. Pitts, R. F., *Am. J. Md.*, 1958, v24, 745.

4. Schreiner, G. E., PROC. SOC. EXP. BIOL. AND MED., 1950, v74, 117.

5. Nelson, N. J., *J. Biol. Chem.*, 1944, v153, 375.

6. Handley, C. A., Telford, J., LaForge, M., PROC. SOC. EXP. BIOL. AND MED., 1949, v71, 187.

7. Handley, C. A., Sigafoos, R. B., LaForge, M., *Am. J. Physiol.*, 1949, v159, 175.

8. Barrett, M. J., *J. Pharm. and Exp. Therap.*, 1950, v100, 502.

9. VanSlyke, D. D., Hiller, A., *J. Biol. Chem.*, 1947, v167, 107.

10. Cohen, J. J., Berglund, F., Lotspeich, W. D., *Am. J. Physiol.*, 1956, v184, 91.

11. Pitts, R. F., Alexander, R. S., *ibid.*, 1944, v142, 648.

12. Miller, J. H., PROC. SOC. EXP. BIOL. AND MED., 1953, v84, 322.

13. Farber, S. J., Berger, E. Y., Earle, D. P., *J. Clin. Invest.*, 1951, v30, 125.

14. Wesson, L. G., Jr., Laular, D. P., *ibid.*, 1961, v40, 1967.

Received February 12, 1962. P.S.E.B.M., 1962, v110.

Hypoglycemic Effect of Zea Styles.* (27459)

E. MENCZEL AND F. G. SULMAN

Department of Applied Pharmacology, Hebrew University-Hadassah Medical School and School of Pharmacy, Jerusalem, Israel

Zea styles, the hairs of the corn ear, were listed in the older pharmacopeias and are still retained in the latest edition of the Swiss Pharmacopeia(1). This drug as decoction or tincture has been assumed to possess diuretic, anticystitic and cardiotonic properties.

Plant products yielding antidiabetic principles were extensively reviewed by Lewis(2), Peters(3) and Goldner(4) without mentioning Zea styles. Decoctions of this drug were, however, employed in southern Europe as a folk remedy in diabetes(5,6). We, therefore, studied the hypoglycemic effect of Zea styles. Mirsky *et al.*(7) demonstrated the hypoglycemic effect of indole acetic acid—also known as the plant growth hormone heteroauxin, isolated from immature Zea kernels (8). Hence, the presence of indole acetic acid in Zea kernels had to be considered when studying the supposed antidiabetic effect of Zea styles.

Materials and methods. Repeated tests indicated that a potent extract could be prepared by macerating Zea styles in distilled water for 24-48 hours. The resulting fermented bulky preparation was boiled for 30 minutes and subjected to pressure expression at 450 kg/cm^2. The liquid extract was adjusted with distilled water to represent 2 g of Zea styles in 10 ml. Fasting and non-fasting male rabbits weighing about 2 kg received oral and subcutaneous doses of the extract equivalent to 2 g Zea styles/kg body weight. Blood samples were drawn from the heart by puncture or from the external auricular veins at hourly intervals prior to and following administration. The blood sugar was analyzed according to the Rappaport-Eichhorn modification(9) of the Hagedorn-Jensen method.

Results. Oral administration of the Zea style extracts to non-fasting animals did not induce hypoglycemia, while the response in fasting animals was not consistent. However, subcutaneous administration to fasting animals invariably produced a significant hypoglycemia (Table I). Substantial reduction in the dose administered (2 g/kg b.w.) decreased or completely eliminated the hypoglycemic effects in proportion to dosage.

The statistical pattern of blood sugar reduction at the third hour following administration of Zea styles extracts compares well with that of crystalline insulin (1 u/kg b.w.) 1 hour after subcutaneous administration to fasting animals. Fig. 1 and 2 represent respectively the histograms of the hypoglycemic effects of insulin and Zea styles, exhibit-

* Generously aided by a grant from Pharmaceutical Section of Manufacturers' Assn. of Israel.

TABLE I. Hypoglycemic Effect of Zea Styles Extracts in Rabbits after S.C. Administration. Extracts of 2 g Zea styles per kg body wt.

Blood sugar levels at different intervals	1 hr	2 hr	3 hr	4 hr
Deviation range from initial blood sugar in mg % (upper limit/lower limit)	+6/–12	+12/–24	+5/–35	–9/–41
Mean reduction—mg %	–3.3	–6.8	–18.9	–25
Stand. dev.	16.4	11.57	12.44	14.49
t student	.613	1.42	3.4	3.91
P	<.50	<.1	>.01	>.01
No. of rabbits	20	19	19	10

ing typical distributions. Frequency and proportional distribution of the hypoglycemic effects of both insulin and Zea styles are shown in Table II. Combining both distributions, the proportional distribution is nearly that of the theoretical gaussian normal curve (10). The differences are negligible; the resulting normal distribution is illustrated in Fig. 3.

Repeated daily subcutaneous administration of Zea styles extracts to non-fasting rabbits exerts progressive hypoglycemia (Fig. 4) with fatal results.

Discussion. Whereas oral administration of Zea styles extracts proved innocuous, serious toxic effects were encountered upon subcutaneous administration. This toxicity is not inherent in the blood sugar reducing principle, since inactive extracts also produced toxic effects. As a rule, the toxic effects were accompanied by hypoglycemia and quite often the rabbits succumbed within 5-12 hours. Intravenous injection of the extract sometimes resulted in intense hypoglycemia followed by death within 2 hours after injection. Non-fasting rabbits receiving orally daily doses of this extract lost weight, whereas repeated daily subcutaneous administration resulted in death of the animals within 2-3 days. Post mortem examination did not reveal significant pathologic lesions.

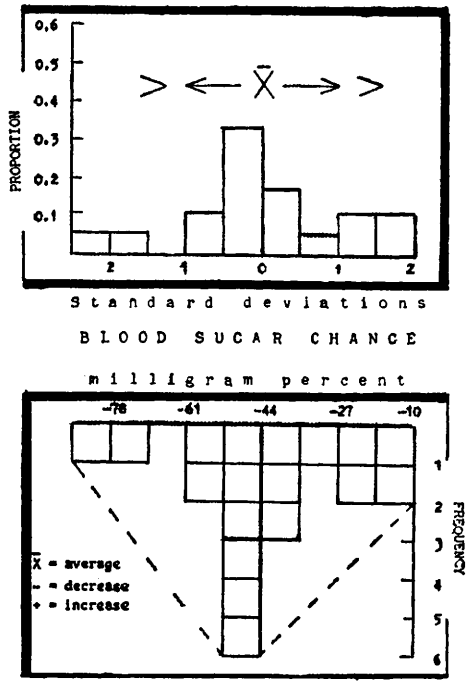
Bearing in mind earlier reports(7) on hypoglycemic effects of heteroauxins, we studied the effect of indole acetic acid on the blood sugar of rabbits. Dosages of 100 mg indole acetic acid per kg body weight of fasting rabbits failed to produce hypoglycemia and no relationship with this plant growth hormone could be established. A further report(11) indicates that indole acetic acid decreases the blood sugar of rats only.

The constituents of Zea styles have not been completely clarified(6,12). They include alkaloids, saponins, glucosides, volatile and fixed oils, reducing sugars, albuminoid substances and an acid named maizenic acid. Their chemical constitution has not yet been determined. The reported results warrant further study as to the nature of the hypoglycemic effect of Zea styles, the chemical structure of the active substance and its separation from the toxic compounds.

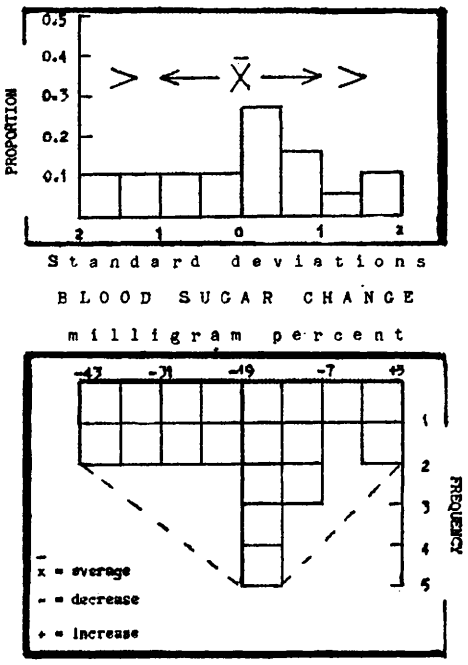
TABLE II. Distribution of Insulin and Zea Styles Hypoglycemias.

Range of hypoglycemic effects	Insulin		Zea styles		Proportion	
	Frequency	Proportion	Frequency	Proportion	Combined	Theoretical
$x-3\sigma \rightarrow x < x-2\sigma$	1	.055	—	—	.027	.0214
$x-2\sigma \rightarrow x < x-\sigma$	1	.055	4	.210	.138	.1354
$x-\sigma \rightarrow x < x-.5\sigma$	2	.111	2	.105	.110	.1500
$x-.5\sigma \rightarrow x < x$	6	.333	2	.105	.216	.1914
$x \longrightarrow x < x+.5\sigma$	3	.166	5	.263	.216	.1914
$x+.5\sigma \rightarrow x < x+\sigma$	1	.055	3	.158	.110	.1500
$x+\sigma \rightarrow x < x+2\sigma$	4	.222	3	.158	.193	.1354
No. of animals	18		19		—	—

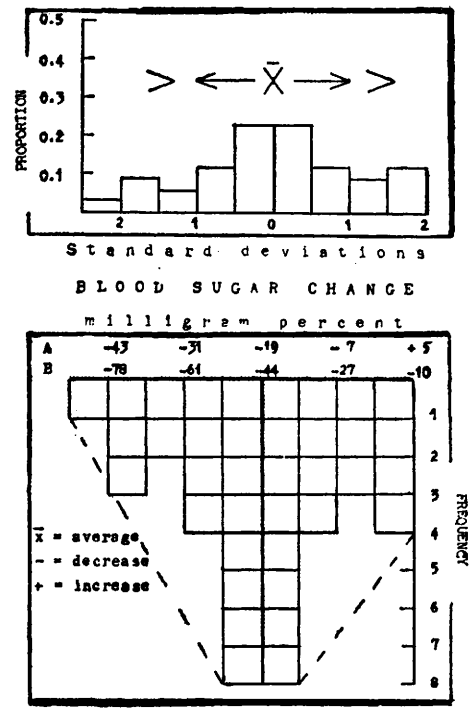
x = Range of hypoglycemic effect
x = Avg reduction (1 hr for insulin, 3 hr for Zea styles extract)
σ = Stand. dev. (sigma)


PROPORTION
Standard deviations
BLOOD SUGAR CHANGE
milligram percent
-78 -61 -44 -27 -10
FREQUENCY
x̄ = average
- = decrease
+ = increase

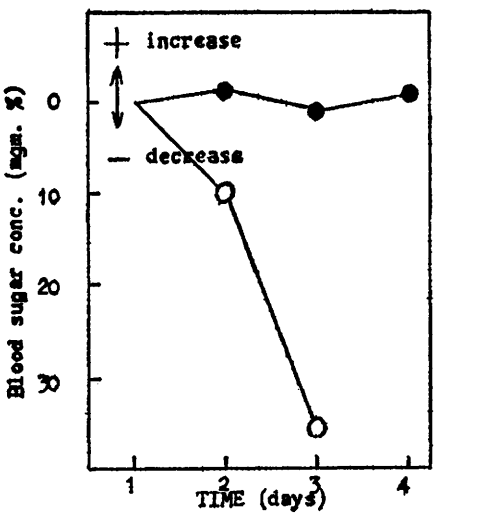
1


PROPORTION
Standard deviations
BLOOD SUGAR CHANGE
milligram percent
-43 -31 -19 -7 +5
FREQUENCY
x̄ = average
- = decrease
+ = increase

2


PROPORTION
Standard deviations
BLOOD SUGAR CHANGE
milligram percent
A -43 -31 -19 -7 +5
B -78 -61 -44 -27 -10
FREQUENCY
x̄ = average
- = decrease
+ = increase

3


+ increase
— decrease
Blood sugar conc. (mgs. %)
0
10
20
30
TIME (days)
1
2
3
4
Zea styles (decoction)
Distilled water

4

FIG. 1. Histogram of hypoglycemic effect of insulin (1 u/kg B.W. 1 hr after s.c. administration).

FIG. 2. Histogram of hypoglycemic effect of Zea styles (2 g/kg B.W. 3 hr after s.c. administration).

FIG. 3. Combined histogram of hypoglycemic effect of: *A*—Zea styles (2 g/kg B.W. 3 hr after s.c. administration) and *B*—Insulin (1 u/kg B.W. 1 hr after s.c. administration).

FIG. 4. Hypoglycemic effect of repeated s.c. administration of Zea styles decoction (2 g/kg B.W. in terms of dried drug).

Summary. Macerated decoction extracts of Zea styles exert consistent hypoglycemic effects in fasting rabbits provided they are administered parenterally. Repeated daily subcutaneous administration of the extract to non-fasting rabbits produces even fatal hypoglycemia. The statistical pattern of the hypoglycemic effect of Zea styles compares well with that of crystalline insulin and the distribution is of the gaussian normal curve. The concomitant toxic effects of the hypoglycemic extract, especially when administered intravenously, cannot be accounted for by its blood sugar reducing principle since we could separate the toxic effect from the blood sugar reducing effect.

Our thanks are due to Dr. P. Farkas for suggesting this study and to Dr. E. Peretz for the statistical evaluation.

1. Pharmacopoea Helvetica, Bern 1953 (German ed.), p. 993.

2. Lewis, J. J., *Physiol. Rev.,* 1949, v29, 75.

3. Peters, G., *Dtsch. Med. Wchschr.,* 1957, v82, 320.

4. Goldner, M. G., *A.M.A. Arch. Int. Med.,* 1958, v102, 820.

5. Farkas, P., personal communication.

6. Gnadt, A. F., *Pharmazie,* 1946, v1, 103.

7. Mirsky, I. A., Diengott, D., Perisutti, G., *Endocrinology,* 1956, v59, 715.

8. Haagen-Smit, A. J., Dandluker, W. B., Wittwer, S. H., Murneek, A. E., *Am. J. Botany,* 1946, v33, 118.

9. Rappaport, F., Eichhorn, E., *Am. J. Clin. Pathol.,* 1950, v20, 834.

10. Dixon, W. J., Massey, F. J., *Introduction to statistical analysis,* McGraw-Hill Book Co., Inc., 2nd ed., 1957, p. 381.

11. Diengott, D., personal communication.

12. Rademaker, C. J., Fisher, J. L., *Am. J. Pharmacy,* 1886, v58, 369.

Received February 28, 1962. P.S.E.B.M., 1962, v110.

Uptake of I^{131} by Rat Organs and Body Fluids Following Injection of Different I^{131} Preparations.* (27460)

V. M. DOCTOR

Department of Physiology and Biochemistry, University of Texas Dental Branch, and Department of Medicine, University of Texas, M. D. Anderson Hospital and Tumor Institute, Houston

Filter paper chromatography of aged solutions of NaI^{131}(1) or of some samples of commercially available NaI^{131}(2,3) show the presence of non-iodide I^{131} component which moves slightly faster than the NaI^{131} band. This compound has been described as "extraneous" I^{131}(1,4,5) or as component "S"(2) or as "U"(3). It is now well established that this compound has chemical and biological properties which are different from that of NaI^{131}(1,2,3,4) and that its presence in radioautograms of radioiodide solutions cannot be caused by chromatographic artifacts(6).

The present report concerns the rate of uptake of NaI^{131} or of "extraneous" I^{131} by rat organs and body fluids following intraperitoneal injection of one microcurie of each compound.

Methods. Isolation of "extraneous" I^{131} and NaI^{131}. Several microcuries of cysteine-free radioiodide solutions (furnished by E.

* This work was supported by a U.S. Public Health Service Senior Research Fellowship and by a grant from Am. Cancer Soc. The author is indebted to Sandra Malicote for valuable technical assistance.