

acid-insoluble ash. The average for the above is 3.02 per cent; with the plants varying in age from 2 to 12 years. Various deductions may be made. However, this is considered as preliminary work, and the results of future years' investigation are necessary before conclusions may be offered.

APPENDIX.

Attention has been called to the difference in alkaloidal content of several lots taken from the tract containing 6-year old plants. (See Table No. 2—compare Nos. 3 and 4 with Nos. 10 and 22.) On the assumption that, apparent loss of alkaloids in the farm plant cured drug was due to the curing process used, several preliminary, but crude tests were carried out in an attempt to ascertain if exposing the freshly washed drug to a high degree of heat, would affect the alkaloidal content.

Ten-gram samples of the powdered Hydrastis were thoroughly wetted with water. These samples were dried in a hot air oven using different temperatures. The length of time to dry the samples approximated about forty-eight hours.

The samples were assayed according to the U. S. P. X method. The following table represents the results obtained from the experiment:

No.	Part.	Temperature.	% Alkaloid.	% Alkaloid before wetting.	% Loss.
4	Root	120-127° C.	1.495	2.67	43.8
3	Root	120-127° C.	1.70	2.83	39.4
12	Fibre	100° C. 6 hrs. 35° 24 hrs.	2.07	2.35	29.0
4	Root	100° C. 6 hrs. 35° 24 hrs.	2.088	2.67	21.8
5	Root	35° C.	2.35	2.62	10.5
2	Root	35° C.	2.234	2.77	19.3

The results would seem to indicate that the maximum temperature for drying the drug is considerably below 35° C. Material has been obtained for carrying on the investigation on fresh plants.

Hydrastine is hydrolyzed into hydrastinine and opianic acid when high heat is applied, or in the presence of oxidizing agents and water as follows:



Complete oxidation of the Hydrastine would yield 54.036 per cent of its weight as hydrastinine.

UNIVERSITY OF WASHINGTON,
COLLEGE OF PHARMACY,
SEATTLE.

THE EFFECT OF CERTAIN HYPOGLYCEMIC DRUGS UPON THE GROWTH OF THE SEEDLINGS OF LUPINUS ALBUS.

BY JOHN C. KRANTZ, JR.

Introduction.—In 1923 Ellis and Eyster (1) studied the effect of insulin and glucokinase upon the growth of maize seedlings. They observed that either of these drugs in concentrations less than 0.005 per cent promoted the growth of these seedlings whereas in concentrations greater than this value a definite retardation of

growth was noticed. In 1924, these same investigators (2) observed that the purification of crude insulin and glucokinase by dialysis left a residue of nondialyzable substances which were the growth-promoting fractions of the crude substances.

It occurred to the author that it would be interesting to test the relative toxicity of commercial insulin of various unitages and compare this with the toxicity of other hypoglycemic drugs by the phytopharmacologic method developed by Macht (3 and 4) and his associates.

EXPERIMENTAL.

Commercial Insulin.—A sample of commercial insulin U-10 was mixed with the nutrient solution (Shive Solution (5)) in which the measured seedlings were planted—the increment of growth was determined after twenty-four hours and compared with the normal growth of the seedlings in Shive Solution. The growth in the nutrient solution is considered one hundred per cent.

Table I shows the results obtained with commercial insulin:

TABLE I.	
Conc. insulin.	Percentage growth.
8 U per 100 cc.	79.8
12 U per 100 cc.	74.9
16 U per 100 cc.	64.6
24 U per 100 cc.	64.1

These results indicate that commercial insulin exerts an inhibiting action upon the growth of the seedlings, but that the retardation is not proportional to the concentration of the unitage of insulin. Repeating this experiment several times with various unitages of commercial insulin the author was unable to secure a significant quantitative relationship between the retardation in growth of the seedlings and the concentration of insulin in units.

Crystalline Insulin.—Through the kindness of Dr. E. M. K. Geiling of the Department of Pharmacology of the Johns Hopkins University, the author obtained a sample of Abel's crystalline insulin (6) for investigation.

Table II records the results of the action of Abel's crystalline insulin upon the seedlings:

TABLE II.	
Conc. of insulin.*	Percentage growth.
4 U per 100 cc.	83.5%
8 U per 100 cc.	85.0%
16 U per 100 cc.	85.0%
24 U per 100 cc.	77.1%

* One mg. is the equivalent of 40 units.

Again it may be observed that in these concentrations crystalline insulin is toxic to the seedlings of lupinus albus, but the author was unable to obtain significant quantitative data.

Synthalin.—Through the kindness of Dr. Eugene Leopold of the Johns Hopkins Hospital a sample of Frank's Synthalin (7) which is decamethylene diguanidine dihydrochloride or $\text{HCl.NH}_2\text{C}:\text{NH.NH}(\text{CH}_2)_{10}\text{.NH.C}:(\text{NH}).\text{NH}_2.\text{HCl}$. was obtained.

Table III records the results of the action of synthalin upon the seedlings:

TABLE III.

Conc. synthalin.	Percentage growth.
4 mg. per 100 cc.	43.1
8 mg. per 100 cc.	32.5
8 mg. per 100 cc.	33.0
16 mg. per 100 cc.	27.7

In Table III the extreme retarding influence of synthalin upon the growth of the seedlings may be observed. It is interesting in this connection to note that the studies of Staub and King (8) indicate that synthalin is a protoplasmic poison.

Neosynthalin.—Through the kindness of Mr. F. E. Bibbins of Eli Lilly & Company a sample of neosynthalin (9) was obtained. On account of the insolubility of this substance in water an alcoholic solution was employed, using the same concentration of alcohol in the control Shive Solutions. Upon dilution with the nutrient solution the neosynthalin precipitated from its alcoholic solution but remained rather uniformly suspended.

Table IV records the results of the action of neosynthalin upon the seedlings:

TABLE IV.

Conc. neosynthalin.	Percentage growth.
1.7 mg. per 100 cc.	77.5
3 mg. per 100 cc.	71.0

Table IV indicates that neosynthalin retards the growth of the seedlings, but not near so markedly as does synthalin.

Glukhorment.—A German preparation by the name of Glukhorment was studied next. This product is claimed to be valuable when administered by mouth in the treatment of *diabetes mellitus*. The product is said to be a mixture of a pancreatic powder and a phosphoric acid derivative of guanidine (10).

Table V records the results of the action of Glukhorment upon the seedlings:

TABLE V.

Conc. Glukhorment.	Percentage growth.
3.3 mg. per 100 cc.	38.2
8.3 mg. per 100 cc.	23.6
13.2 mg. per 100 cc.	20.0

Like synthalin, Glukhorment was very toxic to the seedlings of *lupinus albus*.

Myrtillin.—Through the kindness of Dr. F. M. Allen of Morristown, N. J., a sample of myrtillin (11) was obtained for study.

Table VI records the results of the action of myrtillin upon the seedlings:

TABLE VI.

Conc. myrtillin.	Percentage growth.
34 mg. per 100 cc.	74.8
100 mg. per 100 cc.	40.2
170 mg. per 100 cc.	26.1

In smaller concentrations myrtillin was practically non-toxic to the seedlings, in fact in very high dilution the presence of this substance in the nutrient solution could not be detected on account of its apparently not influencing the increment of growth.

In order to obtain the relative degree of toxicity of these drugs upon the

seedlings several series were grown simultaneously containing insulin, Abel's insulin, synthalin, Glukhorment and myrtillin, respectively.

Table VII records the results of this comparative study:

TABLE VII.

Substance.	Concentration.	Percentage growth.
Insulin	8.5 U per 100 cc.	64.9
	17 U per 100 cc.	58.5
Abel's Crystalline Insulin	0.3 mg. per 100 cc.	87.0
Synthalin	0.3 mg. per 100 cc.	76.8
Glukhorment	0.3 mg. per 100 cc.	78.5
Myrtillin	0.3 mg. per 100 cc.	93.5

In the concentrations employed myrtillin is the least toxic to the seedlings, whereas the guanidine compounds are exceedingly toxic. The commercial insulin 8.5 U per 100 cc. contained (on the basis of Abel's crystalline insulin) approximately 0.2 mg. This would seem to indicate that the extractive material in the insulin preparation, other than insulin, was quite toxic to the seedlings.

CONCLUSIONS.

1. The action of certain hypoglycemic drugs upon the seedlings of lupinus albus has been studied.
2. Certain comparisons of toxicity of these drugs to plant protoplasm have been pointed out.

REFERENCES.

1. M. M. Ellis and W. H. Eyster, *Science*, 58 (1923), 541.
2. M. M. Ellis and W. H. Eyster, *J. Gen. Phys.*, 6 (1924), 653.
3. D. I. Macht and M. B. Livingston, *Ibid.*, 4 (1922), 573.
4. D. J. Macht and J. C. Krantz, Jr., *JOUR. A. PH. A.*, 16 (1927), 211.
5. J. W. Shive, *Physiol. Researches*, 1 (1915), 327.
6. J. J. Abel, *et al.*, *J. Pharm. and Exptl. Therap.*, 31 (1927), 65.
7. Frank, Nothmann and Wagner, *Klin. Wochsch.* (1925), No. 45.
8. H. Staub and O. King, *Ibid.*, 7 (1928), 1365.
9. Nothmann and Wagner, *Ibid.*, 7 (1928), 1996; through *Am. J. Med. Sciences*, 177 (1929), 730.
10. E. B. Salem and T. Nyren, *Acta. Med. Scand. Bd.*, 69 (1928), 69.
11. F. M. Allen, *Am. J. Physiol.*, 81 (1927), 462.

PHARMACEUTICAL RESEARCH LABORATORY,
SHARP & DOHME.

AMINO ALCOHOLS IV.

POTENIOMETRIC MEASUREMENTS OF CERTAIN HOMOLOGUES OF EPHEDRINE.

BY JOHN C. KRANTZ, JR., AND WALTER H. HARTUNG.

INTRODUCTION.

Since the introduction of ephedrine into the practice of medicine by Chen and his associates (1 and 2) and the synthesis of this alkaloid by Fourneau and Kanao (3) many of its homologues and analogues have been studied chemically, pharmacologically and clinically. (Adams, *et al.* (4) and others have prepared several of the homologues of ephedrine and studied their action upon blood-sugar