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Hypoglycemia Induced by Sodium Selenite.

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Since the discovery of insulin (F. G. Banting and C. H. Best[1]), a number of organic compounds, such as guanidine (Collip,[2] Dubin and Corbitt[3]), adenine sulphate and xanthine (Dubin and Corbitt[3]), ergotamine (Lesser and Zipf[4]), 2 thio, 4 or 5 amino-ethylglyoxaline, a sulphur derivative of histidine (MacDonagh[5]), choline (Junkersdorf and Kohl[6]), and dihydroxyacetone (Rabinowitch,[7] Mason[8]), have been found to possess the property of lowering blood sugar. As for inorganic compounds, potassium chloride, according to Kyelin and Engel,[9] induces a slight fall in blood sugar, while calcium chloride, according to Barath,[10] causes a slight rise. Elias, Popescu-Inotesti and Radoslav[11] report a fall in blood sugar in rabbits and dogs induced by both mono and disodium phosphate. Brugsch and Horsters[12] observe that sodium phosphite also diminishes blood sugar.

We wish to report another inorganic compound, sodium selenite, Na_2SeO_3, that induces hypoglycemia. Although selenium is believed to behave pharmacologically like arsenic, it has been shown by Van Dyke[13] that sodium arsenite produces hyperglycemia.

The extent of the hypoglycemia induced by sodium selenite was determined in rabbits that received no food except water for a period of 18 to 24 hours prior to injection of the selenium compound. Blood sugar was determined by the method of Shaffer and Hartmann.[14] The dose administered subcutaneously was 2.5 to 7 mg. per kilo. The minimal lethal dose proved to be 4 mg. per kilo on a diet low in carbohydrate.

The degree of hypoglycemia was in direct proportion to the quantity of the selenium salt injected. Thus, with a small dose, 2.5 mg. per kilo, the normal blood sugar of the animal remained unchanged for 14 hours, when it dropped from 0.118 per cent to 0.085 per cent. With a larger dose, 6 mg. per kilo, the blood sugar dropped from 0.130 per cent before injection to 0.072 per cent the first hour, and to 0.045 per cent the third hour after injection.

The effect of sodium selenite is shown in one of the experiments cited below:

Weight of rabbit, 2,145 grams. Dose: 6 mg. of sodium selenite

per kilo, injected subcutaneously at 2:30 p. m. Animal starved 18 hours prior to injection.

Blood Sugar.

Before injection,	1.050 per cent.
1 hour after injection,	0.087 per cent.
2 hours after injection,	0.048 per cent.

The rabbit went into convulsions at 4:45 p. m. The convulsive movements were somewhat similar to, but not as violent as those observed in strychnine poisoning, but different from those seen in insulin toxemia. The animal died at 6:30 p. m.

This hypoglycemia reflects the efforts of the organism in the direction of detoxication. The organism reduces soluble selenite to free selenium, which in turn is non-toxic. Levine [15] has shown that the reduction of sodium selenite to the free element takes place *in vitro* at 37° C., in the presence of a slightly alkaline solution containing glucose, fructose or galactose, or in a solution slightly acidified with lactic acid. He has further shown that the reduction *in vivo* is partly non-enzymatic and partly the result of a reducing enzyme, the action of which is accelerated by glucose. After histological examination of the tissues stained with eosin and hematoxylin, some organs, especially the liver, show profuse deposits of chocolate colored granules of selenium.

Glycogen in the liver suffers a decrease as a result of the injection of sodium selenite. We have found that the administration of glucose protects the liver cells from degeneration, and prolongs the life of the animal, if selenite has been given in very large doses, and may save it even from death, when the selenite is given in minimal lethal doses. Animals on a diet high in carbohydrate withstand the toxic effects of the selenium salt better than those on a low carbohydrate diet. The experiments of Cathcart and Orr[16] also lead to the same conclusion.

Besides the reduction of selenite to free selenium, another process of detoxication goes on simultaneously, namely, alkylation of selenium, and subsequent expulsion through the respiratory tract of the volatile methyl selenide formed.[17] Rabbits or dogs receiving sodium selenite subcutaneously expire methyl selenide, which has a characteristic and unmistakable odor, detectable in the breath two to three minutes after injection. The odor continues to be present in the expired air for many hours, if the animal survives the dose.

Subcutaneous injection of sodium selenite into the rabbit or dog causes complete withdrawal of free hydrochloric acid from the gastric contents. The probable purpose of this withdrawal of acid is to increase the hydrogen ion concentration of the blood in order to aid

the process of glycogenolysis. That the alimentary tract does influence acid-base balance in the blood is shown by the experiments of Tingl,[18] who demonstrated an increase in blood alkali in the course of digestion.

In the light of our experimental findings, we advocate administration of glucose and the use of diets high in carbohydrate in cases of poisoning with selenite. Tellurium compounds behave in the body similarly to selenium. Since it has been shown that glucose detoxicates sodium tellurite by reduction to free tellurium,[19] we also recommend like treatment in poisoning with tellurites.

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On Specificity of Opalina in the Frog.

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It is well known that the ciliate, *Opalina,* parasitic in the rectum of the leopard frog, *Rana pipiens,* and in the pickerel frog, *R. palustris,* occurs but rarely or not at all in the closely allied adult green frog, *R. clamitans,* and bull frog, *R. catesbiana.* Tadpoles of *R. clamitans* have been found by us to be almost universally para-