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Blood Sugar Changes in the Rat Produced by Salt of Beryllium, Magnesium, and Zinc with Some Observations on Hemoglobin and Red Blood Corpuscles

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BLOOD SUGAR CHANGES IN THE RAT PRODUCED BY SALTS OF BERYLLIUM, MAGNESIUM, AND ZINC WITH SOME OBSERVATIONS ON HEMOGLOBIN AND RED BLOOD CORPUSCLES

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This report is the direct result of research in this laboratory upon the physiological role of several metallic salts. The influence of magnesium salts upon the blood sugar content of rabbits was studied by Underhill (1) who found that hyperglycemia subsequent to magnesium injection was most evident during the period of anesthesia. Meltzer and Auer (2) had shown that an animal anesthetized by an injection of magnesium sulfate could be quickly restored to normal by an intravenous injection of calcium chloride. Underhill (1) showed that the hyperglycemia produced in rabbits anesthetized with magnesium salt was reduced to normal in two or three hours time by calcium chloride. Salant and Wise (3) observed the production of glycosuria in rabbits by zinc salts. They gave results which show that an intravenous injection of zinc malate caused hyperglycemia and glycosuria. These workers report that intravenous injection of calcium chloride did not cause a decrease in the glycosuria resulting from the zinc malate injection. They did not report the effect of calcium chloride upon the blood sugar.

METHODS

Young rats weighing between 130 and 160 grams were used in these experiments. The animals had been reared on our growing ration, which is composed of natural foods and has been used in this laboratory for the growth of rats for many years. Blood samples for glucose, hemoglobin, and erythrocyte counts were obtained, with few exceptions, from the external saphenous vein. In a few cases the blood pressure dropped to such a low level in two to three hours after administration of the metallic salts that it was impossible to obtain samples from the saphenous vein. In these cases blood samples were obtained directly from the heart. The initial blood sugar values were obtained from the unanesthetized animals after a twenty hour fast. All animals at the time they received the test solutions were anesthetized with an intraperitoneal injection

Table I — Blood Sugar Changes Produced by Zinc Chloride, Zinc Chloride and Glucose, and Glucose Administered by Stomach Tube to the Fasting White Rat under Nembutal Anesthesia.

Rat No.	Substance Administered	Volume of solution and mgs. of dissolved substance fed or injected	Glucose mg./100cc. after 20 hr. fast. (Animals not anesthetized)	Glucose mg./100cc. 1 hr. after dose. (Animals anesthetized)	Glucose mg./100cc. 2 hrs. after dose. (Animals anesthetized)	Glucose mg./100cc. 3 hrs. after dose. (Animals anesthetized)
1	$ZnCl_2$	2cc. (30 mg. Zn)	94	125	180	167
2	$ZnCl_2$	2cc. (30 mg. Zn)	80	114	171	190
3	$ZnCl_2$	1cc. (50 mg. Zn)	90	130	133	210
4	$ZnCl_2$ Glucose	2cc. (30 mg. Zn-250 mg. Glucose)	102	140	227	263
5	$ZnCl_2$ Glucose	2cc. (30 mg. Zn-250 mg. Glucose)	109	137	208	N.D.
6	$ZnCl_2$ Glucose	1cc. (50 mg. Zn-250 mg. Glucose)	87.5	125	200	250
7	$ZnCl_2$ Glucose	1cc. (50 mg. Zn-250 mg. Glucose)	95	137	Died	N.D.
8	Glucose	2cc. (250 mg. Glucose)	94	113	104	96
9	Glucose	1cc. (250 mg. Glucose)	82.5	95	116	140
10	Nembutal	1.5cc. (4.5 mg. Nembutal) injected	96.5	90	83	78
11	Nembutal	1.5cc. (4.5 mg. Nembutal) injected	102	90	88	N.D.
12	Nembutal	1.5cc. (4.5 mg. Nembutal) injected	97	83	75	N.D.

N.D. — No determination.

Table II — Changes in Blood Sugar in Various Intervals of Time after the Administration of Beryllium Sulfate by Stomach Tube to the Fasting White Rat under Nembutal Anesthesia

Rat No.	Substance Adminis-tered	Volume of solu-tion and mgs. of dissolved sub-stance fed	Glucose mg./100cc. af-ter 20 hr. fast (Animals not anesthetized)	Glucose mg./100cc. ½ hour after dose (Animals anes-thetized)	Glucose mg./100cc. 1 hour after dose (Animals anes-thetized)	Glucose mg./100cc. 2 hours after dose (Animals anes-thetized)	Glucose mg./100cc. 3 hours after dose (Animals anes-thetized)
1	$BeSO_4$	2cc. (9 mg. Be)	94	94	......	......	......
2	$BeSO_4$	1cc. (9 mg. Be)	90	85	......	......	......
3	$BeSO_4$	1cc. (9 mg. Be)	83	83	113	......	......
4	$BeSO_4$	1cc. (9 mg. Be)	92	90	98	......	......
5	$BeSO_4$	1cc. (9 mg. Be)	109	....	......	136	......
6	$BeSO_4$	1cc. (9 mg. Be)	89	....	......	141	......
7	$BeSO_4$	1cc. (9 mg. Be)	95	....	......	144	......
8	$BeSO_4$	1cc. (9 mg. Be)	83	....	113	150	......
9	$BeSO_4$	1cc. (9 mg. Be)	82	....	121	160	121
10	$BeSO_4$	1cc. (9 mg. Be)	83	....	131	145	160
11	$BeSO_4$	1cc. (6 mg. Be)	90	....	100	84	......
12	$BeSO_4$	1cc. (6 mg. Be)	100	....	106	110	100
13	$BeSO_4$	1cc. (6 mg. Be)	92	....	100	89	......

Table III — The Effect of Calcium Chloride upon Blood Sugar, Hemoglobin, and Red Blood Corpuscle Changes Produced by Administration of Zinc Sulfate by Stomach Tube to the Fasting White Rat under Nembutal Anesthesia

Rat No.	Substance Administered	Volume of solution and mgs. of dissolved substance fed	Volume of solution and mgs. dissolved substance injected subcutaneously	Glucose mg./100cc. after 2 hrs. (Animals anesthetized)	Hemoglobin g./100cc. after 2 hrs. (Animals anesthetized)	RBC million/cmm after 2 hrs. (Animals anesthetized)
1	$ZnSO_4$	1cc. (65mg. Zn)	0	126	21	13.64
2	$ZnSO_4$	1cc. (65mg. Zn)	0	125	23	13.82
3	$ZnSO_4$	1cc. (65mg. Zn)	0	129	....	....
4	$ZnSO_4$	1cc. (65mg. Zn)	1.5cc. (7.5mg. $CaCl_2$)	75	23	13.60
5	$ZnSO_4$	1cc. (65mg. Zn)	1.5cc. (7.5mg. $CaCl_2$)	70	21	11.50
6	$ZnSO_4$	1cc. (65mg. Zn)	1cc. (5mg. $CaCl_2$)	98	23	13.60
7	$ZnSO_4$	1cc. (65mg. Zn)	1cc. (5mg. $CaCl_2$)	103	....	....
8	Glucose	1cc. (250 mg. Glucose)	0	113	15.5	9.65
9	Glucose	1cc. (250 mg. Glucose)	1cc. (5mg. $CaCl_2$)	139	14.6	8.80
10	Na_2SO_4	1cc. (96mgs. SO_4 = 142mgs. Na_2SO_4)	0	84	14.4	8.55

$CaCl_2$ was injected simultaneously with the zinc sulfate.

of nembutal at the rate of 30 mg. per kilogram body weight. Hemoglobin was determined by the Newcomer method, and glucose was determined by the method of Folin and Malmros (4). The salt solutions were administered by stomach tube to rats fasted for 20 hours. For this purpose insulating tubing used in radio work and called "spaghetti" was employed. The concentration of the salts is given in the tables.

Discussion

Table I shows the rise in blood sugar caused by zinc in the form of the chloride; in addition, Table I also shows that the rise in blood sugar which accompanies the administration of glucose is increased by zinc chloride. Nembutal anesthesia causes a lowering of the blood sugar. Table II shows the effect of beryllium sulfate upon the blood sugar. Experiments tend to show that, when compared on a weight basis, beryllium as the sulfate is more toxic than zinc as the sulfate. Table III shows that subcutaneous injection of calcium chloride inhibits the increase of blood sugar caused by zinc sulfate, without diminishing the accompanying rise in hemoglobin and red blood corpuscles. Calcium chloride does not inhibit the blood sugar rise caused by administration of glucose. Calcium chloride injected subcutaneously one hour before or one hour after administration of $ZnSO_4$ did not lower the blood sugar, but when the two salts were administered simultaneously, the hyperglycemia was markedly reduced. Salant and Wise (3), however, did observe that calcium chloride did not affect glycosuria produced by zinc malate in rabbits. The absorption of zinc sulfate is slower than the absorption of zinc chloride as evidenced by the rate of blood sugar increase. The data given in Table IV for the rat agree with the work of Underhill (1) on the effect of $CaCl_2$ on hyperglycemia produced by magnesium sulfate in the rabbit. In addition it was found that

Table IV — The Inhibiting Effect of Calcium Chloride and Nembutal upon the Hyperglycemia Produced by Anesthetic Doses of Magnesium Sulfate upon the Fasting Rat

Rat No.	Volume of solution and mgs. of Mg as $MgSO_4$ dissolved and injected subcutaneously	Treatment of Animals	Volumes and mgs. of $CaCl_2$ dissolved. Sol. injected subcutaneously	Glucose mg./100cc 1.5 hours after dose
1	3/5cc. (14.4mg. Mg)	unanesthetized	none	135
2	3/5cc. (14.4mg. Mg)	anesthetized	none	87
3	3/5cc. (14.4mg. Mg)	unanesthetized	1cc. (5mg. $CaCl_2$)	88
4	3/5cc. (14.4mg. Mg)	anesthetized	1cc. (5mg. $CaCl_2$)	86
5	3/5cc. (14.4mg. Mg)	anesthetized	1cc. (5mg. $CaCl_2$)	87

The calcium chloride and magnesium sulfate were injected simultaneously.

nembutal anesthesia also inhibits the rise in blood sugar caused by subcutaneous injections of magnesium sulfate. Sulfuric acid also causes hyperglycemia and an increase in hemoglobin and red blood corpuscles when administered by stomach tube to rats fasted for 20 hours (Tables V and VI).

Table V — The Effect of Sulfuric Acid Administered by Stomach Tube on the Blood Sugar of the Fasting White Rat under Nembutal Anesthesia

Rat No.	Volume of solution and conc. of acid given	Initial blood sugar (mg./100cc.) after 20 hr. fast (Animals not anesthetized)	Blood sugar (mg./100cc.) 1 hr. after giving acid (Animals anesthetized)	Blood Sugar (mg./100cc.) 2 hrs. after giving acid (Animals anesthetized)
1	1cc. 2N H_2SO_4	102	102	126
2	1cc. 2N H_2SO_4	96	111	121
3	1cc. 2N H_2SO_4	83	105	125
4	1cc. 2N H_2SO_4	89	117	125
5	1cc. 2N H_2SO_4	82	88	143
6	1cc. 2N H_2SO_4	102	123	125

Table VI — The Effect of Sulfuric Acid Administered by Stomach Tube on the Hemoglobin, and Number of Red Blood Corpuscles of the Fasting White Rat under Nembutal Anesthesia

Rat No.	Volume of solution and conc. of acid given	Hemoglobin (gm./100cc.)		Red blood corpuscles million / cmm.	
		Initial after 20 hr. fast (Animals not anesthetized)	Final 2 hrs. later (Animals anesthetized)	Initial after 20 hr. fast (Animals not anesthetized)	Final 2 hrs. later (Animals anesthetized)
1	1cc.2NH_2SO_4	17.0	24+	10.48	14.54
2	1cc.2NH_2SO_4	16.4	22.5	10.86	11.48
3	1cc.2NH_2SO_4	17.5	24+	9.88	12.94
4	1cc.2NH_2SO_4	14.8	24+	9.74	15.28

SUMMARY

Blood sugar may be increased 100-130 per cent above the normal fasting level by administration of certain zinc salts. When the same amount of zinc is given with glucose, the blood sugar may be increased 150-190 per cent above the normal fasting level in three hours. The absorption of glucose from the gastro-intestinal tract is delayed during nembutal anesthesia as evidenced by the blood sugar values when comparison is made with the data of Keil and Nelson (5). Nembutal anesthesia causes a lowering of the blood sugar of fasting rats.

Beryllium sulfate causes an increase in the blood sugar of fasting rats. The rise is not as rapid nor as marked as with a correspondingly toxic dose of zinc sulfate.

Calcium chloride may entirely inhibit the increase of blood sugar caused by zinc sulfate. In depressing the rise in blood sugar caused by zinc sulfate, calcium chloride has no effect upon the rise in hemoglobin and red blood corpuscles caused by zinc sulfate. Calcium chloride alone does not influence the number of red blood cells or hemoglobin values, nor does it have any effect upon blood sugar during the normal rise accompanying glucose absorption. The sulfate ion as sodium sulfate has no effect upon the blood sugar, red blood cell, or hemoglobin values.

The time of injection of calcium chloride relative to the administration of zinc sulfate is important to the inhibitory action of the former upon the blood sugar rise.

Magnesium sulfate causes no effect upon blood sugar when the salt is given by mouth. When subcutaneously injected, magnesium sulfate in proper concentration produces anesthesia. In this condition the blood sugar value rises. The rise in blood sugar produced by anesthetic doses of magnesium sulfate may be inhibited by either calcium chloride or nembutal.

Sulfuric acid also causes hyperglycemia and an increase in hemoglobin and red blood corpuscles when administered by stomach tube to rats fasted for 20 hours.

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