



Blood sugar response of the golden hamster (*Cricetus Auratus*) to intraperitoneal administration of alloxan
by Vernon E Duiker

A THESIS Submitted to the Graduate Faculty in partial fulfillment of the requirements for the degree of Master of Science in Zoology at Montana State College
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Abstract:

Six non-fasted, non-injected hamsters were used to establish normal blood sugar concentration and liver glycogen content. Thirteen additional animals were killed after a 48 hour period of fasting to establish blood sugar levels and liver glycogen content of fasted animals. Forty-six hamsters were divided into nine groups, each group was killed at a set time after the administration of alloxan. Alloxan monohydrate was injected intraperitoneally at the rate of 200 mg. per kg. body weight. Blood samples were obtained by decapitation and blood sugars were run in triplicate on each blood sample. The method of blood sugar determination was; Byrd's modification of the Folin-Wu method. The copper reduced by the glucose was measured by a Leitz Photocolorimeter and averages of the triplicate determinations were recorded as the blood sugars of the animals. The right caudate lobe of the liver was extirpated and fixed in nine volumes of ice cold absolute alcohol saturated with picric acid and one volume of neutral formalin. This material was used for the demonstration of glycogen. The liver sections were stained according to Bensley's modification of the Bauer-Feulgen Procedure. The glycogen was determined by the use of a Densichron Densitometer and recorded as the logarithm of the per cent of light transmitted. The average of the blood sugars, of the six fed animals was 114 mg. per 100 cc. of blood, while the concentration for the thirteen fasted animals was 116 mg. per 100 cc. of blood. Four hours after the administration of alloxan, the maximum blood sugar level of a single experimental animal was 274 mg. per 100 cc. of blood. A minimum concentration of 71 mg. per 100 cc. was obtained 168 hours after administration of alloxan which excluded this reaction from the secondary hypoglycemia of the triphasic blood sugar response. The overall glycogen content of the treated animals was 0.076 as compared to 0.141 for the non-treated animals. However, the former was within the range 0.028-0.104 of the fasted non-treated animals. It was assumed that the drop in the glycogen content was due to the effects of fasting rather than to the effects of alloxan administration. It was concluded that, alloxan administration intraperitoneally at the rate of 200 mg per kg. body weight had no effect on the blood sugar nor on the glycogen content of the liver.

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by
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ABSTRACT

Six non-fasted, non-injected hamsters were used to establish normal blood sugar concentration and liver glycogen content. Thirteen additional animals were killed after a 48 hour period of fasting to establish blood sugar levels and liver glycogen content of fasted animals. Forty-six hamsters were divided into nine groups, each group was killed at a set time after the administration of alloxan. Alloxan monohydrate was injected intraperitoneally at the rate of 200 mg. per kg. body weight. Blood samples were obtained by decapitation and blood sugars were run in triplicate on each blood sample. The method of blood sugar determination was Byrd's modification of the Folin-Wu method. The copper reduced by the glucose was measured by a Leitz Photocolorimeter and averages of the triplicate determinations were recorded as the blood sugars of the animals. The right caudate lobe of the liver was extirpated and fixed in nine volumes of ice cold absolute alcohol saturated with picric acid and one volume of neutral formalin. This material was used for the demonstration of glycogen. The liver sections were stained according to Bensley's modification of the Bauer-Feulgen Procedure. The glycogen was determined by the use of a Densichron Densitometer and recorded as the logarithm of the per cent of light transmitted. The average of the blood sugars of the six fed animals was 114 mg. per 100 cc. of blood, while the concentration for the thirteen fasted animals was 116 mg. per 100 cc. of blood. Four hours after the administration of alloxan, the maximum blood sugar level of a single experimental animal was 274 mg. per 100 cc. of blood. A minimum concentration of 71 mg. per 100 cc. was obtained 168 hours after administration of alloxan which excluded this reaction from the secondary hypoglycemia of the triphasic blood sugar response. The overall glycogen content of the treated animals was 0.076 as compared to 0.141 for the non-treated animals. However, the former was within the range 0.028-0.104 of the fasted non-treated animals. It was assumed that the drop in the glycogen content was due to the effects of fasting rather than to the effects of alloxan administration. It was concluded that, alloxan administration intraperitoneally at the rate of 200 mg. per kg. body weight had no effect on the blood sugar nor on the glycogen content of the liver.

INTRODUCTION

Blood Sugars: A fatal hypoglycemic blood sugar with a concentration of less than 15 mg. per 100 cc. of blood 2-4 hours after the intravenous administration of 70 mg. of alloxan per kg. body weight was first observed in rabbits by Jacobs (1937). Dunn and co-workers (1943) found that alloxan produced selective necrosis in the islets of Langerhans in rabbits, showing a fall of blood sugar to 59 mg. per cent. Studies of the blood sugar response of animals treated with varying amounts of alloxan have been extensive.

Blood Sugars in Dogs: Manhoff (1948) maintained dogs for three days on water before injecting 75 mg. of alloxan per kg. body weight. He reported blood sugar levels ranging from 112-750 mg. per 100 cc. of blood 1-19 days after administration. Goldner (1947) reported blood sugar levels of 98-356 mg. per cent in 17 pancreatectomized dogs 1-48 hours after intravenous injection of varying amounts of alloxan. Blood sugars ranging from 28-600 mg. per 100 cc. of blood were observed by Shipley (1947) in dogs one-fourth to 48 hours after intravenous administration of 75 mg. of alloxan per kg. body weight after vagotomy and thoracic sympathectomy, and vagotomy, thoracic sympathectomy, and sham operations had been performed. Houssay (1947) reported blood sugars between 28 and 471 mg. per 100 cc. of blood one-half to 48 hours in pancreatectomized chloralosed dogs which had received intravenous injections of 100-200 mg. of alloxan per kg. body weight.

Blood Sugars in Rabbits: Hard (1944) injected rabbits intravenously with doses of alloxan ranging between 10 and 300 mg. per kg. body weight and reported blood sugar concentration of 39-400 mg. per 100 cc. of blood 1-12 days after administration. Goldner (1944) reported blood sugar levels of 37-507 mg. per 100 cc. of blood 1-48 hours after intravenous injection of 200 mg. of alloxan per kg. body weight and 6-8 units of protamine zinc insulin. He also reported blood sugar concentrations of 30-148 mg. per 100 cc of blood for the same time period and same dosage of alloxan in adrenalectomized rabbits. Rabbits receiving intravenously 200 mg. of alloxan per kg. body weight gave blood sugar levels of 190-640 mg. per cent one hour to one week after administration, as reported by Bailey (1943). Kendall (1945) reported that blood sugar concentrations in rabbits injected intravenously with doses of 50-125 mg. of alloxan per kg. body weight ranged from 17-490 mg. per 100 cc. of blood, one hour to 50 days after injection.

Blood Sugars in Rats: Lazarow (1946) injected rats intravenously with alloxan in various doses of 15-200 mg. per kg. body weight. He reported blood sugar averages of 109-933 mg. per cent 1-72 hours after administration. Shipley (1947) injected male paralytic rats intravenously with 100 mg. of alloxan per kg. body weight. The Blood sugars of these rats ranged between 44 and 823 mg. per cent 1-23 days after administration. Palay (1946) recorded blood sugar levels of 25-800 mg. per 100 cc. of blood in rats receiving 40 mg. of

alloxan per kg. body weight. He compared these results with blood sugar levels of 90-160 mg. per 100 cc. of blood in rats in which the same dose of alloxan was preceded by an intravenous injection of neutralized cysteine hydrochloride in amounts ranging from 52-1180 mg. per kg. body weight. In testing the antagonism of the diabetogenic action of alloxan by pentnucleotides, Emerson (1946) injected rats intraperitoneally with pentose nucleotides obtained from yeast nucleic acid at 350 mg. of nucleotides per kg. body weight 30-45 minutes before intravenous injection of 40 mg. of alloxan per kg. body weight. The blood sugar concentration reported ranged up to 600 mg. per 100 cc. of blood 1-600 hours after the initial treatment began.

Blood Sugars in Guinea Pigs: Blood sugar levels of 114-124 mg. per cent 1-7 hours after administration were reported by Griffiths (1948) after injecting 200 mg. of alloxan per kg. body weight subcutaneously, intracardially, and intraperitoneally.

Blood Sugars in Birds: Scott (1945) reported no changes in the blood sugar levels resulting from intravenous injections of alloxan in various amounts in barn owls, horned owls, pigeons, ducks, and chickens. The dose of alloxan varied from 50-200 mg. per kg. body weight for periods of from 2-64 days in increasing quantities. The blood sugar response of these birds was between 100 and 180 mg. per cent. The changes observed were considered to be normal variations.

Blood Sugars in Sheep and Calves: McCandless reported blood sugar ranges between 14 and 255 mg. per cent in fasted and non-fasted

sheep 1-38 hours after intravenous injection of alloxan in doses of 75-125 mg. per kg. body weight. In other work by McCandless (1949), Guernsey bulls 2-3 weeks old received progressively higher doses of alloxan intravenously, starting at 65 mg. per kg. body weight and ending with 175 mg. per kg., for periods up to 22 days. The blood sugars of these calves ranged from 22-275 mg. per 100 cc. of blood one-half to 48 hours after administration.

Blood Sugars in Hamsters: Harris (1946) studied the histological effects of alloxan on the golden hamster. He reported terminal blood sugars of 458-822 mg. per 100 cc. of blood 2-4 days after intravenous administration. Harris made no attempt to study the changes in the blood sugars over timed reaction periods.

Liver Glycogen: Lackey (1944) reported the mean value for chemical determination of liver glycogen in control rats as 3.056 per cent and for alloxan-treated animals as 0.806 per cent. The rats had received an intraperitoneal injection of 200 mg. of alloxan per kg. body weight as a single dose. The alloxan-treated animals used to demonstrate the liver glycogen were those which had survived three or more days and had developed moderate to severe diabetes. Carrasco-Formiguera (1950) reported quantitative chemical estimation of liver glycogen as 0.35-0.80 per cent in 24-hour fasted rabbits. In animals receiving 200 mg. of alloxan per kg. body weight the liver glycogen was 0.16-0.68 per cent three hours after feeding intragastrically 30 cc. of a 10% solution of a totally neutralized lactic acid per

kg. body weight. The liver glycogen in rats given only lactic acid-lactate feeding (same dosage as in the foregoing) was 1.38-4.80 per cent in three animals 4 hours after feeding.

The work outlined in this paper was designed to study the effects of intraperitoneal injection of alloxan on the blood sugar level in the hamster for different reaction periods. In addition, determinations of liver glycogen were made in order to study the effects of various blood sugar levels on the liver glycogen content.

METHODS

The hamsters used were divided into three groups. Group 1 was the non-treated animals; these received no alloxan or were they fasted. In Group 2 the animals, known as the fasted non-injected group, received no alloxan but were fasted for a period of 48 hours. Group 3, which will be referred to as "experimental", was divided into nine timed reaction periods. Each reaction group was killed after a set time interval following alloxan administration in order to obtain the blood samples and the right caudate lobe of the liver. All animals of Group 3 were fasted for a period of 24 hours before alloxan administration and not more than 24 hours after administration.

The animals were reared in round cages with an adequate diet of Ralston Purina laboratory chow and fresh water. When selected, their weights ranged between 60 and 106 grams with an average of 85.6 grams. All hamsters were young, mature adults, 25-40 weeks old, in a

non-hibernating condition.

The animals in Group 1 were used to establish normal blood sugar and liver glycogen levels. Special care was taken to select the animals so that the weight range did not exceed 10 grams. To facilitate the drawing of an adequate amount of blood, each animal was decapitated and the blood was collected in a clean watch glass. The blood drawing was completed within 75 seconds after decapitation. Three 0.1 cc. samples were drawn up in a pipette and analyzed for blood sugar by Byrd's (1925) modification of the Folin-Wu method. The reduced copper was measured by the use of a Leitz Photocolorimeter using the filter #428. The efficiency of Byrd's modification of the Folin-Wu method in the recovery of blood sugar from a blood sample has been found to be 100 per cent as compared to the Folin-Wu method (Byrd, 1925).

The blood samples were drawn, diluted successively with 0.7 cc. of distilled water, 0.1 cc of a 10% solution of sodium tungstate, and 0.1 cc of two-thirds normal sulfuric acid. This dilution was carried out first because of the fast coagulation of the blood, and then the right caudate lobe of the liver was extirpated. This procedure was carried out so that an aliquot of blood representing the amount of glucose in the entire sample was thus obtained.

The trimmed liver was placed in nine volumes of ice cold absolute alcohol saturated with picric acid and one volume of neutral formalin for a period of 12 hours in accordance with Bensley's method as described by Glick (1949). The liver was then transferred to

dioxane for a total of 10 hours with the dioxane solution being changed after a 5 hour period. The tissue was held for one and one-half hours in a mixture consisting of melted paraffin (two-thirds) and dioxane (one-third). It was then held for one and one-half hours in melted paraffin after which it was embedded in 56-58 degree C paraffin. The tissue was sectioned at a thickness of 10 μ .

Every twentieth serial cross section was taken for the histological demonstration of glycogen. Glycogen was stained by the use of Bensley's modification of the Bauer-Feulgen method as described by Glick (1949). After staining, the slides were passed through dilute solutions of HCl and NaOH to obtain a "true" reaction of the glycogen to the Feulgen reagent. "True" designates those reactions of aldehydes which, after being treated with the Feulgen reagent and decolorized by dilute NaOH, were restored to their original color intensity by dilute HCl. The original intensity of the color reaction of the "pseudo" aldehydes cannot be restored by this procedure. The twenty-first serial cross section was used as a negative control by digesting out the glycogen with saliva and staining the liver in the same manner as above.

The procedure for decapitation, blood sugar determination, and liver lobe preparation for the animals of Group 2 was the same as for the animals of Group 1. However, the animals of Group 2 were subjected to a 48 hour fasting period before the blood samples and right caudate lobe of the liver were obtained.

After a period of 24 hours fasting, Group 3 animals received intraperitoneally a single injection of 200 mg. per kg. body weight of a freshly prepared 2 per cent solution of alloxan monohydrate (Eastman Kodak Co.). The site of the injection was approximately 6 mm. to the left of the linea alba and 15 mm. posterior to the thoracic cage. A #26 one-half inch needle attached to a 20-40 unit Eco insulin syringe (Eisele and Co.) was used to make the injection. In making the injection, a check was made in each case in order to determine whether or not the needle had entered an abdominal organ instead of the abdominal cavity by drawing back the plunger to observe the presence or absence of blood in the needle. If no blood was found, the injection was made.

The injected hamsters were allowed to remain alive for periods of 1,2,4,8,12,24,48,72, and 168 hours after injection. In each case the animals were subjected to a 24-hour fast before alloxan administration. Those which were kept less than 24 hours received no further food. The intention of the fast was to obtain low levels of glycogen which would be more or less uniform throughout the entire group. Those which were kept alive for 48-168 hours after treatment were fed immediately after injection. However, in order to deplete the liver glycogen, the food was removed 24 hours prior to decapitation (Carrasco-Formiguera, 1950).

Under normal conditions, the glycogen content of the liver does not remain constant throughout an entire 24 hour period. According to

Deane (1944a) and van Well (1941), who studied the variation of the glycogen content of the mouse liver, there are high and low levels which occur in all individuals at approximately the same time of day. Therefore, the animals were decapitated on successive days at approximately 7:30 P.M. It was hoped that in this manner errors due to the normal periodic changes would be minimized.

Loveland (1931) in demonstrating the diminution of the glycogen store in the rabbit placenta during pregnancy estimated the glycogen content visually as demonstrated by Best's Carmine method as four plus equal to maximal glycogen and one plus equal to minimal glycogen. Graflin (1941) arranged a sequence that a given liver contained respectively more or less histologically demonstrable glycogen than the liver preceding or following it in the series. On the other hand, Deane (1944b) used the plus symbol to indicate that only scattered cells in the lobule contained glycogen, one or more plus's indicate an appreciable quantity present.

The optical density of the stained liver tissue on the slides was obtained showing the relative glycogen content of the liver lobe. The optical density is represented as the log of the per cent of light transmitted. This was assumed to be proportional to the amount of glycogen present in the stained section of the liver tissue. A Densichron Model 2150 Densitometer was used to measure the transmitted light and a Bausch and Lomb micro-projector provided the necessary light source. A microscope diaphragm was placed over the probe unit of the

densitometer to adjust the aperture size, thus enabling measurements to be made on very small areas of the liver sections. Zero readings were obtained for each slide by adjusting the meter needle to the zero position. This reading was the standard reading upon which all the other readings were based. The section, on which the light transmittance was to be determined, was then placed over the aperture. Readings of the optical density, which represented the comparative concentration of "true" glycogen, were taken on each twentieth section. Approximately 30 readings were made on each slide. This same procedure was repeated using the negative control sections in which the glycogen was removed by saliva digestion. The optical density representing the glycogen content was obtained by subtracting the average optical densities of the negative control slides from the average optical density of the "true" glycogen slides.

EXPERIMENTAL DATA

Table I shows the weight, blood sugar level, and liver glycogen index of the six animals used in Group 1. The blood sugar content expressed in mg. per 100 cc. of blood, is the average of the triplicate determinations which were made on each blood sample. The average blood sugar content of the check animals was 114 mg. per 100 cc. of blood with a range of 102-126 mg. per 100 cc. The average index of the glycogen content of the liver lobes was 0.141 with a range of 0.058-0.210

TABLE I.

Weight, Blood Sugar, and Liver Glycogen Index of
Non-fasting and Non-injected Hamsters.

Animal No.	Weight (grams)	Blood Sugar (mg. per 100 cc.)	Index of Liver Glycogen
N1	91.5	126 ± 4	0.110
N2	90.0	121 ± 1	0.129
N3	86.5	102 ± 3	0.210
N4	87.0	116 ± 7	0.170
N5	88.5	104 ± 4	0.167
N6	93.0	111 ± 9	0.058
Avg.	89.4	114 ± 5	0.141

The weights, blood sugar values, and liver glycogen indexes of the thirteen animals used in the fasted non-injected group are presented in Table II. Blood sugars averaging 116 mg. per 100 cc. and ranging between 93 and 163 mg. per 100 cc. of blood were obtained. Since slides A1, A3, and A4 were counterstained with Delafield's Hematoxylin thus obscuring the red-violet color of the glycogen, these slides were not used for the glycogen content determination. The average index of the liver glycogen was 0.045 with the range being 0.028-0.104.

Table III includes the reaction time, total number of fasting hours, body weight, blood sugar, and liver glycogen index of animals receiving alloxan. Two hamsters died after the injection, and autopsies were performed but the cause of death was undetermined. Index readings were not taken on slides W1, W3, and W4, since they

were counterstained with Delafield's Hematoxylin, and Z3 and Z4 sections were ruined in staining.

Figure 1 shows the blood sugar content of the individual animals of the various groups. Each point represents the blood sugar concentration of an individual animal. Figure 2 shows indexes of liver glycogen content.

TABLE II.

Weight, Blood Sugar, and Liver Glycogen Index of
48-Hour Fasted and Non-injected Hamsters.

Animal No.	Weight (grams)	Blood Sugar (mg. per 100 cc.)	Index of Liver Glycogen
A1	75.5	133 ±6	-----
A2	74.0	126 ±8	0.036
A3	84.5	113 ±3	-----
A4	89.0	112 ±3	-----
A5	75.0	114 ±7	0.042
A6	70.0	163 ±14	0.028
A7	82.5	94 ±5	0.037
A8	82.0	93 ±4	0.043
A9	69.0	106 ±4	0.059
A10	85.0	121 ±2	0.039
A11	70.0	113 ±5	0.029
A12	65.0	96 ±1	0.042
A13	60.0	119 ±2	0.104
Avg.	75.5	116 ±5	0.045

TABLE III.

Weight, Blood Sugar, and Index of Liver Glycogen of
Alloxan Injected Hamsters.

Animal No.	Reaction Time (Hours)	Total Hours Fasting	Weight (grams)	Blood Sugar (mg. per 100 cc.)	Index of Liver Glycogen
R1	1	25	98	208 ± 6	0.017
R2			100	124 ± 4	0.028
R3			89	131 ± 9	0.030
R4			83	125 ± 3	0.146
S1	2	26	95	113 ± 2	0.012
S2			98	108 ± 5	0.030
S3			89	100 ± 4	0.074
S4			101	92 ± 7	0.095
T1	4	28	94	103 ± 1	0.030
T2			99	274 ± 12	0.094
T3			88	96 ± 1	0.094
T4			92	101 ± 2	0.116
U1	8	32	86	84 ± 1	0.054
U2			92	79 ± 0	0.058
U3			96	108 ± 2	0.082
U4			90	143 ± 4	0.067
V1	12	36	97	103 ± 2	0.088
V2			82	123 ± 3	0.102
V3			90	93 ± 4	0.216
V4			101	100 ± 0	0.216

(Continued)

Table III. (Continued)

Animal No.	Reaction Time (Hours)	Total Hours Fasting	Weight (grams)	Blood Sugar (mg. per 100 cc.)	Index of Liver Glycogen
W1	24	48	78	117 ±8	-----
W2			76	137 ±5	0.060
W3			87	141 ±4	-----
W4			91	178 ±10	-----
W5			74	123 ±6	0.065
W6			71	155 ±4	0.048
W7			82	84 ±1	0.043
W8			81	111 ±2	0.040
W9			76	114 ±4	0.046
W10			85	103 ±7	0.012
W11			84	died	-----
W12			69	118 ±3	0.051
W13			68	119 ±2	0.073
W14			73	100 ±3	0.063
X1	48	24	82	109 ±4	0.100
X2			85	111 ±8	0.093
X3			99	101 ±11	0.114
X4			104	102 ±5	0.110
Y1	72	24	79	102 ±1	0.060
Y2			81	122 ±8	0.090
Y3			105	died	-----
Y4			106	112 ±2	0.096
Z1	168	24	85	111 ±4	0.072
Z2			86	107 ±2	0.065
Z3			94	71 ±5	-----
Z4			71	99 ±0	-----

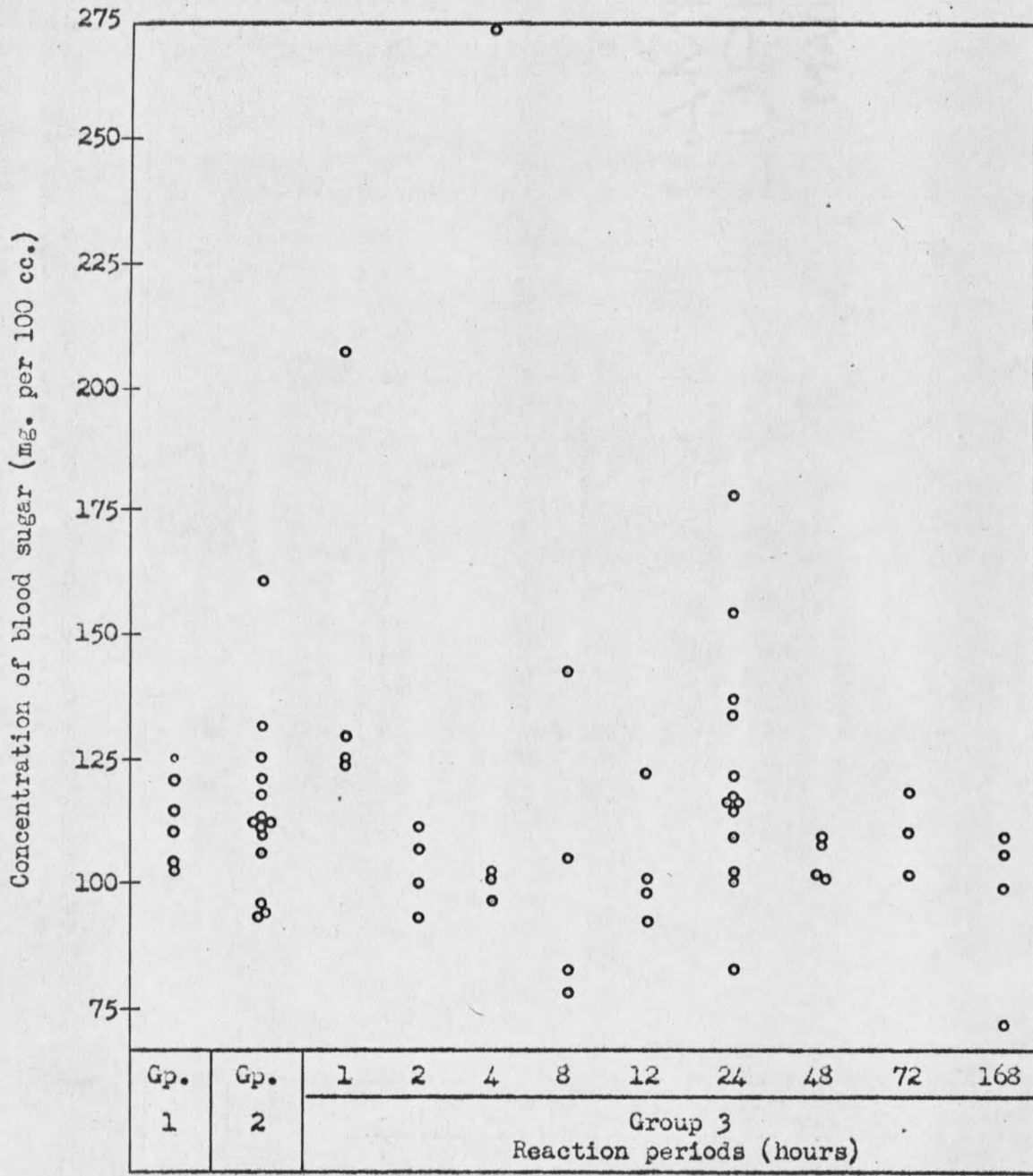


Figure 1.

Scattergram showing the variations in blood sugar content

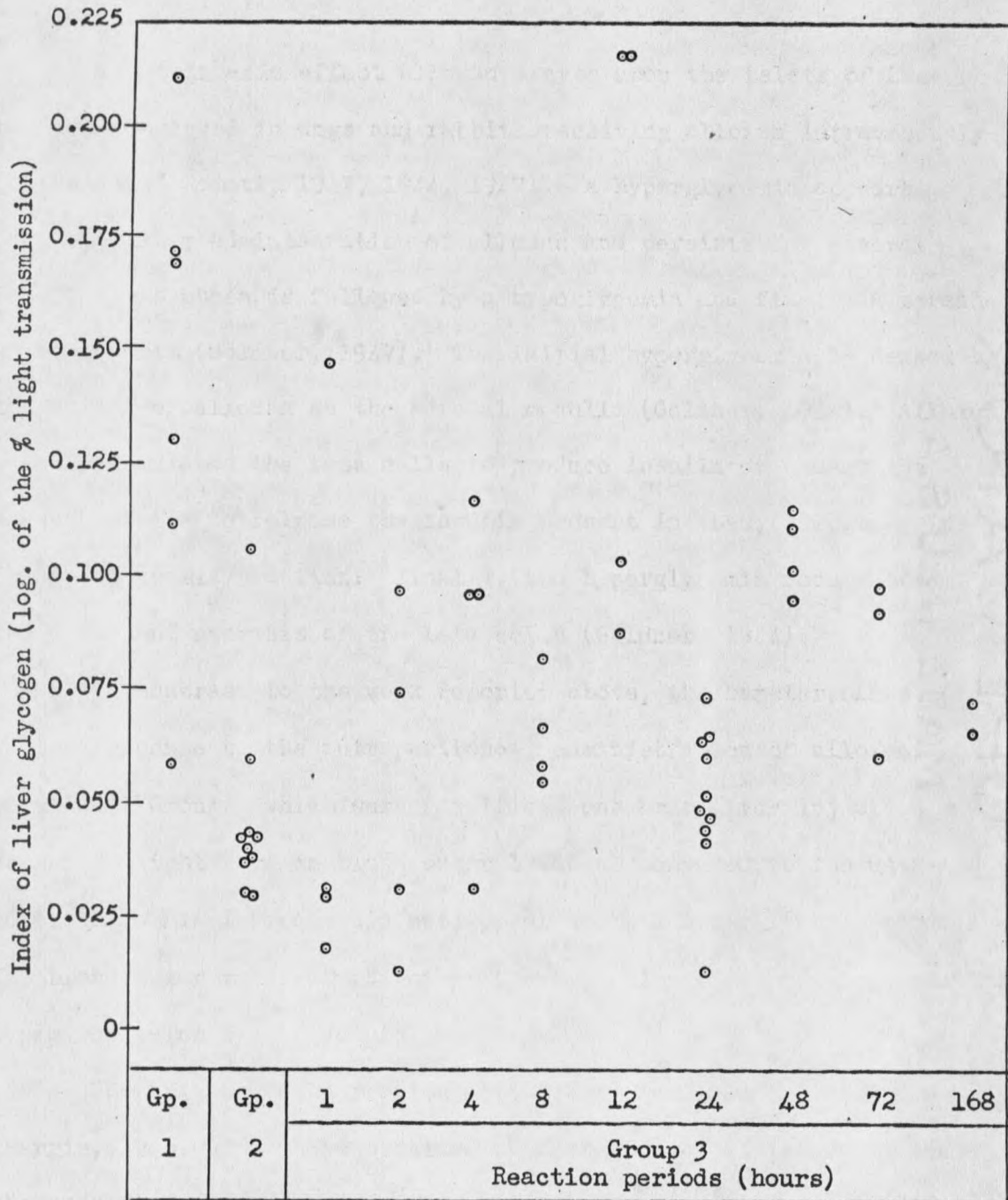


Figure 2

Scattergram of relative liver glycogen content

DISCUSSION

The triphasic effect alloxan exerts upon the islets of Langerhans has been observed in dogs and rabbits receiving alloxan intravenously (Goldner and Gomori, 1943; 1944, 1947). A hyperglycemia appears promptly after administration of alloxan and persists for several hours. This phase is followed by a hypoglycemia and finally a permanent hyperglycemia (Goldner, 1947). The initial hyperglycemia is caused by the action of alloxan on the adrenal medulla (Goldner, 1944). Alloxan either stimulates the beta cells to produce insulin or causes the affected cells to release the insulin present in them, resulting in the hypoglycemic reaction. Finally, the hyperglycemia results from the permanent necrosis of the beta cells (Goldner, 1944).

In contrast to the work reported above, the hamster shows little response to the intraperitoneal administration of alloxan. Animals in Group 3 which were sacrificed one hour after injection showed a slight rise in blood sugar level as compared to the untreated controls. This increase did not appear to be a hyperglycemic condition. The blood sugar value of the other treated animals did not indicate any hypoglycemia or hyperglycemia.

Comparison of the results obtained by intravenous injection (Harris, 1946) with those obtained by intraperitoneal injection (in the present work) emphasizes the variations which occur due to different injection methods in hamsters. The scattergram reading (Figure 1) shows a maximum blood sugar value of 111 mg. per 100 cc.

of blood 48 hours after alloxan administration, while the intravenous method resulted in 647 mg. per 100 cc. By the intravenous method a maximum blood sugar value of 720 mg. per 100 cc. of blood 72 hours after injection was recorded. Results of the intraperitoneal injection show a maximum blood sugar level of 122 mg. per 100 cc. of blood for the same period. Harris (1946) reported a reading of 822 mg. per 100 cc. of blood 96 hours after injection. The experiment presented in this paper did not include a group which was held for 96 hours after injection, but the maximum figure obtained from the 168 hour group, 111 mg. per 100 cc. of blood, does not show a noticeable blood sugar increase.

Bailey (1946) found that alloxan disappeared from the blood of rabbits five minutes after intravenous injection. He attributes the disappearance of the alloxan to its reaction with the sulfhydryl group of glutathione, the alloxan being reduced to dialuric acid which has no diabetogenic effect. In hamsters receiving intraperitoneal injection the alloxan may be converted into dialuric acid before it can exert any diabetogenic effect.

To determine the effects of starvation, a group of fasted non-injected animals was starved for 48 hours before blood samples were taken. There is little indication from these results that starvation tends to alter blood sugar level in the direction of the hypoglycemic reaction. However, the true picture may be masked by utilization of stored liver glycogen. Because of the failure to develop a marked hypoglycemic reaction, it is assumed that pronounced changes in blood

sugar levels would be due to effects of alloxan.

Harris (1946) reported the probable diabetogenic dose of alloxan when administered intravenously to be approximately 60 mg. per kg. body weight. Since the intraperitoneal administration of 200 mg. per kg. body weight did not result in the triphasic response reported above, the effective dose by this method has not been determined.

The distribution of the liver glycogen values obtained from densitometer readings is recorded in Figure 2. Readings from the non-treated animals show a wide range in glycogen values. In contrast to Group 1, the animals of Group 2 show a lower liver glycogen value. The normal blood sugar level of Group 2 animals, Figure 1, may have resulted from the transfer of liver glycogen to glucose. The data on the treated animals do not show a correlation between blood sugar levels and liver glycogen values, as indicated by the results obtained for animals S4, T2, T3, and V3. However, there is a noticeable low glycogen index in the animals of Group 3. Only six of the thirty-nine animals show index readings higher than the maximum readings of the fasted non-injected group, but the glycogen index readings of these six animals are within the range recorded for the non-treated group. From these data it is postulated that the low glycogen readings of this group are due to the effects of starvation.

SUMMARY

Hamsters when injected intraperitoneally failed to show the triphasic blood sugar response.

The liver glycogen content of treated animals did not vary appreciably from those of the fasted animals. Glycogen content of treated groups was lower than the glycogen content in the untreated. This decrease was attributed to the effects of fasting rather than to the effects of alloxan.

Two hundred mg. per kg. body weight of alloxan monohydrate, administered intraperitoneally, did not result in a diabetogenic condition in the golden hamster.

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