

بعض الدراسات على الكفاءة الوظيفية للبنكرياس

في الجاموس والأبقار

٣ - احداث مرض البول السكرى تجريبيا

م . حسن ، أ . عامر ، ع . بيومي ، س . العمروسي

استخدم لتنفيذ هذه التجربة خمس عجول بقرية تتراوح أعمارها بين  $1\frac{1}{4}$  -  $3\frac{1}{4}$  سنة حقنت بمحلول ٥٪ من الالوكزان في الوريد الودجى ولقد وضعت هذه الحيوانات تحت الملاحظة الاكلينيكية كما وقد جمعت عينات دم وبول وبراز والسائل المعوى قبل وبعد ١ ، ٢ ، ٤ ، ٧ ، ١٥ يوم من الحقن وتبين بتحليل النتائج مما يلي :

- ١ - انتابت الحيوانات حالة من القلق الوقتى تبعها هدوء نسبي وبعد مرور عشر ساعات من الحقن اصيبت الحيوانات بحالة من الاغماء بدأت بعدها تعود الحيوانات الى حالتها الطبيعية بحلول ١٦ ساعة من الحقن .
- ٢ - زاد تبول الحيوان ابتداءً من ال ٢٤ ساعة الأولى بعد الحقن وكانت كل العينات ايجابية لاختيار السكر .
- ٣ - زيادة مستوى السكر فى سيرم الدم طوال مدة التجربة .
- ٤ - لم يتأثر مستوى انزيمات البنكرياس فى الدم .
- ٥ - زاد تركيز انزيمى جلوتامك اكسال ترانس امينز وجلوتامك بيروفك ترانس امينز فى سيرم الدم بينما ظل مستوى الفوسفاتيز القاعدى والحمضى عند المعدل الطبيعى .
- ٦ - ظهرت زيادة طفيفة فى مستوى البروتين والجليسرايدات فى السيرم فى حين أن كمية الدهون الكلية والكوليسترول لم تتأثر بحقن الالوكزان .

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Depts. of Medicine & Pathology,  
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SOME STUDIES ON PANCREATIC FUNCTION  
IN CATTLE AND BUFFALOES

3. ALLOXAN DIABETES

(With 14 Figures and 4 Tables)

By

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SUMMARY

Diabetes was induced in 5 male cattle by injection of alloxan. Each animal received single dose of 5% alloxan solution intravenously. Blood, faecal, urine and duodenal fluid samples were collected before and 1,2,4,7 & 15 days post alloxan injection ( P.A.I. ). Recorded results indicated:-

- 1- Momentary restlessness for about  $\frac{1}{2}$  hour where respiratory and pulse rates increased. The animals returned to normal condition after 16 hrs P.A.I. Ten hours later P.A.I. the animals were fainting but not commatosed.
- 2- Polyuria with apparent glucosuria.
- 3- Increased serum glucose level during the whole course of experiment.
- 4- Pancreatic enzymes ( lipase, Amylase & Trypsin ) were not affected.
- 5- Elevated S-GOT & S-GPT while alkaline and acid phosphatase enzymes activity was still in the normal level.

INTRODUCTION

It has been shown that the intravenous or intraperitoneal administration of aqueous solution of alloxan causes permanent diabetes in rabbits or rats (Dunn & Mclethie, 1943), dog ( Goldner and Gomori, 1945 ), cat (Peralta, 1945) and sheep (Dye and Woodward, 1947). The response, however, varied from one species to another. Available literature lacks

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any information about the diabetogenic effect of Alloxan in large ruminants. The present study was planned to evaluate the pathophysiological change occurring in the endocrine part of the pancreas, in large ruminants, after the injection of diabetogenic dose of alloxan.

#### MATERIALS & METHODS

Five healthy male cattle with body weight ranging from 300-500 kg., aging between 1.5-3.5 years were used. Food was withheld 24 hours before experiment. Animals were intravenously injected with single dose of 5% freshly prepared alloxan. The injection was done after technique described by Jarrett (1946), Dye and Woodward (1947) and Lukens, (1948).

Samples of blood were collected from the jugular vein, before and  $\frac{1}{2}$ , 1, 2, 4, 6, 8, 10, 12, 24, hours as well as 2, 4, 7, 15 days post alloxan injection where blood sugar was estimated according to Trinder, (1969) and sugar curve plotted.

Another samples of blood, faeces, urine and duodenal fluid were collected before and 1, 2, 4, 7, & 15 days post alloxan injection (P.A.I.).

These blood samples were analysed for amylase, lipase, S-GOT, S-GPT, alkaline and acid phosphatase enzymes activities. Total proteins, total lipids, triglycerides and cholesterol levels were also determined. Faecal samples were examined quantitatively for trypsin and fat. Methods adopted here were previously reported by Hassan et al (1980).

Urine samples were tested for the presence of reducing sugars by the aid of Combur 8 Test strips (Boehringer Mannheim GmbH Diagnostica, W-Germany). Duodenal fluid samples were analysed for pancreatic trypsin. Dosing, time of sampling and slaughtering were as follows:-

## INDUCED ALLOXAN DIABETES

## Time of Sampling After Alloxan Injection

No. of Animals	Age (years)	Weight (Kg)	Dose of Alloxan (gm)	Time of Sampling (days)					
1	1.5	350	31	1	2	4	7	15	-----
2	3.5	400	35	1	2	4	7	-----	-----
3	2.5	300	27	1	2	4	-----	-----	-----
4	2.5	300	27	1	2	-----	-----	-----	-----
5	1.5	300	27	1	-----	-----	-----	-----	-----

## RESULTS AND DISCUSSION

Tables 1,2,3 & 4 and figures 1-14 presented the biochemical changes observed in blood, faeces and duodenal fluid of experimental animals post alloxan injection (P.A.I.).

Major signs included transient restlessness followed by depression. Animals became normal with the apparent physiological activities after 16 hrs. P.A.I. However, 24 hrs. P.A.I. polyuria was evident. These signs were positively correlated with the triphasic fluctuation of blood sugar level (Fig. 11) Glucosuria was also evident at the 2<sup>nd</sup> day P.A.I. The comparison of the results of alloxan injection with other species of monogastric animals was sometimes necessary as the literature lacks similar picture of ruminants.

Rather similar findings were reported in canines, following alloxan injection, by Bailey, (1947), lukens, (1948), Ettinger(1975) and others.

## Pancreatic Enzymes:

Since the injection of alloxan produced selective necrosis of the beta cells of the pancreatic islands and did not affect the acinar tissue (Fig. 12), the pancreatic enzymes (Amylase, lipase, & trypsin) were slightly affected still remain within the normal physiological limits. Similar results were recorded in sheep by Dye & Woodward (1947)

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and in other species by Goldner & Gomori, (1945), Peralta, (1945) and others.

Gradual increased S-GOT & S-GPT levels were evident from the beginning of the experiment. Maximal levels were evident at the 15<sup>th</sup> day P.A.I. (Table II). On the other side acid and alkaline phosphatase enzymes activities, fluctuated upward and downwards (Table II). Increased S-GOT and S-GPT activities accompanied the fatty liver changes and other tissue changes in the liver ( Fig. 14 ) of experimental animals. Fatty metamorphosis and liver cirrhosis in canines with diabetes mellitus induced similar results (Ettinger, 1975).

#### Total serum Protein:

Slightly affected hepatic tissue was reflected on total serum protein picture with subsequent slight changes (Table III & Fig. 10). The obtained results were in agreement with those described in dogs by Ivy et al, (1951), Milman et al, (1951), Scharff and Wool, (1966) and Rogers et al, (1957a). These authors concluded that administration of alloxan in experimental animals usually, but not always is accompanied by increased total serum protein level.

#### Total lipids

Fluctuated levels were observed P.A.I. but were within the normal physiological range. (Table III). Sterky et al, (1963) could not detect any elevation in total serum lipids in diabetic patients. Slight increase, on the contrary, was recorded in diabetic dogs by Work and Knowles (1961) and Schrade et al (1963).

Alloxan injection in experimental animals resulted in a gradual increase in triglyceride level from 0.42 to 0.90 g/l (Table III). Total serum cholesterol level, on the other hand insignificantly changed P.A.I.

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## INDUCED ALLOXAN DIABETES

Table (I)

Changes IN Pancreatic Enzyme (Lipase And Amylase) In Serum And Trypsin In Duodenal Fluid And Faeces Before And After I.V. Injection With Diabetogenic Dose of Alloxan.

Time of Specimens	Before Injection		After 1 day		After 2 days		After 4 days		After 7 days		After 15 days	
	No. of cases	5 cases	5 cases	4 cases	4 cases	3 cases	3 cases	2 cases	2 cases	One case		
Amylase u/100 ml		78.00 (70-80)	72.20 (60-85)	68.20 (60-78)	67.30 (60-74)	69.50 (67-72)	84.00					
Lipase ml of 0.05 M NaOH		0.74 (0.-0.9)	0.72 (0.6-0.9)	0.58 (0.5-0.7)	0.57 (0.5-0.6)	9.55 (0.5-0.6)	0.70					
Trypsin in Duodenal fluid U/Lit.		16.40	15.40	14.80	13.40	12.20	16.00					
Trypsin In Faeces		+++++	+++++	+++++	+++++	+++++	+++++					

Assiut Vet.Med.J.Vol. 7, No. 13614, 1980.

Table (II)

Changes In Liver Enzymes (GOT, GPT, Alkaline Phosphatase And Acid Phosphatase) Before And After Injection With Biabetogenic Dose Of Alloxan.

Time of specimens	Before Injection	After 1 day	After 2 days	After 4 days	After 7 days	After 15 days
No. of cases	5 cases	5 cases	4 cases	3 cases	2 cases	One case
GPT	8.10	8.20	10.20	12.00	15.00	25.00
U/Lit.	(6.5-10)	(7-10)	(10-10.5)	(0-14)	(15-15)	
GOT	27.00	30-00	38.80	40.70	41.50	48.00
U/Lit.	(24-37)	(24-44)	(28-47)	(30-48)	(35-48)	
Alkaline Phosphatase U/Lit.	18.20	28.60	24.80	22.00	18.00	22.00
	(11-22)	(22-33)	(22-33)	(11-33)	(13-33)	
Acid Phosphatase	3.00	3.16	3.08	2.80	2.75	3.00
U/Lit.	(2.5-4.0)	(2.8-3.5)	(2.5-4.0)	(2.5-3.0)	(2.5-3.0)	

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Table (III)

Changes In Serum Organic Constituents (Total Protein, Total Lipids, Triglycerides, Cholesterol And Glucose), And Fat In Faeces Before And After Injection With Diabetogenic Dose of Alloxan.

Time of specimens	Before	After	After	After	After	After
	Injection	1 day	2 days	4 days	7 days	15 days
No. of cases	5 cases	5 cases	4 cases	3 cases	2 cases	One case
Total Protein g/100 ml	6.10 (6-6.3)	7.46 (6.5-8)	9.30 (7.9-10.5)	7.70 (6.8-9.5)	7.50 (6-9)	6.80
Total Lipids mg/100 ml	612 (450-700)	556 (450-660)	560 (400-660)	593 (450-700)	575 (550-600)	720
Triglycerides g/Lit.	0.42 (0.3-0.5)	0.48 (0.4-0.6)	0.55 (0.4-0.6)	0.67 (0.5-0.8)	0.80 (0.7-0.9)	0.90
Cholesterol mg/100 ml	150 (120-170)	179 (136-210)	193 (150-250)	192 (120-185)	170 (160-180)	180
Glucose mg/100 ml	38 (30-40)	87 (60-150)	133 (100-160)	203 (150-300)	170 (120-220)	170
Fat In Faeces (Qualitative Test)	-ve	-ve	-ve	-ve	-ve	-ve

*Assist. Vet. Med. J. Vol. 7, No. 13614, 1960.*

Table (IV)

Individual Blood Sugar Fluctuation, Following I.V. Injection Of A Diabetogenic Dose Of Alloxan.

Case No.	Weight of Animals Kg.	Age Year	Dose of alloxan gm	Blood Sugar level (mg/100 ml) Before And After Injection at Alloxan													
				0	¼h	1h	2h	4h	6h	8h	10h	12h	24h	48h	96h	168h	360h
1	350	1.5	30	40	100	160	210	260	200	40	20	35	70	160	300	220	170
2	400	3.5	35	40	50	60	100	150	43	24	20	25	60	150	160	120	-
3	300	2.5	27	30	85	130	160	180	100	30	15	25	70	120	150	-	-
4	300	2.5	27	40	50	60	70	80	40	20	15	20	85	100	-	-	-
5	300	1.5	27	40	90	130	220	260	220	40	20	40	150	-	-	-	-
Mean			90 mg/ kg.B.W.	38	75	110	152	186	121	31	18	29	87	133	203	170	170

h = hour.

B.W.= Body weight.

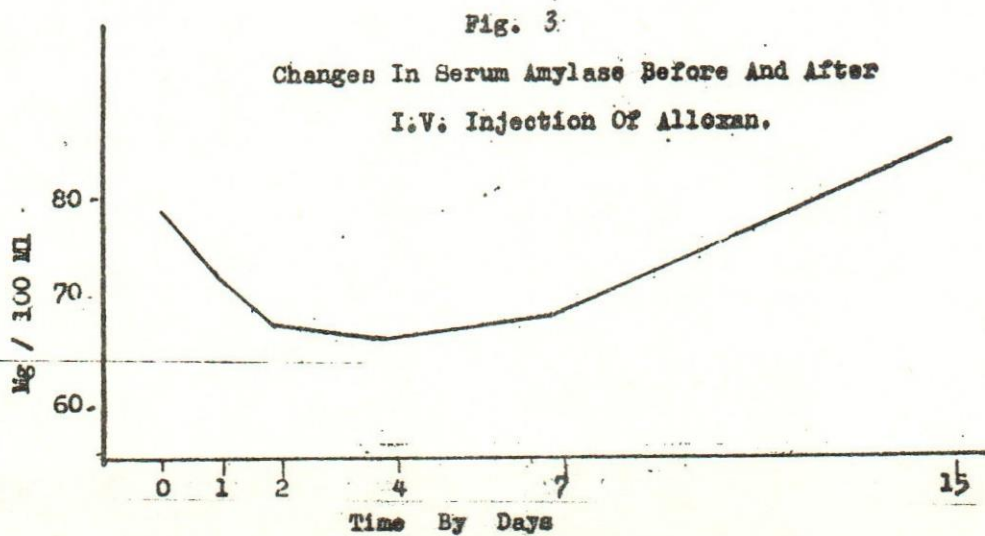
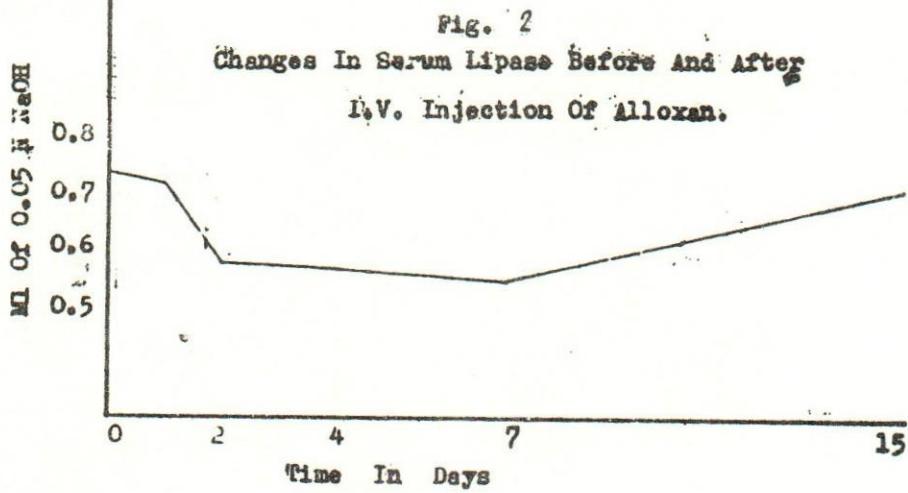
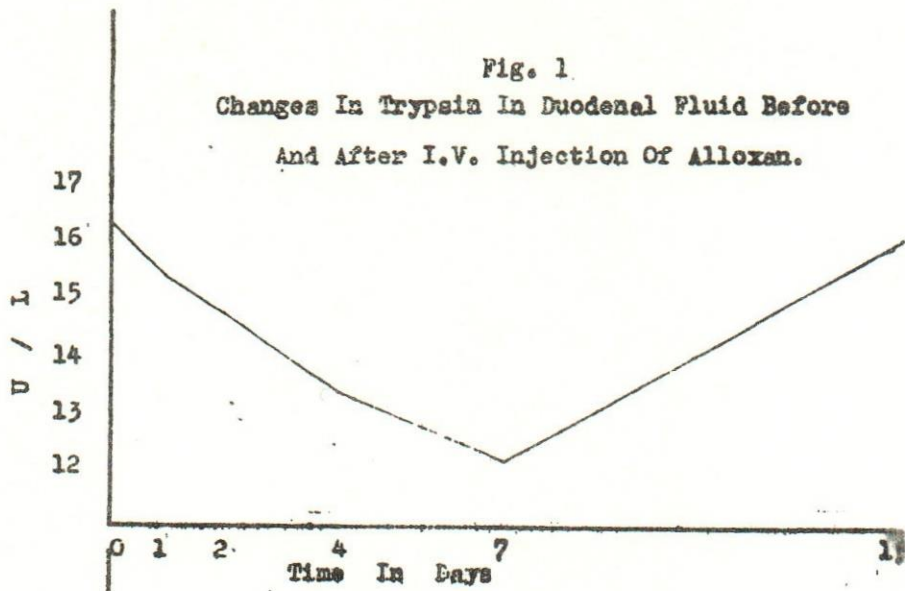


Figure 1: Plot of  $\ln(\frac{1}{1-x})$  versus  $x$  for  $x \in [0, 1]$ . The curve starts at (0,0) and increases monotonically, passing through (0.5, 0.693) and (1, 1).



Figure 2: Plot of  $\ln(\frac{1}{1-x^2})$  versus  $x$  for  $x \in [0, 1]$ . The curve starts at (0,0) and increases monotonically, passing through (0.5, 0.347) and (1, 0.693).



Figure 3: Plot of  $\ln(\frac{1}{1-x^3})$  versus  $x$  for  $x \in [0, 1]$ . The curve starts at (0,0) and increases monotonically, passing through (0.5, 0.143) and (1, 0.347).



Fig. 4  
Changes In GOF Before And After I.V.  
Injection Of Alloran.

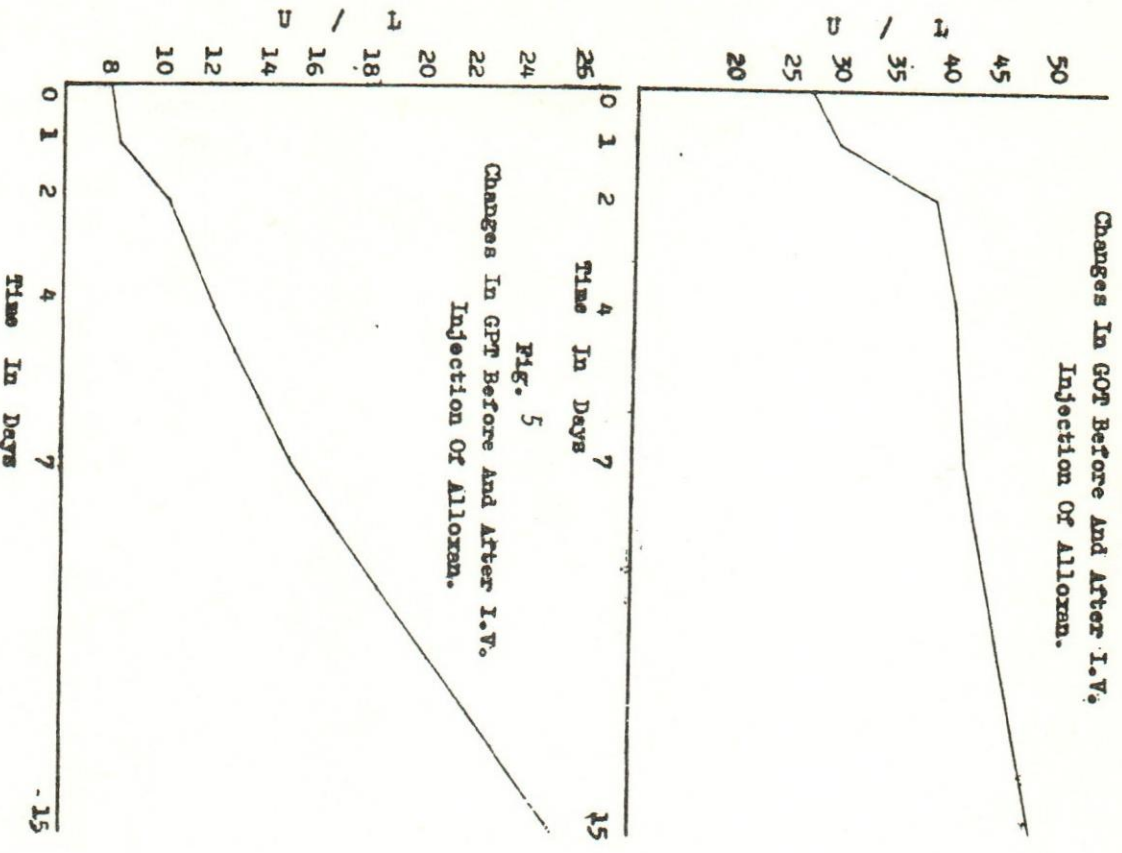


Fig. 5  
Changes In GPT Before And After I.V.  
Injection Of Alloran.

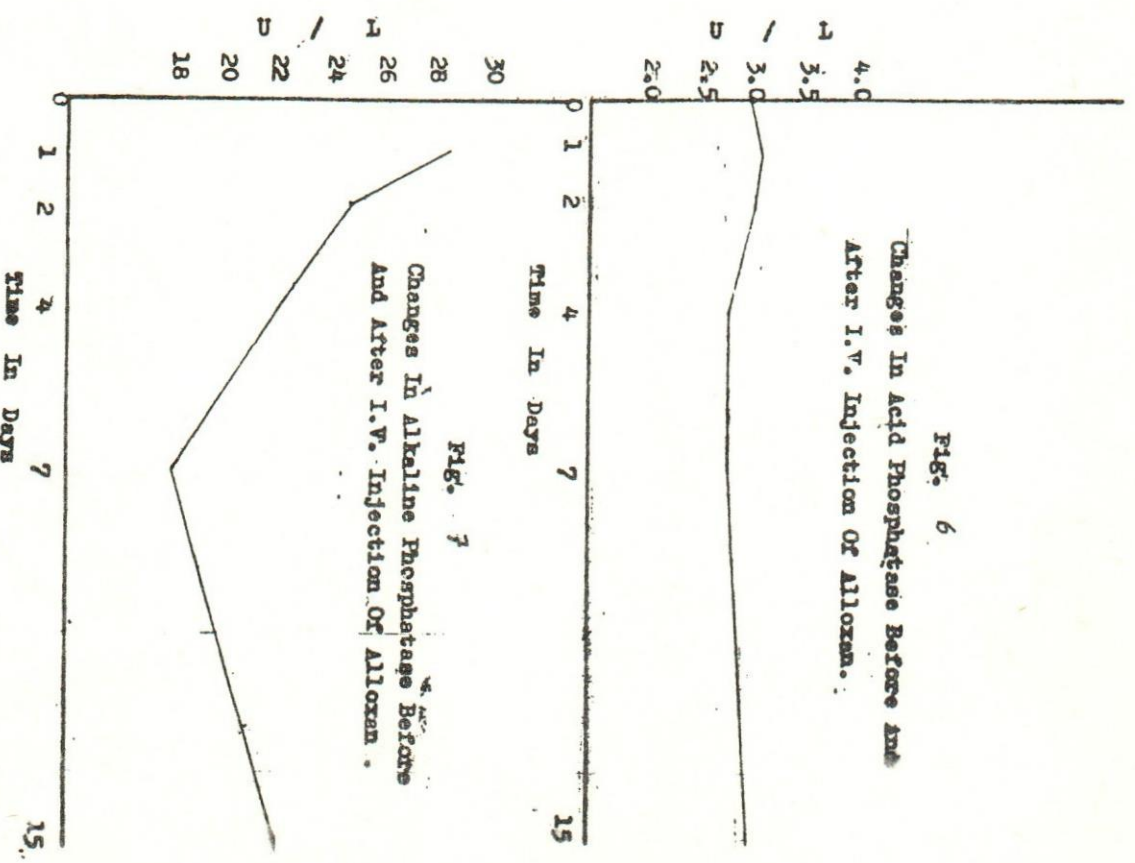


Fig. 6  
Changes In Acid Phosphatase Before And  
After I.V. Injection Of Alloran.

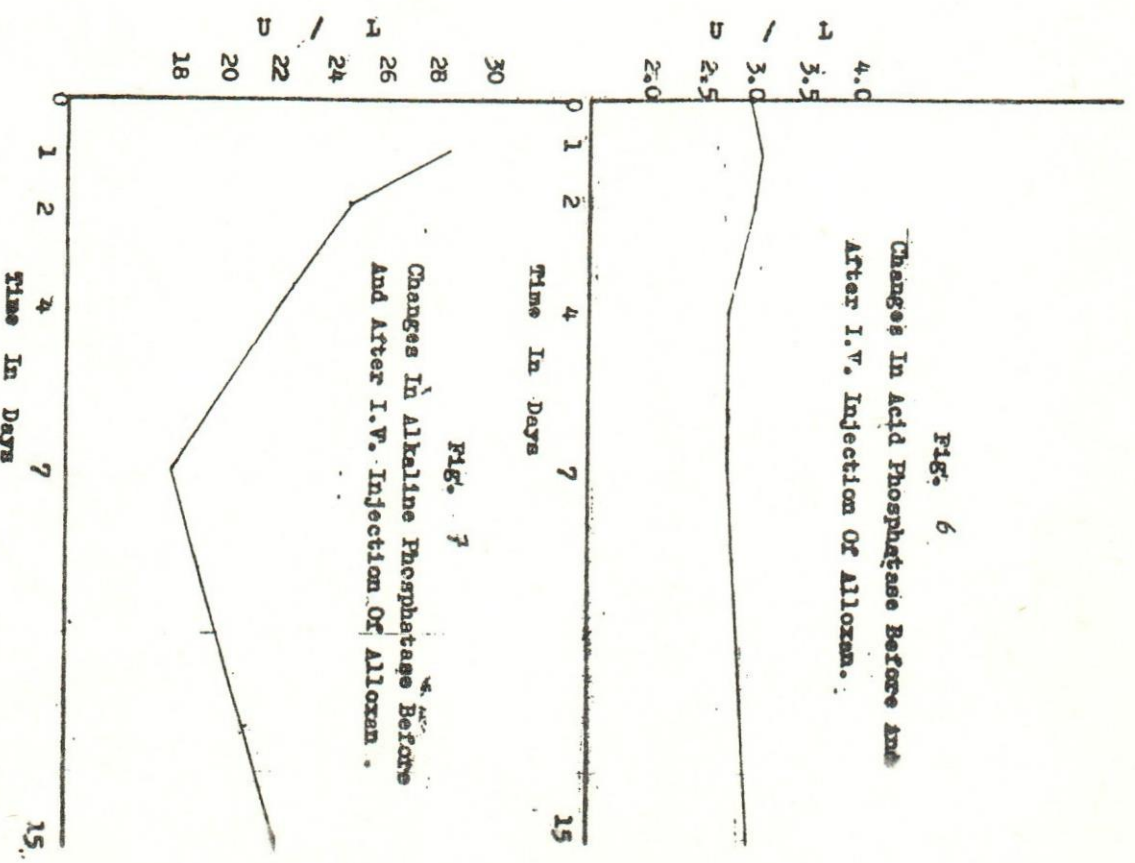


Fig. 7  
Changes In Alkaline Phosphatase Before  
And After I.V. Injection Of Alloran.

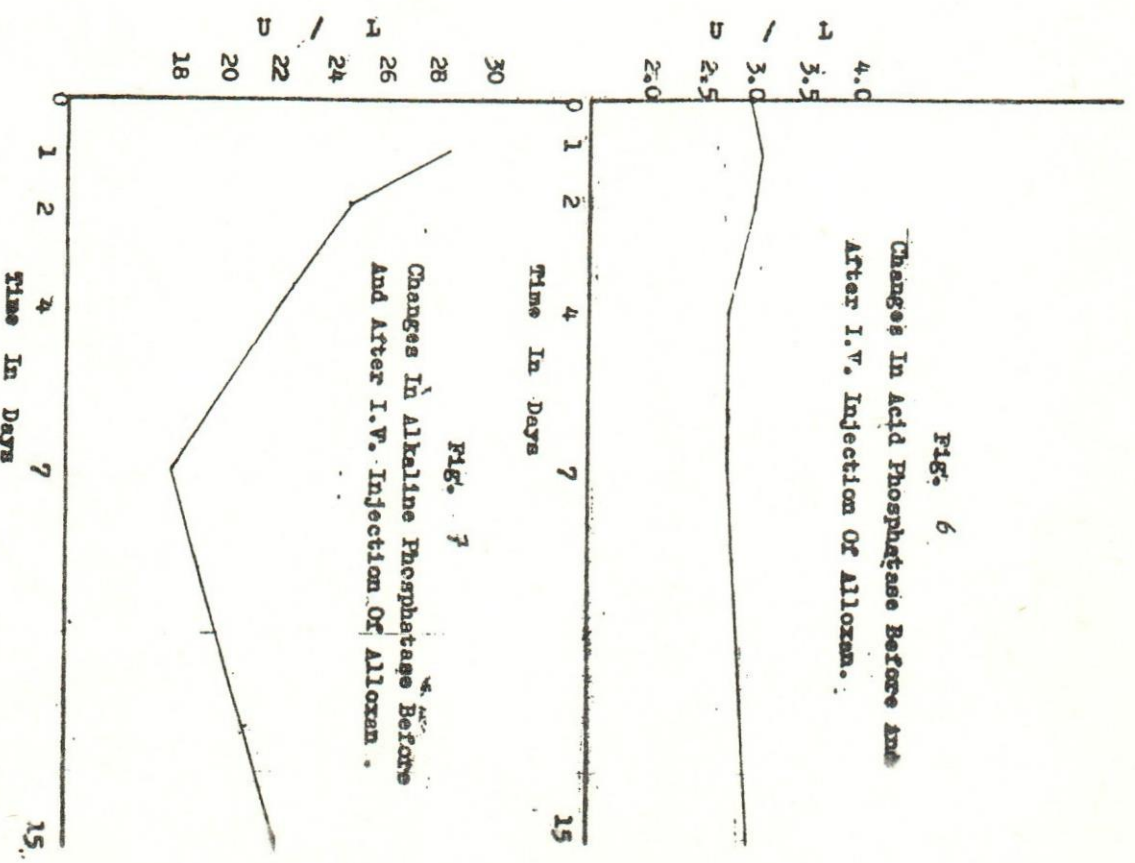






Fig. 8  
 Changes In Triglycerides Before And After  
 I.V. Injection Of Alloxan.

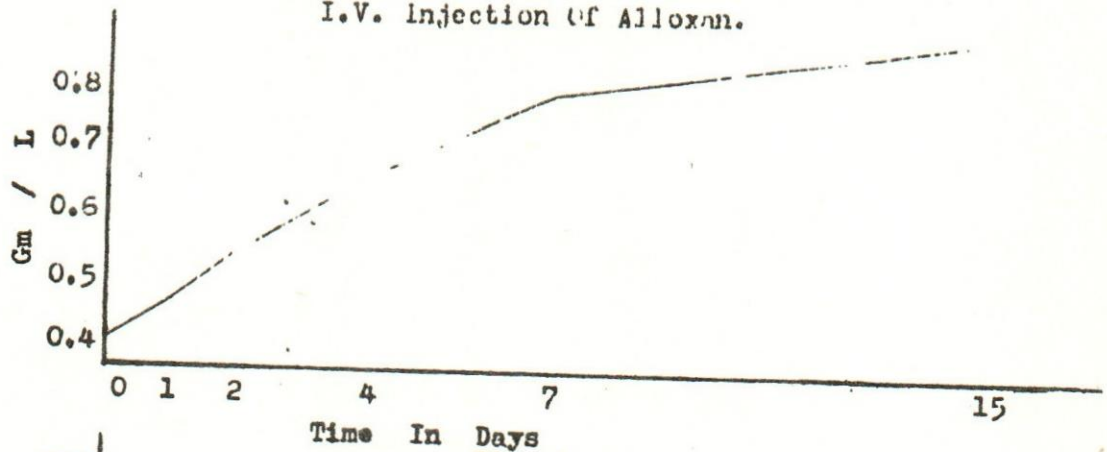


Fig. 9  
 Changes In Total Lipids Before And After  
 I.V. Injection Of Alloxan.

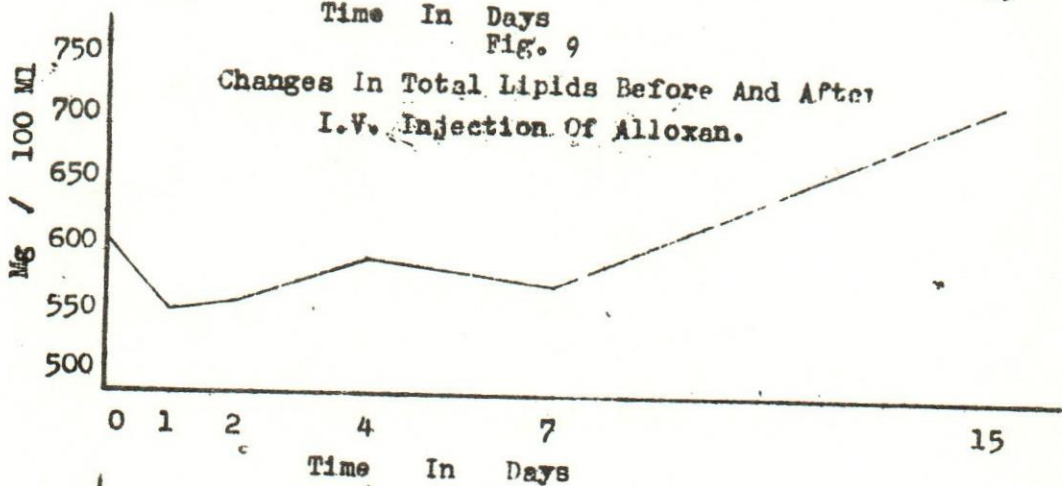
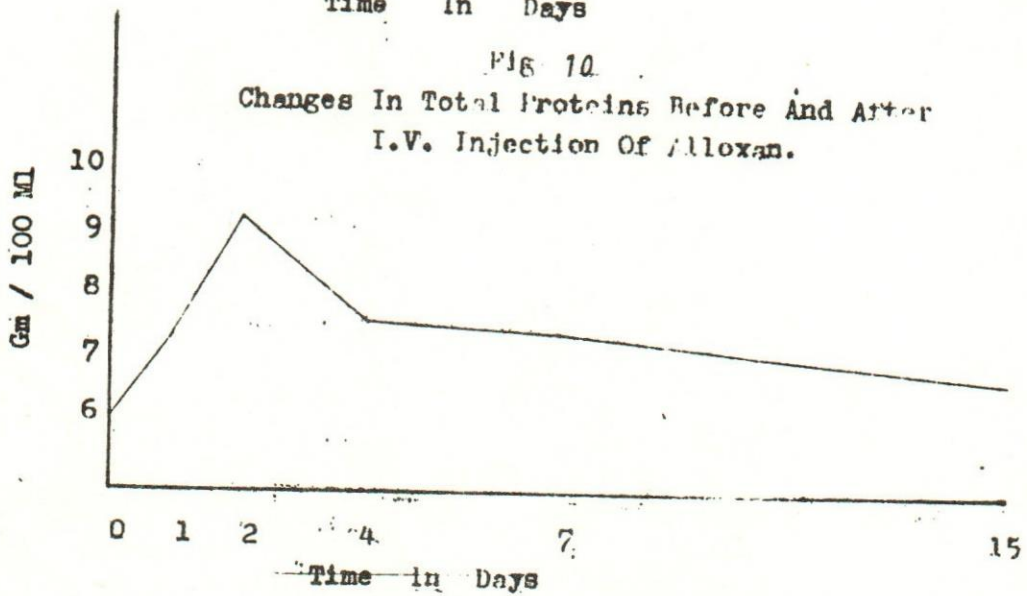


Fig. 10  
 Changes In Total Proteins Before And After  
 I.V. Injection Of Alloxan.



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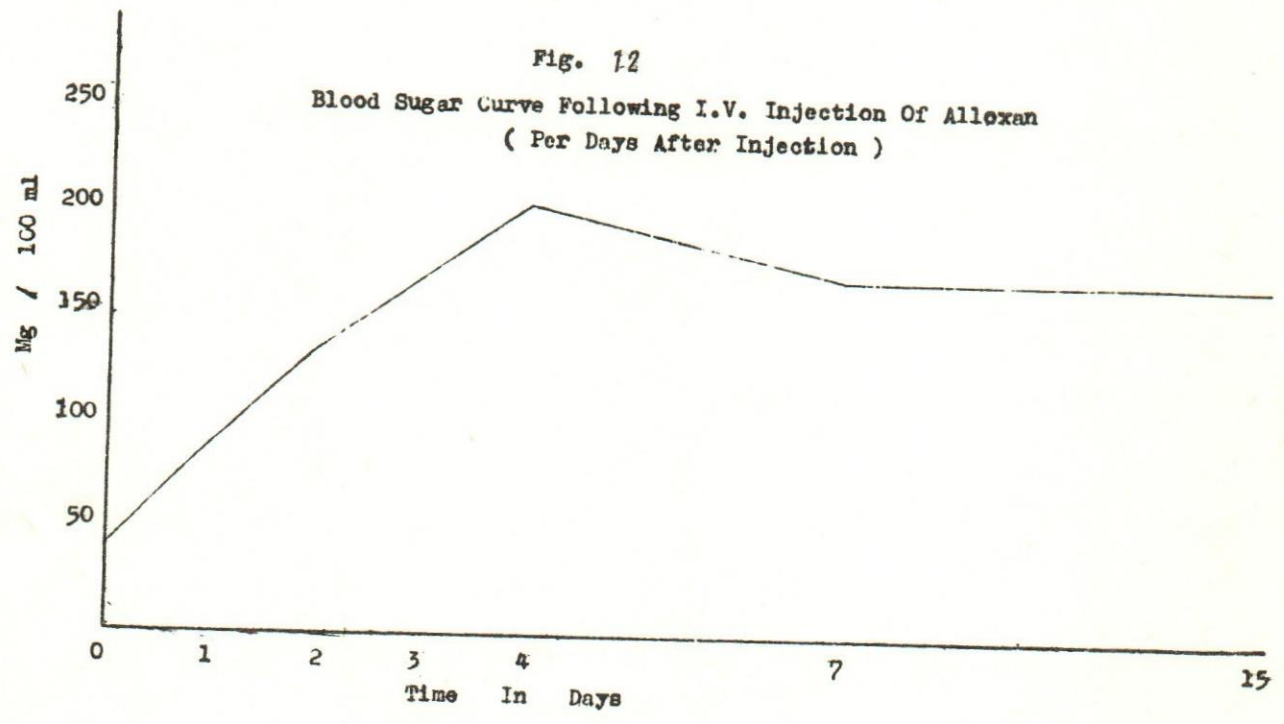
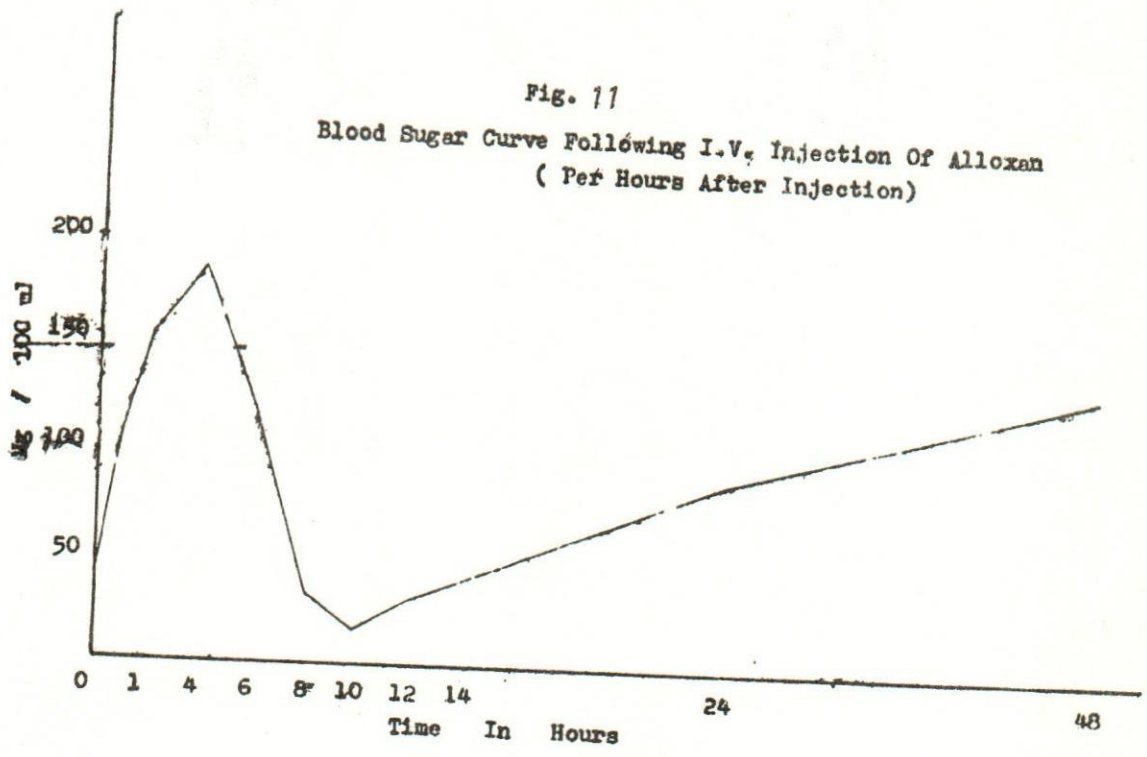


Fig. 11  
 Dependence of the rate of polymerization on the concentration of the initiator



Fig. 12  
 Dependence of the rate of polymerization on the concentration of the monomer



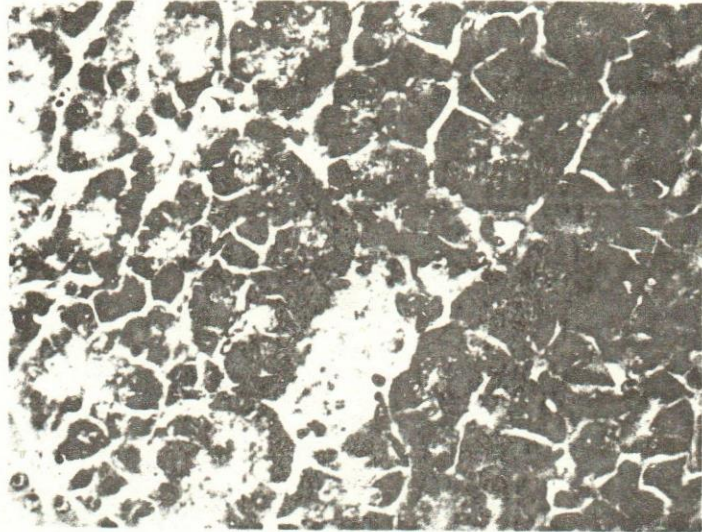


Fig. 13: Pancreas Showing Necrotic Changes in Islets of Langerhans. H&E. (X 40. 12.5).

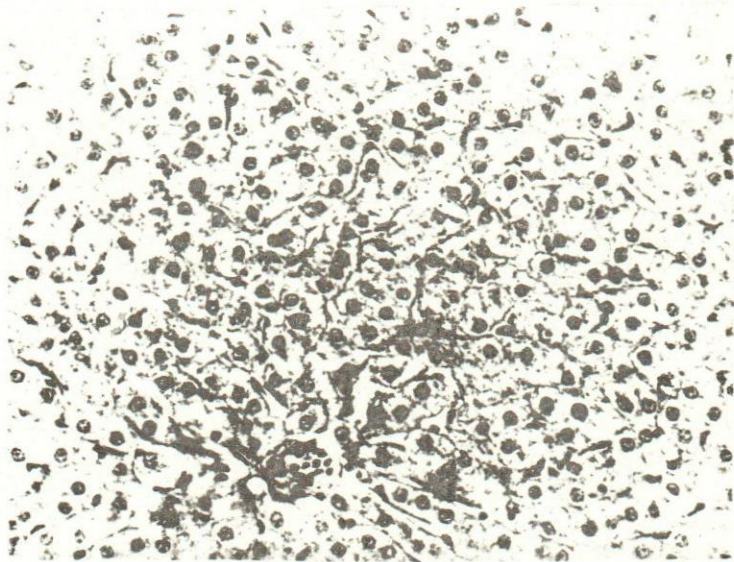


Fig. 14: Liver Showing Dystrophic Changes. H&E. (X 25. 12.5).

