CHAPTER III

EFFECT OF CORTICOSTERONE ADMINISTRATION ON THE METABOLIC ACTIVITIES OF KIDNEY OF BLUE ROCK PIGEON (*COLUMBA LIVIA*)

Glucocorticoids are known to have gluconeogenic and diebetogenic actions in mammals (Ingle, 1952; Welt *et al.*, 1952). Long and Lukens, as early as 1936 reported that adrenalectomy decreased blood glucose concentration in alloxan diabetic rats. Bates and Garrison (1971) have also reported glucosuria in rats treated with corticosterone and dexamethasone either alone or in combination. The effect of glucocorticoid is initiated when the hormone binds to stereospecific intracellular receptor protein in target tissue (Funder *et al.*, 1973). Kidney is one of the target tissues of glucocorticoid over and above being a well characterized target tissue of aldosterone (Herman *et al.*, 1968; Swaneck *et al.*, 1970). Glucocorticoids not only influence intermediary metabolism in the kidney but also play a role in Na^+ homeostasis (Sinha, 1982). One of the major metabolic activities of the kidney is gluconeogenesis (Krebs, 1963) which is greatly influenced by glucocorticoids (Landala, 1960).

Avian kidney is also the predominant gluconeogenic tissue unlike in mammals where liver has a clear edge over kidney. Although, the ultimate machinery that is concerned with

gluconeogenesis may be similar in mammals and birds, the control of gluconeogenesis in the avian kidney especially by corticosterone is not well elucidated. In this context, the involvement of corticosterone in regulating the activities of some of the enzymes concerned with glucose metabolism in the kidney as well as blood sugar level, was investigated in blue rock pigeon.

MATERIALS AND METHODS

Adult, domesticated variety of blue rock pigeons of both sexes weighing around 250-300 gms were used in the experiment. The birds were acclimated to laboratory conditions for two weeks and fed ad libitum. The birds were divided into two groups. Birds of one group were injected with corticosterone (2 µg/gm body weight) dissolved in 0.9 % saline. Control birds received only the vehicle (0.9 % saline). A total of five intraperitoneal injections were given, being administered every alternate day. 24 hrs after the last injection both experimental and control birds were sacrificed by decapitation. Prior to decapitation the blood was drawn from wing vein for measuring the blood glucose level. Kidney was quickly excised and used for enzyme estimations. The enzymes estimated were G-6-Pase, Alkaline phosphatase, acid phosphatase, transaminases (GOT,GPT), Na^+-K^+-ATPase, phosphorylase and LDH. Glycogen and protein contents were also estimated. The methods followed for these estimations are given in Chapter 1.

Table I : Effect of corticosterone injection on the metabolic activities of the kidney of Blue Rock Pigeon (Columba livia).(Mean ± S E)

Parameters	Normal	Control	Experimental
Protein	13.956 ± 1.038	12.274 ± 0.50	17.120 ± 0.786 ***
Alk Pase	1.378 ± 0.191	0.321 ± 0.041	0.183 ± 0.035 NS
Ac Pase	0.834 ± 0.113	0.244 ± 0.020	0.305 ± 0.031 NS
GOT	90.4 ± 21.3	122.89 ± 9.24	126.69 ±13.07 NS
GPT	151.620 ± 26.391	32.93 ± 2.67	59.25 ± 5.65 **
Na^+-K^+-ATPase	133.30 ± 57.20	36.35 ± 1.78	28.28 ± 2.52 NS
Phosphorylase	233.56 ± 21.963	20.57 ± 2.47	252.58 ± 54.07 **
G-6-Pase	0.113 ± 0.022	0.143 ± 0.019	0.167 ± 0.03 NS
LDH	16.50 ± 5.30	7.049 ± 0.532	14.61 ± 1.32 **
Glucose	120.00 ± 6.260	92.57 ± 4.83	178.28 ± 8.05 ***
Glycogen	0.033 ± 0.009	0.034 ± 0.003	0.016 ± 0.003 ***
Body weight	290 ± 4.47	281 ± 4.00	275 ± 8.0
Total Kidney weight	1.59 ± 0.07	1.27 ± 0.07	1.32 ± 0.12

** $P < 0.01$, *** $P < 0.001$, NS - Not significant.

EXPLANATIONS TO GRAPHS - CHAPTER III

Fig.1. Graphs showing the effect of corticosterone administration on glucose level and glycogen content in the kidney of blue rock pigeon.

Fig.2. Graphs showing the effect of corticosterone administration on GOT and GPT activities in the kidney of blue rock pigeon.

Fig.3. Graphs showing the effect of corticosterone administration on acid phosphatase and G-6-Pase activities in the kidney of blue rock pigeon.

Fig.4. Graphs showing the effect of corticosterone administration on Alk Pase and Na^{+}-K^{+}-ATPase activities in the kidney of blue rock pigeon.

Fig.5. Graphs showing the effect of corticosterone administration on LDH activity in the kidney of blue rock pigeon.

Fig.6. Graphs showing the effect of corticosterone administration on phosphorylase activity and protein content in the kidney of blue rock pigeon.

FIG. 1 : EFFECT OF CORTICOSTERONE

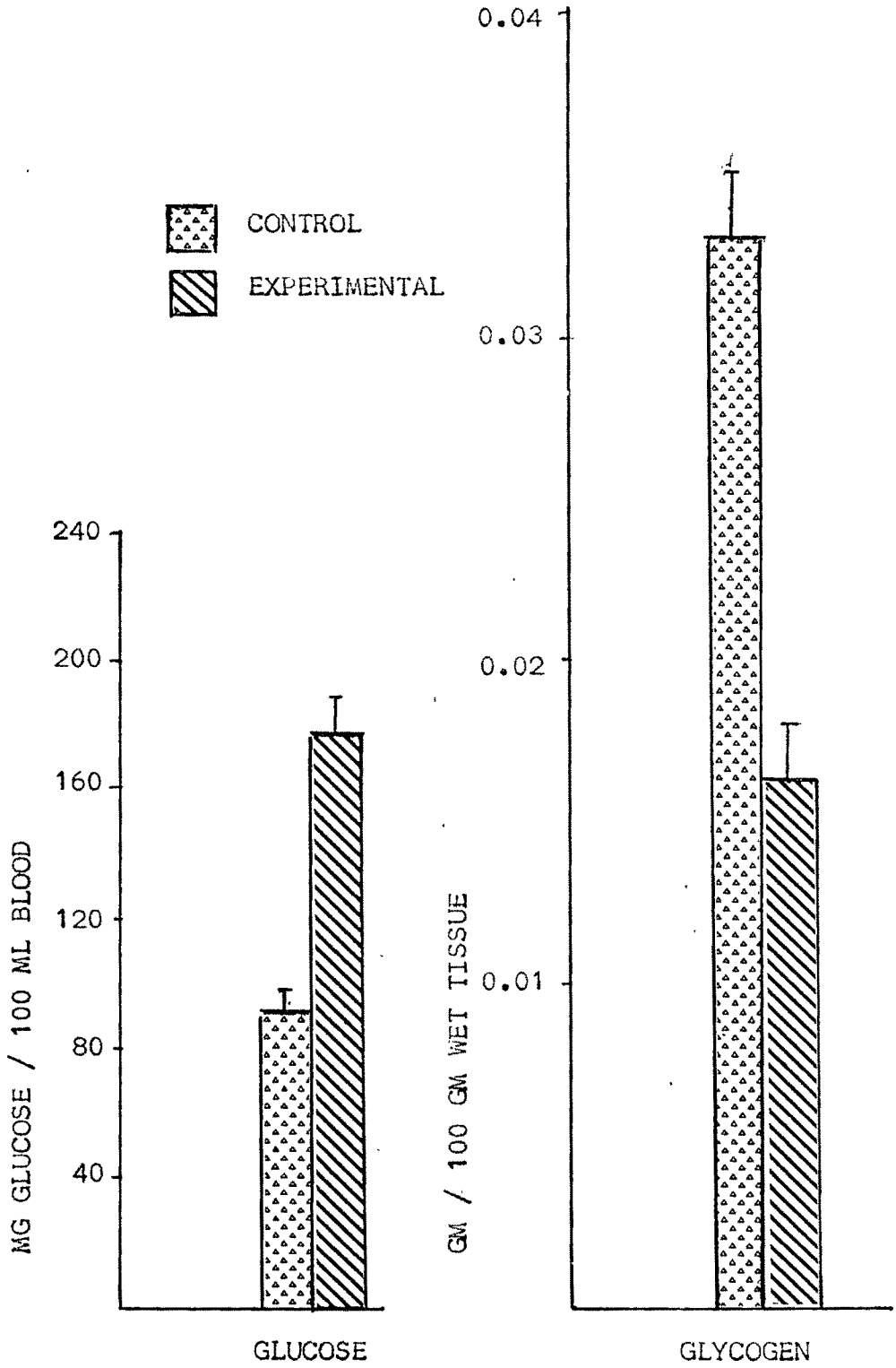


FIG. 2 : EFFECT OF CORTICOSTERONE

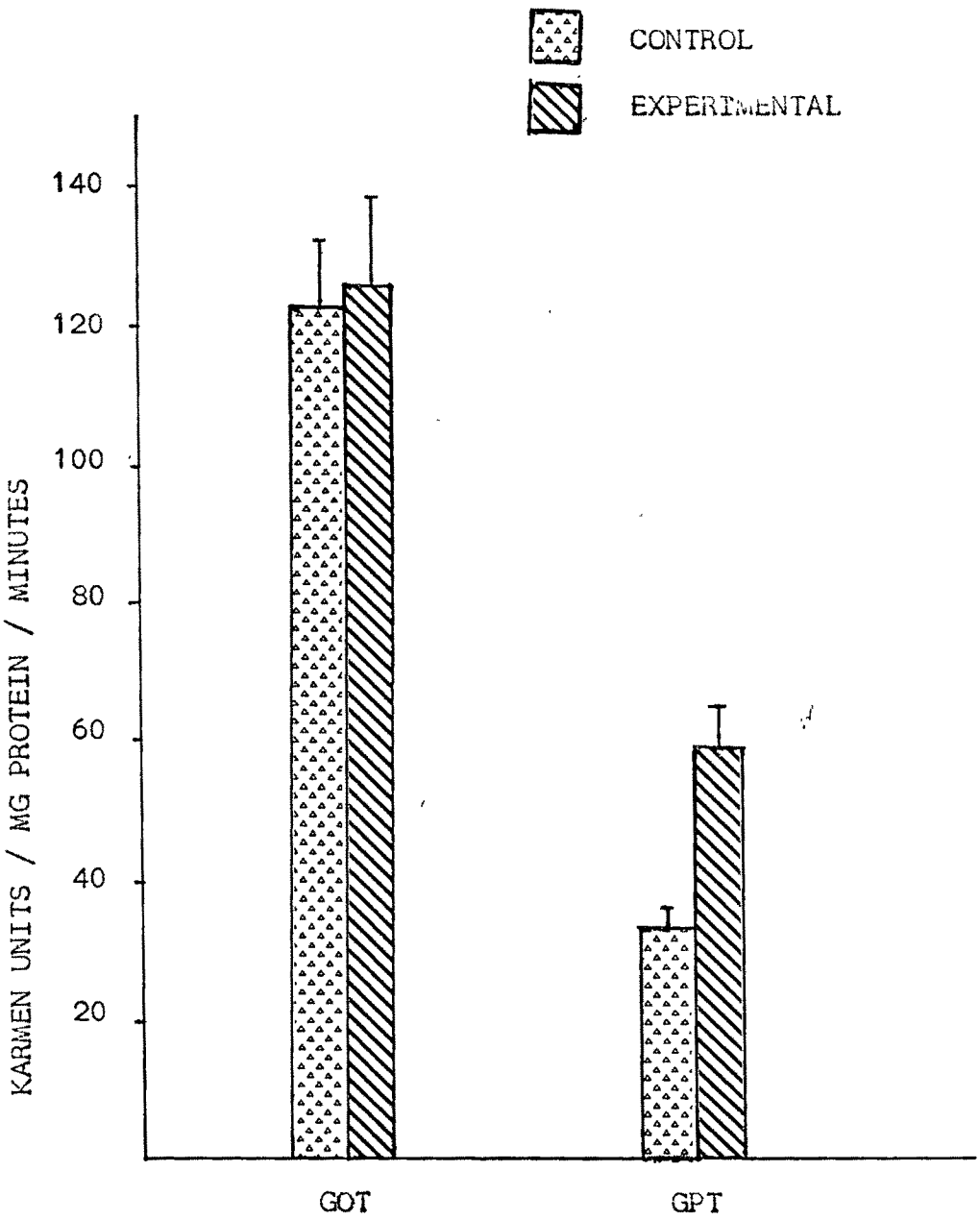


FIG. 3 : EFFECT OF CORTICOSTERONE

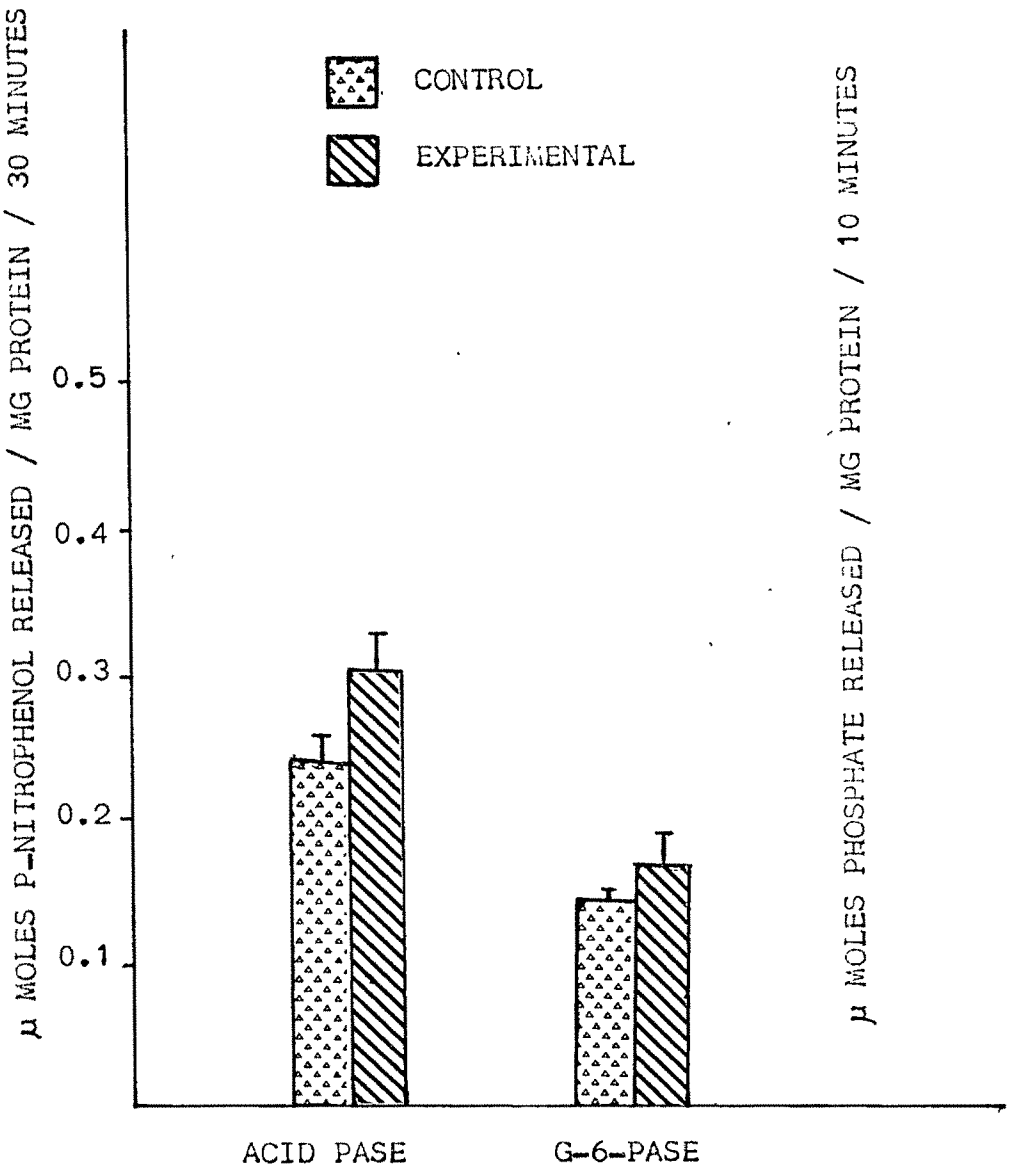


FIG. 4 : EFFECT OF CORTICOSTERONE

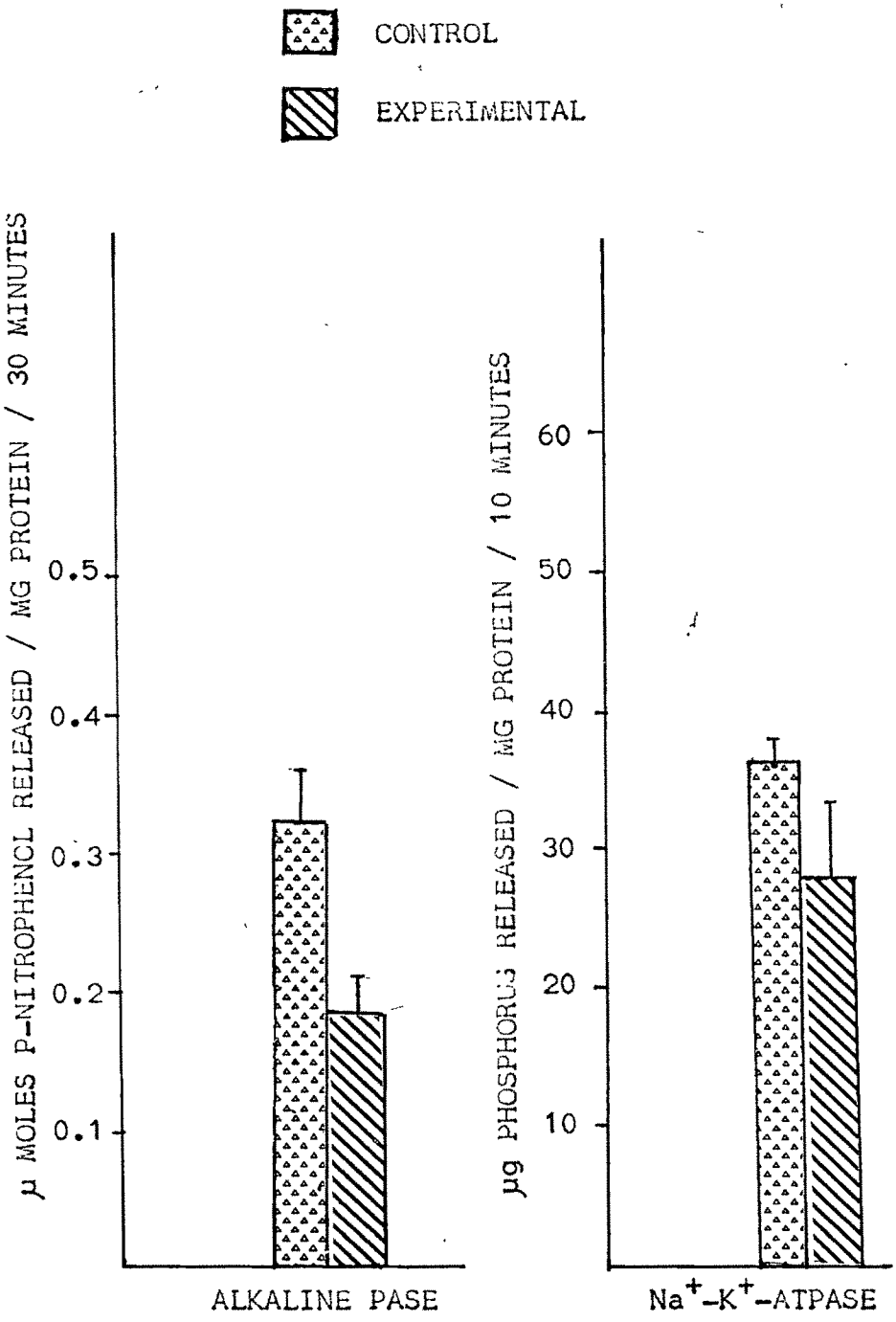


FIG. 5 : EFFECT OF CORTICOSTERONE

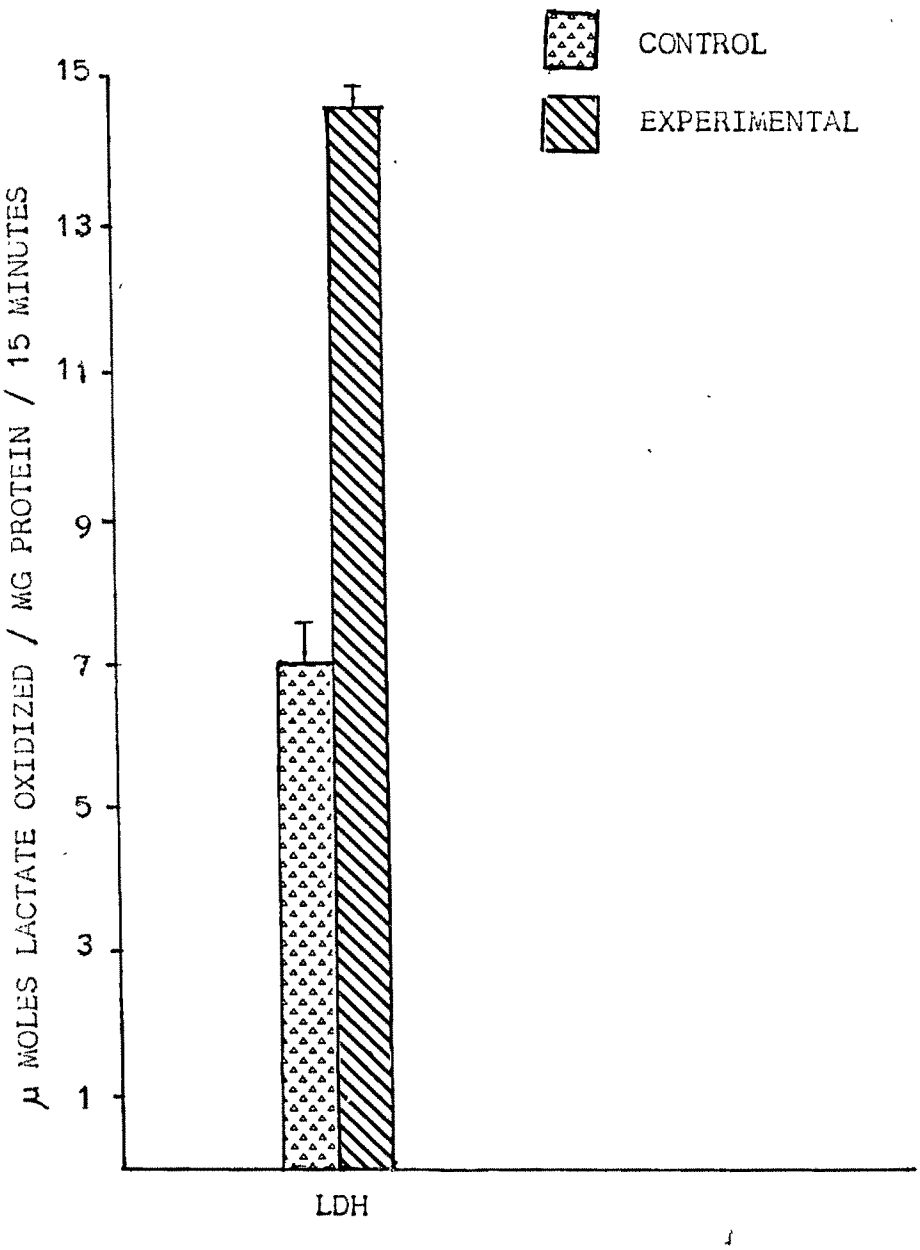
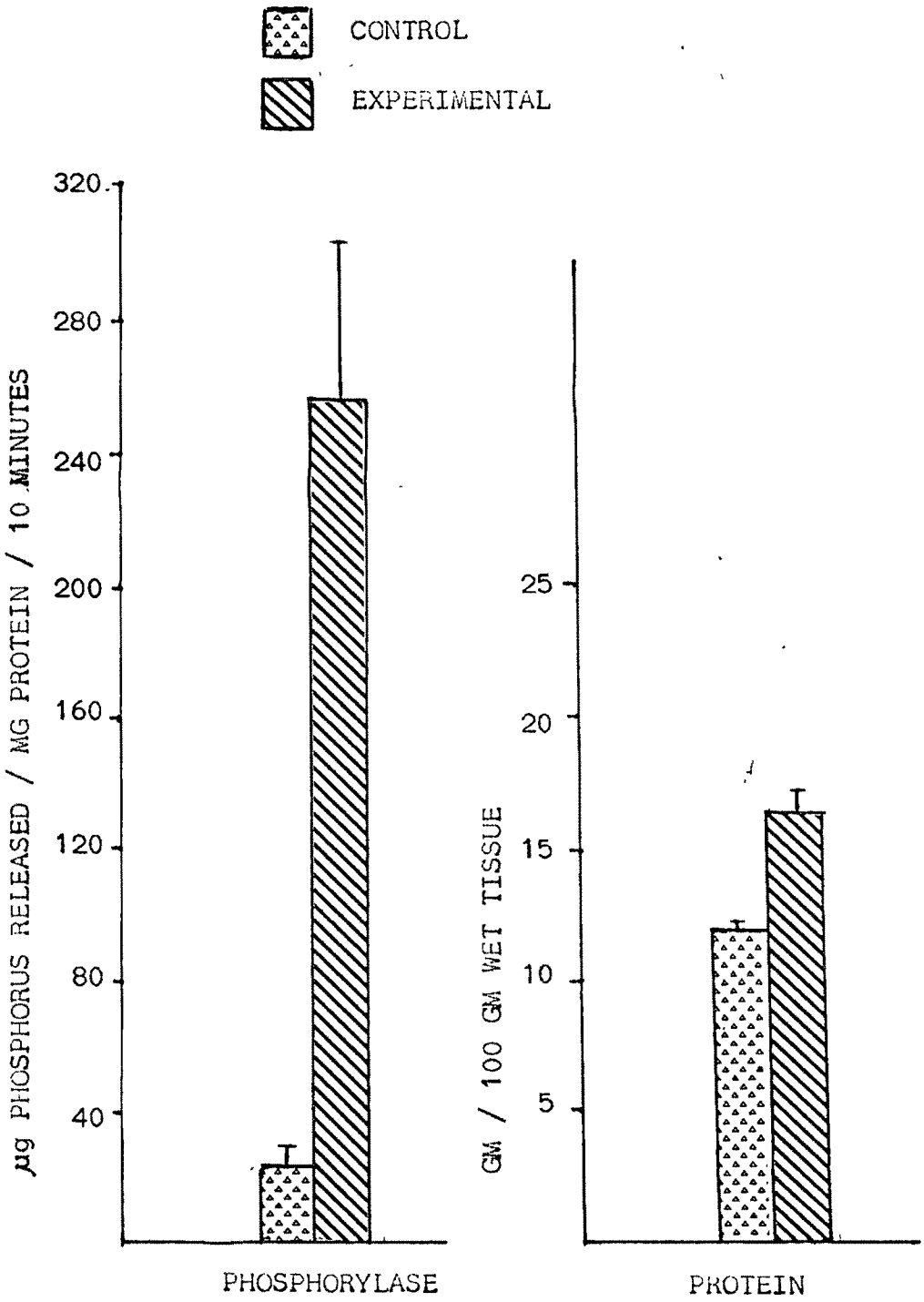


FIG. 6 : EFFECT OF CORTICOSTERONE



RESULTS

Results are presented in Table 1 and Figs. 1 to 6. When the enzyme values of control and experimental pigeon kidney were compared, it was observed that corticosterone administration did not produce any appreciable change in the activity of phosphatases in the kidney of pigeons. G-6-Pase also did not show any significant variation in the experimental pigeon from what was observed in that of control birds. Activity of Na^+-K^+-ATPase too was unaffected by corticosterone administration. Phosphorylase, on the other hand, showed a significant increase in experimental birds. A similar increase was also observed in the activity of LDH in the kidney of corticosterone treated pigeon. Of the two transaminases (GOT and GPT), GPT showed an increase in activity in significant proportion.

Corticosterone administration produced a hyperglycaemic response in pigeons, glucose level increasing from 90.6 in the controls to 178.3 (mg/100 ml) in the experimentals. Kidney glycogen content was found to decrease significantly in experimental birds. Protein value on the other hand showed a significant increase.

DISCUSSION

Elevation of glucose in the blood due to corticosterone treatment indicated this hormone's hyperglycaemic effect. The major portion of extra glucose released into the blood stream might have come from the liver. Since glycogen content of the

corticosterone treated pigeon kidney was found to decrease, it is reasonable to believe that some of the glucose might have originated from kidney too. Kidney slices (Benoy and Elliot, 1937; Krebs, 1963) or perfused kidney (Bahlmann et al., 1965; Nishiit-Sutsuji et al., 1967) are known to release glucose into the medium when incubated or perfused with various gluconeogenic precursors . In the kidney, major part of glucose that is released under corticosterone influence must necessarily be from glycogen, as phosphorylase activity showed tremendous increase. However, there was no increase in the activity of G-6-Pase. Since there is apparently no on/off mechanism of control of glucokinase and glucose-6-phosphatase, these two enzymes are always simultaneously in operation, and both of them are characterized by a k_M that exceeds the usual concentration of either glucose or G-6-P, their activities are essentially being controlled by substrate concentrations (Hers and Hue, 1983). Thus, increase in G-6-P due to high activity of phosphorylase suffices to induce increased release of glucose into blood stream after its dephosphorylation by G-6-Pase. Since the glycogen store is mearge in the kidney, G-6-P may also be generated by gluconeogenesis. One of the most readily available precursor for gluconeogenesis is lactate. In fact, the major role of gluconeogenesis mechanism in normal physiological state (as against starvation) is conversion of lactate into glucose. Corticosterone treatment also induced two fold increase in LDH activity in kidney of

pigeon indicating enhanced conversion of lactate. At the same time a limited elevation of conversion of amino acids into glucose must be also taking place in the kidney. Increased GPT activity to a certain extent indicate this possibility.

Apart from a moderate stimulatory effect on gluconeogenesis, corticosterone must also be inhibiting glucose uptake and its utilization by kidney. All the phosphatases studied were either not effected by corticosterone treatment or are down regulated.

Moderate accelaration of gluconeogenesis was all that could be expected to be induced by glucocorticoids as the birds were not under stress of food deprivation. Moreover, since corticosterone administration was not supplemented with other hormones such as glucagon or catecholamines (which are usually secreted more during starvation), gluconeogemic machinery can not be expected to be activated to its maximum level.

Concerted action of these hormones (corticosterone, glucagon and catecholamines) is essential to elevate gluconeogenic rate to a maximum level. Adrenalectomized rats did not increase their rate of gluconeogenic activity during starvation or diabetes (Exton, 1979). Furthermore, gluconeogenesis was found to be less sensitive to stimulation by glucagon in adrenalectomized animals. The absence of synergic actions of other hormones (glucagon and catecholamines) probably account for the milder effect of corticosterone administration on the gluconeogenesis in the kidney of pigeon.