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Histological and Physiological study of the effect of prazosin hydrochloride on liver and kidney of rats (*Rattus norvegicus*)

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Abstract: This study was conducted at the laboratory of department of biology, faculty of science/university of Kufa, 40 male rats that was used.The present study was conducted to investigate the effect of Prazosin hydrochloride on some organs in male rats (*Rattus norvegicus*), after administration of prazosin hydrochloride at three doses (25,50,75) mg/kgb.wt. for eight-weeks, liver and kidney showed severe histopathological changes, at high doses,the results revealed a significant increase in urea levels from (36.391±1.674 to 82.155±1.448), uric acid levels from (4.376±0.138 to 8.1252±0.0928), and creatinine levels from (1.4262±0.1055 to 3.9324±0.0342), at high doses of prazosin when compared with control groups.
Keyword: Hypertension, Prazosin hydrochloride, liver, kidney.

Introduction

Hypertension is a community healthiness problematic and a term used to describe HBP. It is a disorder that occurs as a result of recurrently raised blood pressure exceeding 140 over 90 mmHg whereby a systolic pressure above 140 with a diastolic pressure above 90.Though, normal blood pressure is below 120/80; interpretations between 12/8 and 139/89 is called pre-hypertension. Systolic blood pressure is the pressure in the arteries as the heart agreements and pumps blood onward into the arteries while diastolic represents pressure as a result to relative of the arteries after contraction.[1,2]. It has been called a silent assassin as it is usually deprived of symptoms. Hypertension takes a long time before diagnosed thereby causing major health problems as stroke and other cardiovascular diseases. Injury to organs as the liver, brain, heart, kidneys and eye and so on are the extended term effect of high blood pressure disease [3].

Prazosin hydrochloride are indicated in the treatment of high blood pressure, can be used alone or in combination with other antihypertensive groups such as diuretics or beta-adrenergic blocking agents[4]. Trazocin, Doxazocin, and Prazosin are a selective alpha-1 receptor blockers that all have similar three α-1 receptors subtypes, this distinguished from other blocker Tamsulosin, study has been that alpha (α1a AR) relieve bladder based irritability symptoms, in contrast blockade of the α-1 b- adrenergic receptors leads to orthostatic hypotension; a side effect associated with non-select alpha blockers[5].

Hypertension is closely related to kidney diseases[6]. The kidney is the major excretory organ in the body. The main function is to filter the blood to remove any potential toxic molecules, metabolic products (such as creatinine and urea) and any extra fluid in order to maintain normal blood volume[7]. The kidney also plays an important role in reabsorbing water and some important molecules such as electrolytes (sodium and potassium) and proteins[8].Blood filtration occurs in the nephron, the functional unit of the kidney[9]. Normally, each kidney

has more than one million nephrons. Each nephron consists of tubules and glomerulus where blood filtration occurs. The glomerulus contains a filtration membrane which consists of three layers: the endothelium, the epithelial podocyte and the basement membrane[10].

Methods:

Preparation of Prazosin Hydrochloride (Miniperss) solution:

The Prazosin was obtained from (Pfizer lab,Germany) at concentration (5mg/kg) , the Prazosin hydrochloride dose (25, 50, 75 mg/kg.b.wt.) were prepared by dissolving (10)g from Prazosin in (100)ml from distill water to make stock solution and different concentration from stock solution were prepared.

Experimental animals:

40 rats (*Rattus*norvegicus) of male sex weighing (210-290)g,the animals were housed in aplastic caged. The caged were embedded with in wooden shelves in the animal house of Faculty of Science, University of Kufa, under standard environment condition (temperature 25-28 ºC and 12 hr,light-dark cycle) and allowed access to standard laboratory water and feed. They were divided in to four groups[10] animals for each group.

Group 1: as a control, animals were treated with (0.5 ml/kg) of distilled water, giveorally,
Group 2: The animals were treated with (0.5 ml) of volume dose from prazosin at concentration25 mg/kg for 8 weeks, giveorally,
Group 3: The animals were treated with (0.5 ml) of volume dose from prazosin at concentration50 mg/kg for 8 weeks, give orally,
Group4: The animals were treated with (0.5 ml) of volume dose from prazosin at concentration75 mg/kg for 8 weeks, give orally.

Measurement of weights:

The weight of male rats were measured by sensitive balance (Shimadzu- Japan), depending on method of[1] 1.

Preparation of histological sections :

We make it depending on method by[12].

Determined of Urea, uric acid, and creatinine Concentration in Serum: by using kits is supplied by biomerieux, France[13].

Bio-statistical analysis:

The results were expressed as (mean ± standard deviation), t- test was used for the comparison between control and other groups in the measured parameters[14].

Results and discussion:

The histological results in figures (2),(3)showed histopathological changes in liver of rats that treated with prazosin at dose respectively 25, 50mg/kg b.wt.for 8-weeks, that represented as hemorrhage spots on the parenchyma of the liver ,as well as degenerative , necrotic cells beside blood clots inside central vein , and irregular central vein, The figures (4),(5),(6),histological section of rats that treated with prazosin at 75mg/kg b.wt. for 8-weeks, blood clots inside central vein, dilation in the central vein, hemorrhage spots, and aggregation of inflammation cells especially lymphocytes, when compared with control.

The histo-pathological changes occurred in the liver of treated rat with prazosin especially in a high dose which lead to liver dysfunction .Hepatic metabolism is a mechanism that converts drugs and other compounds into products that are more easily excreted and that usually have a lower pharmacological activity than the parent compound[15].

Vacuolization of the cytoplasm and nucleus of the liver cells appeared at first in the hepatocytes of the peripheral zone of the hepaticlobules, extending gradually toward the center.This may be due to the direction of the lobular blood supply, vacuolization and damage of liver cells were noted by other investigators following treatment with different agents. Results also showed a remarkable cellular infiltration in the hepatic tissue, abundance of leucocytes, in general, and lymphocytes, in particular, are a prominent response of body tissues facing any injurious impacts, the serum level of AST and ALT were significantly elevated in prazosin treated rats compared with the control group. This elevation is attributed to damaged liver cells since these enzymes are located in the cytosol and released into the blood following liver damage, the data suggest that prazosin is a potential anticancer agent that induces apoptotic in tissue that agree with[16].

The histological results in figure (7) revealed normal structure of kidney, figures(8),(9),showed histopathological changes in kidney of rats that treated with prazosin at dose respectively 25, 50mg/kg b.wt. for 8-weeks, that represented as irregular shape of tubules, hemorrhage spots, necrotic cells of tubules, and sloughing in the epithelial lining of tubules. The histopathology results of this study due to the effect of prazosin in producing kidney damage as clear pathological changes were seen in the glomerulus, tubules, and blood vessels at 8-weeks, besides this, total serum protein was markedly decreased and the uric acid and urea were greatly increased, the cytoplasmic and nucleus vacuolization is mainly a consequence of considerable disturbance in lipid inclusions and fat metabolism occurring during pathological changes. Also, vacuolar degeneration, the Drug concentration in the blood is affected by capillary constriction leading to a decrease inglomerular filtration of that drug which minimizes its effect and protects the tubular cells, may be affect the shrinkage and atrophy of the glomeruli.

The cells of the proximal and distal convoluted tubules became edematous leading to distention and sloughing of most microvilli and destruction of others. These may be due to a decreased reabsorption of the glomerular filtrate which counteracts the toxicity of the drug. damage in the cell lining of the collecting tubules in the kidney of rats when administered excessive quantities of alpha blocker drug prazosin hydrochloride, sever hemorrhage that occur in the tissue due to exudate from blood capillary, a metabolite may be have higher activity as toxic materials. By products of the drugs that are excreted via kidneys may also cause cellular damage leading to kidney dysfunction[17].

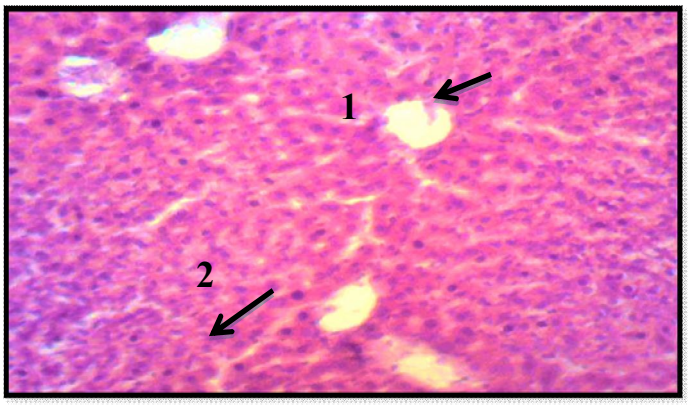
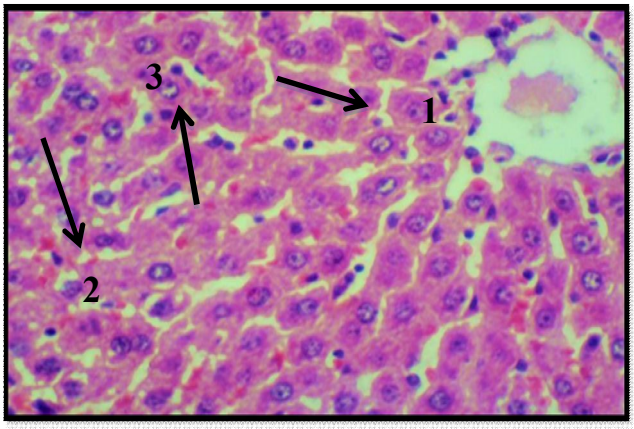
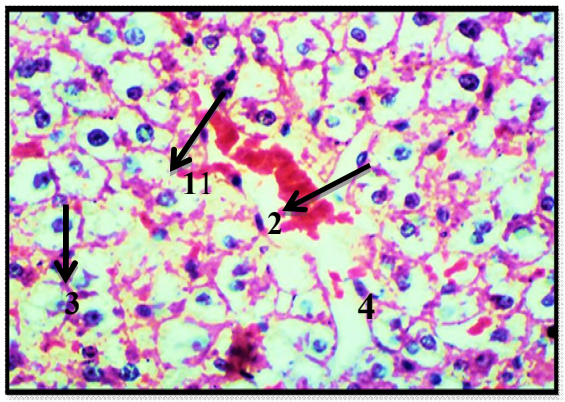


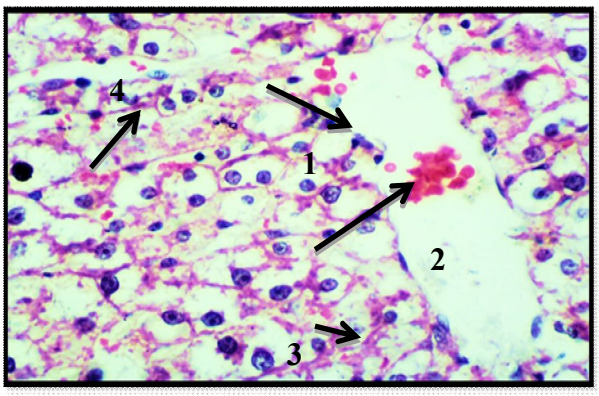
Figure (1) : liver control of rats demonstrated: 1-central vein. 2-hepatic traid.



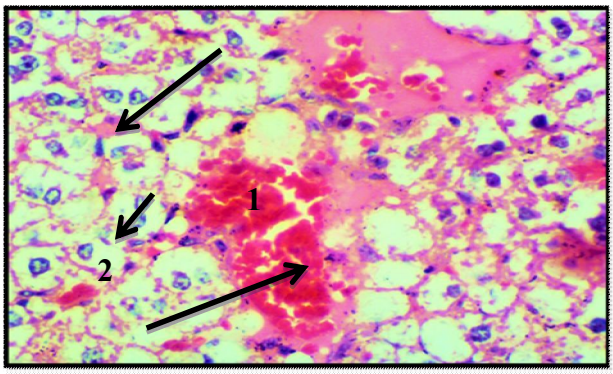
Figure(2): liver section of rats treated with prazosin at dose 25mg/kg. demonstrated:1-irregular shape of central vein. 2- necrotic cells. 3-hemorhage spots like pin heads.(H&E stain X40)



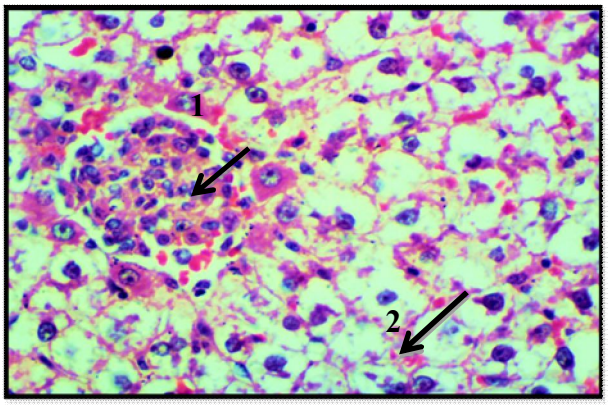
Picture(3):liver section of rat by treated with pz. At dose 50mg/kg. b.wt.strated: 1- blood clot inside central vein.2-irregular shape of central vein.3-necrotic cells. 4- hemorrhage spots.(H&E stain X40).



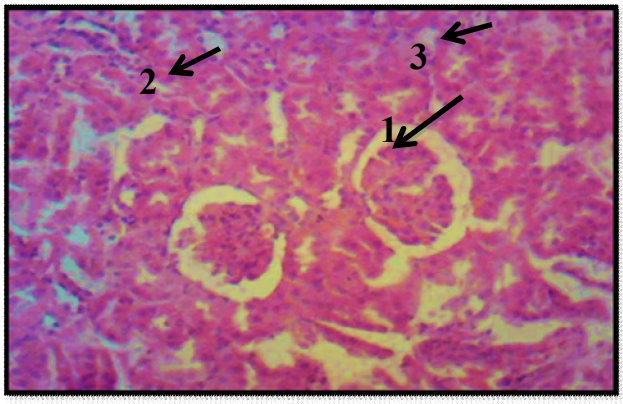
Picture(4):liver section of rats by treated with pz.at 75mg/kg.b.wt. demonstrated: 1- irregular shape of central vein.2- blood clot inside c.v. 3-nectrotic cells. 4-hemorhage spots like pin head.(H&E stain X40).



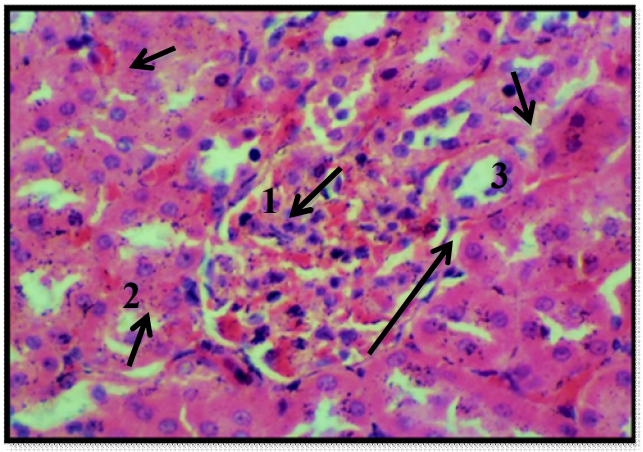
Picture(5):liver section of rats by treated with pz.at 75mg/kg.b.wt. demonstrated: demonstrated:1-blood clots inside tissue.2-nectrotic cells. (H&E stain X40)



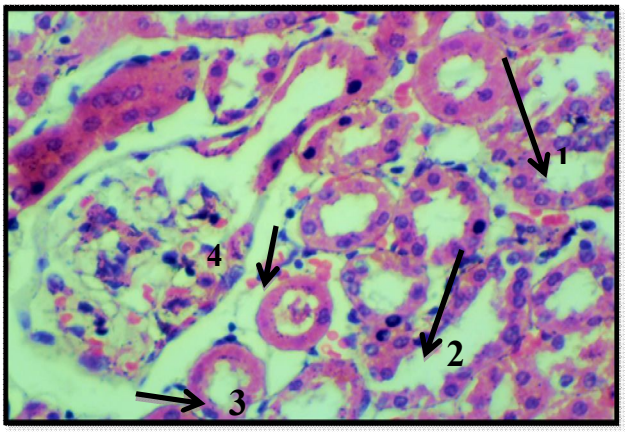
Picture(6): liver section of rats by treated with pz.at 75mg/kg.b.wt. demonstrated: demonstrated: 1-agregation of inflammatory cells (lymphocytes). 2-fatty degeneration. (H&E stain X40)



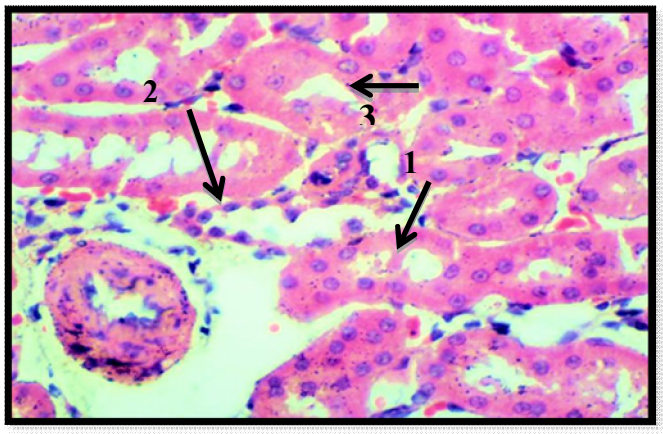
Picture(7): kidney control showed: 1-glomerulus. 2-proximal tubules.3-distal tubules.(H&E stain X40)



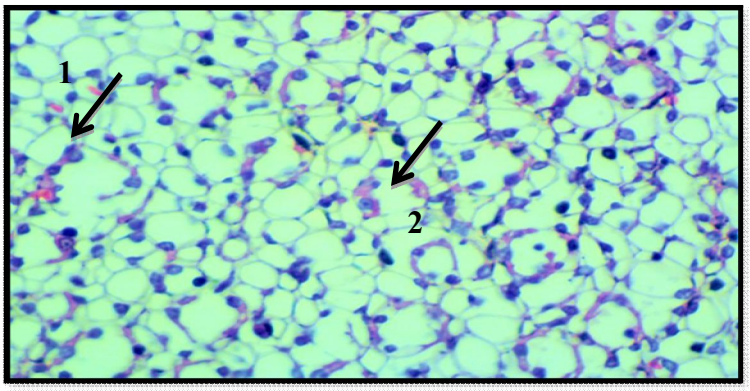
Picture(8):kidney section of rat by treated with pz. At dose 50mg/kg b.wt.demonstrated:1-hemorhage inside glomerulus, and in the other position of tissue. 2- necrotic cells of tubules. 3- irregular shape of tubules (proximal and distal tubules). (H&E stain X40)



Picture(9): kidney section of rat by treated with pz. At dose 50mg/kg b.wt.demonstrated: 1- irregular shape of distal tubules.2-irregular shape of proximal tubules.3-nectrotic cells of kidney tubules. 4-hemorrhage spots.(H&E stain X40)



Picture(10): kidney of rat that treated with pz. at dose 75mg/kg. b.wt. demonstrated: 1-iregular shape of kidney tubules(distal and proximal). 2-necrotic cells. 3- changed the tunica media of germinal artery.(H&E stain X40).



Picture (11):lipomain the medulla of kidney rat that treated with prazosin at dose 75mg/kg.b.wt. demonstrated: adipocytes were distributed among the collecting tubules.1-adipocytes. 2-collecting tubules.(H&E stain x40).

Effect of prazosin on urea uric acid and creatinine measurments:

The results in figures (1), (2), and (3) showed a significant raise ($p<0.05$) in urea, uric acid, and creatinine levels in the group treated with Prazosin when compared with control. Groups of the animals Prazosin at concentrations 25, 50, and 75mg/kg/b.wt. for 8 weeks showed a significant increment in urea and uric acid levels in contrast with control group,the take of Prazosin that caused chronic renal impairment were associated with urea, uric acid and creatinine elevation and considered as indicators of kidney impairment, where the serum creatinine level doesn't rise until at least half of the kidney nephrons are destroyed renal injuries may contribute to low level of serum protein that might have resulted from remarkable release into urine due to inflammation of the glomeruli and tubules or may be attributed to necrosis, in the catabolism of protein after administration of Prazosin, if renal function becomes progressively worse, as indicated by serum creatinine levels, an interruption or discontinuation of thiazide therapy should be considered, creatinine is end products of protein metabolism are widely distributed in the body. Creatinine is found especially in muscles combined with phosphoric acid in the form of creatine phosphate[18] .

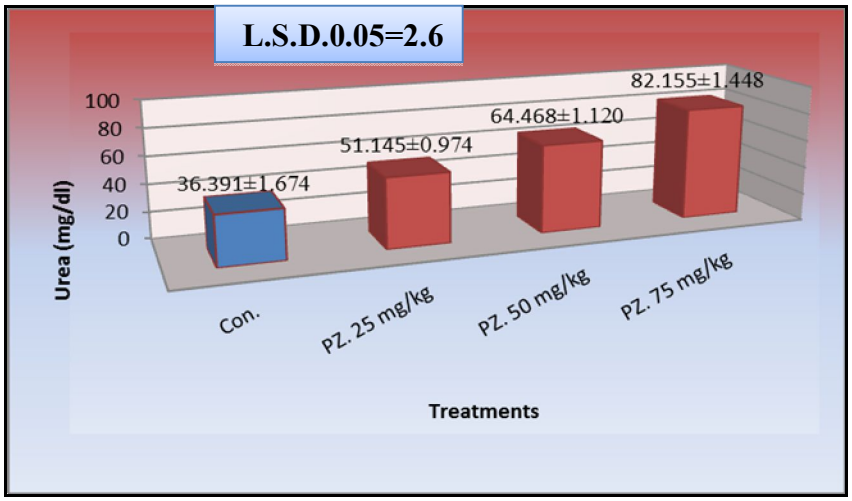


Figure (1): Effect of prazosin at in the serum levels urea in male rats.Values are mean ±SE. *Significantly different at $p<0.05$.

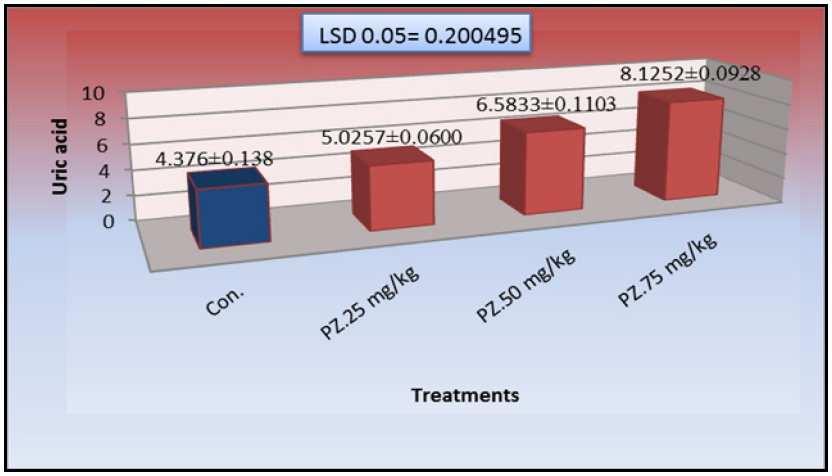


Figure (2): Effect of prazosin at in the serum levels uric acid in male rats. Values are mean ±SE. *Significantly different at p<0.05.

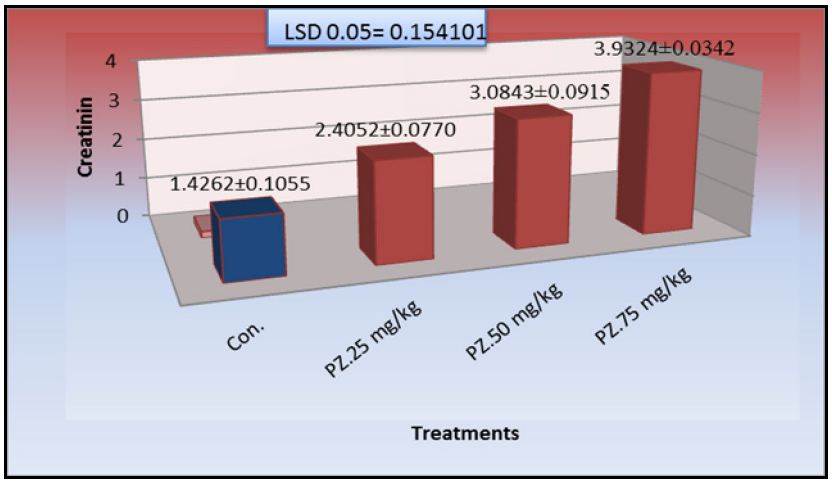


Figure (3): Effect of prazosin at in the serum levels creatinine in male rats. Values are mean ±SE. *Significantly different at p<0.05

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