

## Protective effects of sulpiride treatment on kidney functions of female albino rats exposed to noise stress.

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### Abstract

**Background:** Noise is the most stressful factor for experimental animals. So these studies aim to clarify its effect on some physiological and histological parameters.

**Material and methods:** 36 Female rats were divided into four groups (6/each):1-control, 2-treated with sulpiride drug,3- noise exposure (90db/3h per day for 30days), 4-noise + drug

**Results:** drug recorded no significant change in all the studied parameters. Noise stress recorded a significant increase in creatinine, total lipids, TG, Cholesterol, HDL-C, LDL-C and no significant changes in urea, uric acid.

It has been detected that sulpiride drug ameliorated most of these parameters. Concerning the histological and histochemical studies sulpiride treatment showed no detectable changes in the kidney tissue with exception of increased lymphocytes. Exposure to noise showed many dystrophic changes in the kidney tissue, but drug treatment improved all the previous changes and this indicates the protective effect of sulpiride against noise exposure.

**Conclusion:** It is useful to use sulpiride drug in people who exposed to noise stress.

**Key words:** Noise,Sulpiride drug , Albino rats, Physiological parameters, Histopathology and histochemistry.

### Introduction

Stress as noise is a part of everyone's life every day. From getting kids ready for school to fighting traffic to the demands of work, the average person goes up against the nemesis called stress multiple times daily. From waking up to sleeping our bodies are in a constant battle to maintain the balance. Noise is a kind of stress which is defined as unwanted sound. Noise is a pervasive aspect of many modern community and work environments. Acute noise exposures activate the autonomic and hormonal systems, leading to temporary changes such as increased blood pressure, increased heart rate and vasoconstriction. After prolonged exposure, susceptible individuals in the general population may develop permanent effects, such as hypertension and ischemic heart disease that are associated with exposures to high sound pressure levels. (Tomoyuki, 2004).

According to Samson *et al.* (2006) noise exposure over 90 decibel (db) becomes a stressor and contributes to the genesis and manifestation of several multifactorial diseases, chronic annoyance and permanent behavioral alterations.

Antidepressant drugs are the most successful drug in patients with clearly defined characteristics including psychomotor retardation, sleep disturbance, poor appetite and weight loss. However, a variety of different chemical structures have been found to have antidepressant activity. Their number is constantly growing, but as yet no group has been found to have a clear therapeutic advantage over the others (Katzung, 2008). Sulpiride is the most favorite drug which is used to tolerate stress symptoms (Panzani *et al.*, 2011).

People exposed to stress take one or some drugs to avoid the effect of stress even without a doctor's prescription. So, in this study we try to illustrate the effect of

one of the antidepressant drugs (**sulpiride**) which is generally used by people to avoid the effect of stress. The present study deals with the possible protective effect of sulpiride against noise in female albino rats from the physiological, histological and histochemical points of view.

## Material and Methods

### **1-Experimental animals:**

36 Normal white female albino rats weighing (150±30) gms were taken from the farm of National organization for control and Research. They were kept under observation for one week before the beginning of the experiment to acclimatize. The chosen animals were housed in cages and exposed to artificial light for 14hrs and 10hrs complete darkness at normal atmospheric temperature. All animals were fed on standard diet contained protein, fibers, fats, ash, carbohydrates, and supplied with vitamins and minerals mixture with continuous supply of water.

### **2-Sulpiride administration:**

The drug was administered orally by gastric tube at a dose of 0.28mg/100mg body weight/day for one month. The dose for the rat was calculated according to the Paget's formula on the basis of the human dose (**Paget and Barns,1964**)

## Methods:

### **(I) Animal groups:**

24 female albino rats were divided into 6 main groups each group contained 6 rats.

**Group1:** Normal rats served as negative control (without any treatment for one month).

**Group 2:** Rats treated with the sulpiride drug at dose of (0.28mg/100mg body weight/day for one month).

**Group 3:** Rats exposed to noise only for one month over 90dB,3h/day.

**Group 4 :** Rats exposed to noise and treated with the drug for one month.

### **a)Application of noise:**

Prepared Noise was applied by 5 different sources of unharmonic and high intensity music.

### **Physiological studies:**

Serum urea and creatinine were measured according to the method of Junge *et al.*(2004), serum uric acid was done using the method of Tietz (2006). Total lipid concentration was done according to the method of Knight *et al.*(1972), serum cholesterol level was measured according to the method of Tietz (1995), serum Triglycerides(TG) was done according to the method of Stein and Myers(1995), serum HDL-cholesterol and LDL-C were measured according to method of Sugiuchi (2005).

### **Data analysis:**

The obtained results were statistically analyzed by using the student (T test) according to the method of Snedecor and Cochran (1980), P<0.05 considered significant while P<0.01 highly significant.

### **Histological and histochemical studies:**

Rats from control and treated groups were sacrificed after month and small pieces of kidney was taken for the histological and histochemical studies. Small pieces of kidney was fixed in 10% neutral buffered formal solution and Carnoy's fluid for the histological and histochemical studies. Paraffin section were prepared 5µm thickness and stained with Harris haematoxylin and eosin (**Drury and Wallington, 1980**). Proteins were detected by mercuric bromophenol blue method (**Mazia et al.,1953**). Polysaccharides were detected by PAS (periodic acSchiff)method (**Pearse,1977**). Mallory's trichome stain for demonstrating collagen fibers (**Pearse,1977**).

## Results

Uric acid and Urea no significant change were recorded in all groups (table 1.2).

**Table (1): serum Uric acid(mg/dl) in female albino rats after exposure to stress (noise) sulphiride , dual effect.**

parameter		Group			
		control	drug	Noise alone	Noise +drug
Uric acid (mg/dl)	Mean	3.4	3.4	3.05	3.1
	±SE	0.15	0.19	0.09	0.05
	P		N.S	N.S	N.S
%Of change			0	-10.2	-8.8

**Table (2): serum Urea level (mg/dl) in female albino rats after exposure to stress (noise) sulphiride, dual effect.**

parameter		Group			
		control	drug	Noise alone	Noise +drug
Urea (mg/dl)	Mean	28.7	28.7	26.1	27.2
	±SE	1.5	1.2	1.6	1.7
	P		N.S	N.S	N.S
%Of change			0	-9.0	-5.2

**Table (3): serum Creatinine level (mg/dl)in female albino rats after exposure to stress (noise) sulphiride , dual effect.**

parameter		Group			
		control	drug	Noise alone	Noise +drug
Creatinine (mg/dl)	Mean	0.55	0.48	1.9	1.7
	±SE	0.04	0.1	0.2	0.1
	P		N.S	<0.05	<0.05
%Of change			-11.7	225	192

Both groups of rats (exposed to noise or noise + drug) showed significant increase ( $P < 0.05$ ) when compared with control group (Table 3).



**Table (4): serum Total lipid level (mg/dl) in female albino rats after exposure to stress (noise) sulpiride , dual effect.**

parameter		Group			
		control	drug	Noise alone	Noise +drug
<b>Total lipid (mg/dl)</b>	<b>Mean</b>	<b>197</b>	<b>195</b>	<b>210</b>	<b>203</b>
	<b>±SE</b>	<b>1.8</b>	<b>1.4</b>	<b>1.6</b>	<b>1.3</b>
	<b>P</b>		<b>N.S</b>	<b>&lt;0.01</b>	<b>&lt;0.05</b>
<b>%Of change</b>			<b>-1.0</b>	<b>6.5</b>	<b>3.0</b>

Table (4) noise exposure group was highly significant increase (P<0.01) and noise exposure and treated with sulpiride showed significant increase (P<0.05) when compared with control group.

**Table (5): serum Triglycerides level(mg/dl) in female albino rats after exposure to stress ((noise) sulpiride , dual effect.**

parameter		Group			
		control	drug	Noise alone	Noise +drug
<b>Triglycerides (mg/dl)</b>	<b>Mean</b>	<b>66.6</b>	<b>68.1</b>	<b>103.3</b>	<b>96.3</b>
	<b>±SE</b>	<b>1.5</b>	<b>1.2</b>	<b>1.6</b>	<b>1.7</b>
	<b>P</b>		<b>N.S</b>	<b>&lt;0.01</b>	<b>&lt;0.01</b>
<b>%Of change</b>			<b>2.2</b>	<b>55.1</b>	<b>44.5</b>

**Table (6): serum Cholesterol (mg/dl) level in female albino rats after exposure to stress (noise) sulpiride, dual effect.**

parameter		Group			
		control	drug	Noise alone	Noise +drug
<b>Cholesterol (mg/dl)</b>	<b>Mean</b>	<b>118.1</b>	<b>115</b>	<b>169.4</b>	<b>132</b>
	<b>±SE</b>	<b>1.9</b>	<b>1.4</b>	<b>1.6</b>	<b>1.8</b>
	<b>P</b>		<b>N.S</b>	<b>&lt;0.01</b>	<b>&lt;0.01</b>
<b>%Of change</b>			<b>-2.6</b>	<b>43.4</b>	<b>11.7</b>

**Table (7): serum HDL- Cholesterol level (mg/dl) in female albino rats after exposure to stress (noise) sulpiride , dual effect.**

parameter		Group			
		control	drug	Noise alone	Noise +drug
<b>HDL- Cholesterol (mg/dl)</b>	<b>Mean</b>	<b>65.3</b>	<b>62.0</b>	<b>77</b>	<b>69.9</b>
	<b>±SE</b>	<b>1.6</b>	<b>1.6</b>	<b>1.2</b>	<b>2.0</b>
	<b>P</b>		<b>N.S</b>	<b>&lt;0.01</b>	<b>&lt;0.01</b>
<b>%Of change</b>			<b>-5.0</b>	<b>17.9</b>	<b>7.0</b>

Data represented in tables (5,6,7,8) showed that (TG,HDL-C, LDL-C) levels of noise exposure group or noise exposure and treated with sulpiride recorded highly significant increase ( $P<0.01$ ) of the (TG,HDL-C, LDL-C) level when compared with control group.

**Table (8): serum LDL- Cholesterol (mg/dl) level in female albino rats after exposure to stress (noise) sulpiride , dual effect.**

parameter		Group			
		control	drug	Noise alone	Noise +drug
<b>LDL- Cholesterol (mg/dl)</b>	<b>Mean</b>	<b>51.1</b>	<b>49.2</b>	<b>91.4</b>	<b>60.1</b>
	<b>±SE</b>	<b>3.3</b>	<b>2.5</b>	<b>2.4</b>	<b>2.0</b>
	<b>P</b>		<b>N.S</b>	<b>&lt;0.01</b>	<b>&lt;0.01</b>
<b>%Of change</b>			<b>-3.7</b>	<b>0.8</b>	<b>17.6</b>

Regarding LDL/HDL -Cholesterol no significant change were recorded in all groups (table 9).

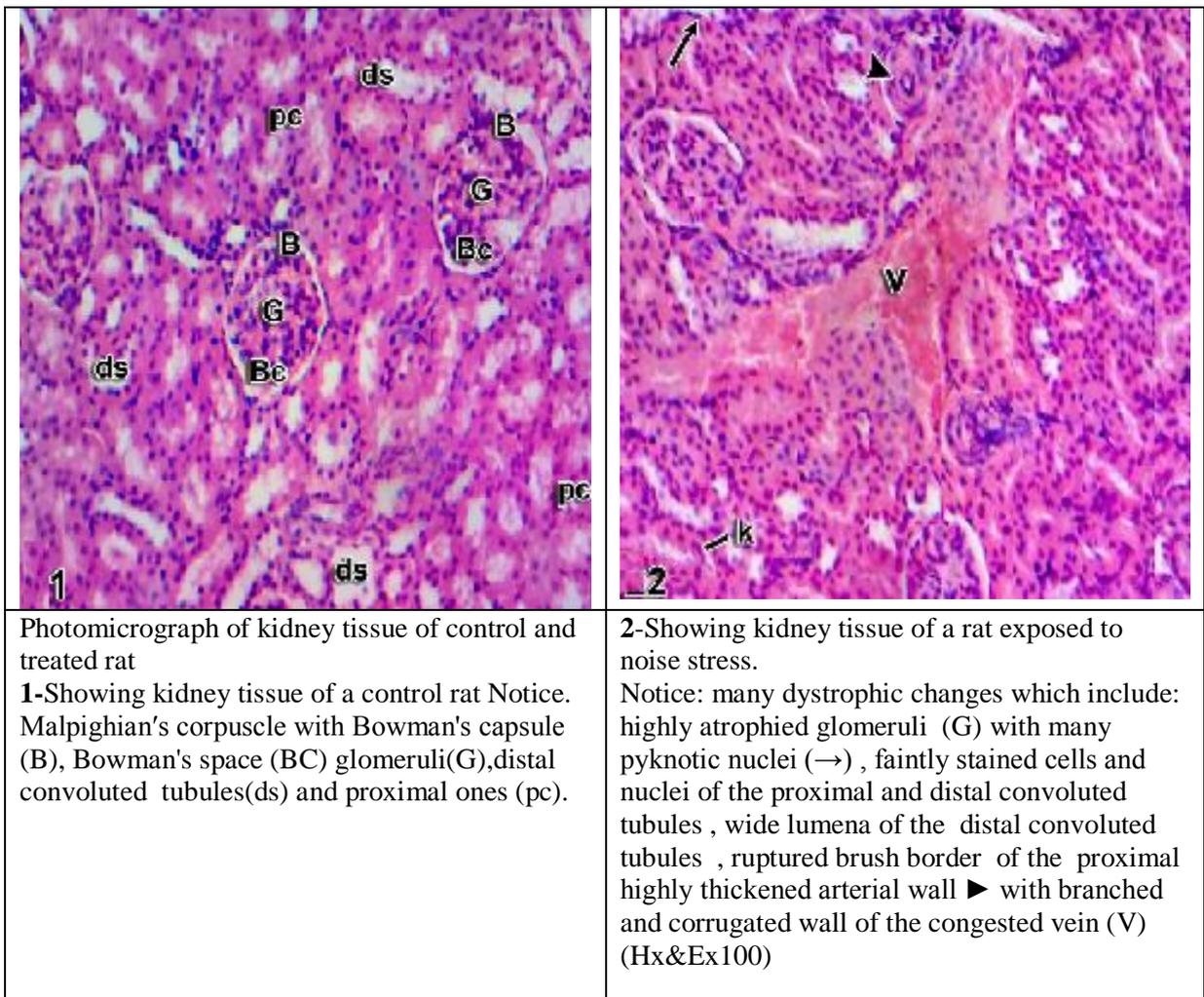
**Table (9): serum LDL/ HDL- Cholesterol (mg/dl) level in female albino rats after exposure to stress (noise) sulpiride , dual effect.**

parameter		Group			
		control	drug	Noise alone	Noise +drug
<b>LDL/HDL- Cholesterol (mg/dl)</b>	<b>Mean</b>	<b>0.8</b>	<b>0.8</b>	<b>1.2</b>	<b>1.2</b>
	<b>±SE</b>	<b>0.8</b>	<b>0.1</b>	<b>0.1</b>	<b>0.2</b>
	<b>P</b>		<b>N.S</b>	<b>N.S</b>	<b>N.S</b>
<b>%Of change</b>			<b>0</b>	<b>0.5</b>	<b>0.5</b>

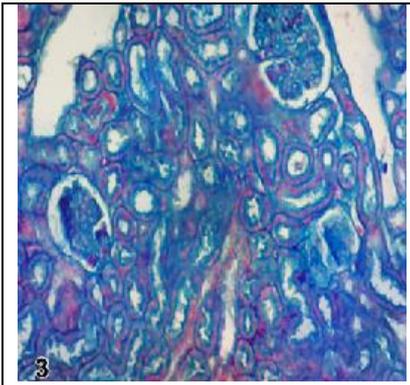
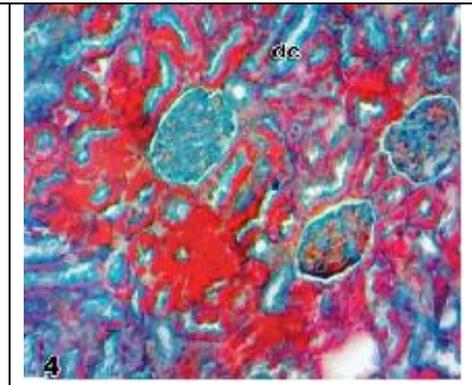
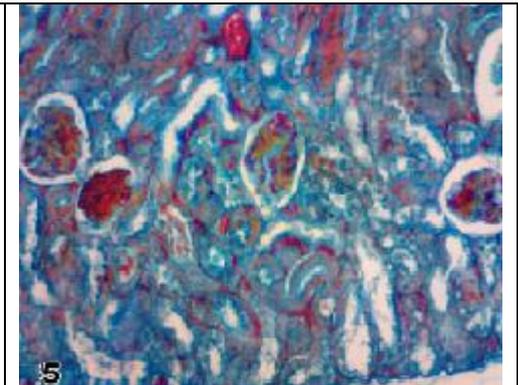
Drug treatment showed no detectable histological or histochemical changes in liver or kidney tissues with the exception of increased lymphocytes especially in the portal area of the kidney tissue.

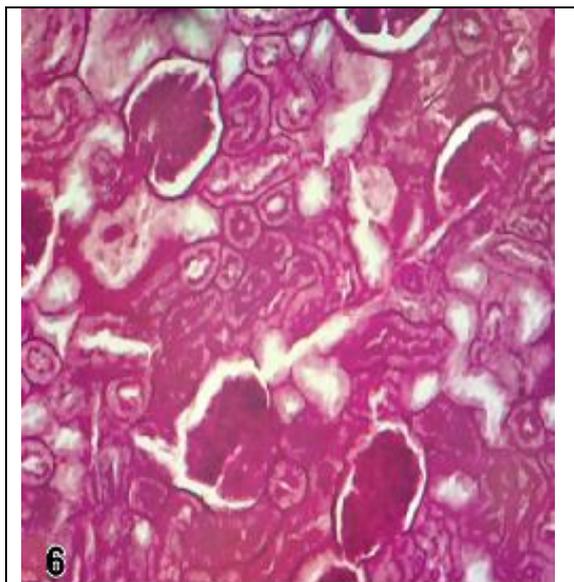
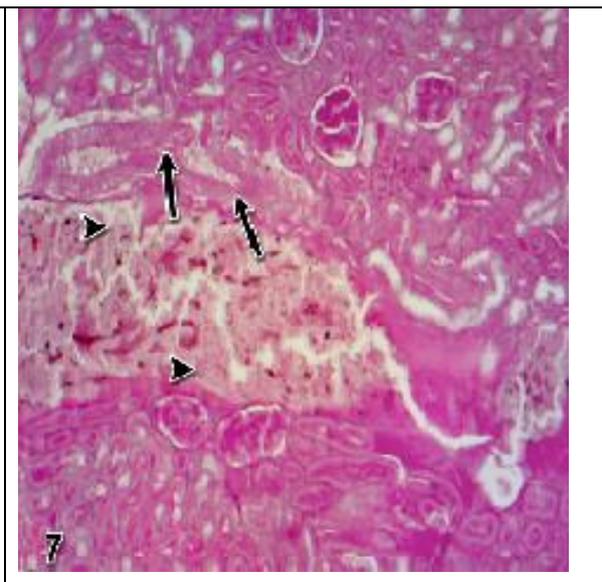
Exposure of rats to noise showed several dystrophic changes in the kidney tissue compared with the control group (Fig. 1). These changes include: highly atrophied glomerulus's, faintly stained cells and nuclei of the convoluted tubules with wide lumina of the distal ones, ruptured brush borders of the proximal ones, thickened arterial walls with branched and corrugated walls of the congested vein. Kidneys of group noise + drug showed normal histological appearance .Increased collagen fibers were realized in the kidney tissue of noise group (Fig. 4) compared with the control group (Fig. 3). Also

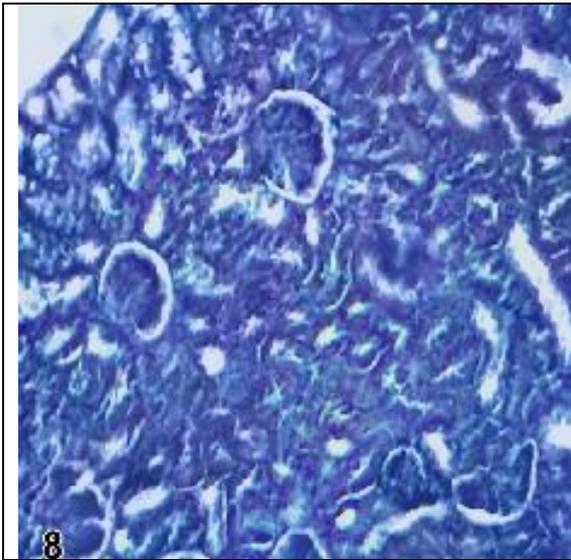
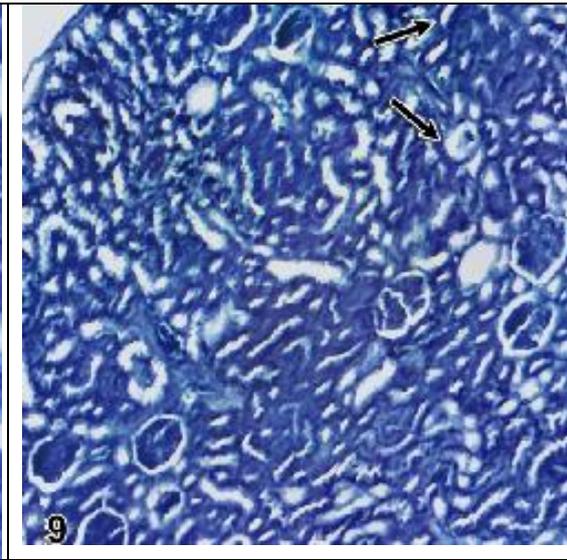
kidney tissue of group noise+ drug showed also increased collagen fibers in the convoluted tubules and Bowman's capsules (Fig. 5) .Kidney tissue of noise group showed poor stain affinity of PAS +ve materials in the haemolysed RBCs (Fig. 7) with moderately stained tunica media and adventitia of the highly distorted renal artery compared with the control group (Fig. 6) . Kidney of group noise+ drug showed normal stain affinity of PAS+ ve materials. Poorly stained glomeruli of the kidney cortex of noise group were detected, but some of them were atrophied and deeply stained (Fig. 9) compared with the control one (Fig. 8), also convoluted tubules were faintly stained .Drug treatment post- exposure to noise returned total protein to the normal level.





		
<p><b>3:</b> Showing thin collagen bundles supporting walls of the blood vessels, proximal and distal C.T, blood capillaries and Bowman's capsules of kidney tissue of a control rat. <b>(Mallory's trichrome stain x100)</b></p>	<p><b>4:</b> -Showing highly increased collagen fibers in the walls of the distal convoluted tubules (dc) and inside the glomeruli . Common fibrosis was detected in most proximal C.T and numerous brightly stained hemorrhagic areas in the kidney tissue of a rat exposed to noise stress. <b>(Mallory's trichrome stain x100)</b></p>	<p><b>5:</b> - Showing increased collagen fibers in between and around <b>cells</b> of the convoluted tubules and the Bowman's capsule of the kidney of a rat exposed to noise and treated with the drug. <b>(Mallory's trichrome stain x100)</b></p>

	
<p><b>6-</b> Showing normal distribution of polysaccharides in the kidney cortex of a control rat. deeply stained glomeruli , Bowman's capsules ,brush border of The proximal C.T and cells of the distal C.T, but cells of the proximal ones were less stained. <b>(PASx100)</b> .</p>	<p><b>7:</b> Showing distribution of polysaccharides in the kidney cortex of a rat exposed to noise. moderately stained tunica media and adventitia of highly elongated and distorted renal artery (→), faintly to moderately stained endothelial lining of the vein (&lt;) which contained poorly stained haemolysed RBCs. <b>(PASx100)</b></p>

	
<p><b>8:</b> Showing normal distribution of total protein in the kidney tissue of a control rat. Deeply stained glomeruli, cells of the proximal and distal convoluted tubules with less stained brush border. (<b>Mercuric bromophenol blue x100</b>)</p>	<p><b>9:</b> Showing total protein in the kidney tissue of a rat exposed to noise stress. Some atrophied glomeruli were deeply stained, while some of them were poorly stained (→), some convoluted tubules were faintly stained. (<b>Mercuric bromophenol blue x100</b>)</p>

## Discussion

### 1-Kidney functions test:

The present study showed significant increase ( $p < 0.05$ ) in serum creatinine in rat exposed to noise, noise+ drug. The abnormal out comes in the present study could have resulted from kidney function impairment such as generation in the poroximal convoluted tubules (**Senior, 2009**).

(**Matsumoto et al., 2009**) recorded an increase in creatinine serum in rat exposed to noise stress which may be due to increase catabolism in muscle and tissue that appear to act as a stimulus to synthesis of more serum creatinine.

According to **Andrey(2010)** noise stress causes hyperthyroidism which is one of the disease characterized by disturbances creatinine metabolism. Consequently it is of interest that hypothyroidism also associated with reduced kidney transaminase activity. It may be that the effect of hyperthyroidism on kidney transamedinase is actually mediated by the increase level of blood creatinine which occur in the disease.

### 2-lipid profile:

The present results revealed that plasma lipid significantly increased when exposed

to noise stress in adult female rats .Plasma lipid response to stress varies from stressor to other according to severity and combination of more than stressor (**Willis et al.,2009**) .The alteration in plasma lipid depends on the type and severity of stress as well as several individual characteristics , such as heightened neuroendocrine or autonomic reactivity to stressors. So, stress may influence lipid concentration and metabolic thought variety of physiological and behavioral mechanisms (**Blumenth et al,2000**).

**Radahmadi et al. (2006)** demonstrated that all type of plasma cholesterol levels increased in response to stress particularly LDL-C which constitutes the bad type of cholesterol. **Brenna et al. (1992)** mentioned that stress induced increase in plasma level of cholesterol and triglyceride. **Willis et al. (2009)** mentioned that stress induced an elevation in serum total cholesterol concentration which may persist through the recovery period, increased triglyceride level, fatty acids, LDL-C and HDL-C.

The rate clearance of lipid also increases in some stressful situation. **Meraihi et al.(1990)** observed that Hyperlipidamia under noise stress may be due to decreased insulin secretion . Insulin has an

antagonistic effect upon catecholamine mediated lipolysis . Sulpiride drug ameliorated the effect of noise of most measured parameter.

#### **The histopathological and histochemical studies:**

In 2008, **Katzung** stated that the sulpiride is a drug with relatively minor adverse effects .It has been regarded by some psychiatrists as the safest neuroleptic. Exposure of female rats to noise caused many deleterious changes in the kidney cortex. Highly thickened arterial walls were detected with haemolysed RBCs inside these arteries with numerous hemorrhagic areas in between the convoluted tubules .Increased kupffer cells and ruptured brush borders of proximal convoluted tubules with atrophied glomeruli were also observed. Hypertension is an established risk factor for congestive heart failure long-term exposure to pressure overload induces left ventricular remodeling and cardiac hypertrophy, subsequently resulting in heart failure (**Zhang and Kaufman 2008**). Reactive oxygen species (ROS) increased in response to mechanical stress, this increase in ROS induces apoptosis

( **Katzung, 2008**), and contributes to the progression of heart failure( **Samson et al .,2005**). Effects of noise on the immune status have also been reported (**Archana and Namasivayam, 2000**). Thus, noise exposure contributes to genesis and manifestation of several multifactor diseases, of chronic annoyance, and permanent behavioral alterations. According to **Agarwal (2005)** stresses led to oxidative stress which contributes to renal injury .This injury seems to be predominantly localized to the renal proximal tubules and this injury was realized in the destructed brush borders of proximal convoluted tubules observed in the present study. The previous results discuss the injury observed in the glomeruli and cells of proximal convoluted tubules in the kidney cortex of rats exposed to noise in the present study. Signs of improvement were observed in the kidney cortex of rats exposed to noise and treated with the drug, **Zhang and Kaufman( 2008)** declared that increased size and number of kupffer cells reflect

clearly the active defense mechanism against the toxic substances and proliferation of the kupffer cells is achieved in order to engulf hepatic cell breakdown products. Normal distribution of collagen fibers was observed in the kidney cortex of control rats and those treated with the drug, but highly increased collagen fibers with common fibrosis were detected post exposure to noise. Increased collagen fibers observed in the present study may lead to rapid healing .This opinion was discussed by **Zhang et al. (2006)** who reported that increased collagen may lead to rapid healing, rapid differentiation of cells and appearance of a new network of blood vessels, Increased collagen fibers were still noticed in kidney cortex of rats treated the drug and exposed to noise. Normal distribution of polysaccharides was observed in kidney cortex of rats treated with the drug compared with the control group, but some cells of convoluted tubules were less stained. Highly decreased polysaccharides were observed in the kidney cortex of rats exposed to noise this injury may be responsible for decreased total protein observed in the present study. Thickened and deeply stained arterial walls observed in the present study was also detected by another authors (**Gu et al.,1998;Agrwal,2005**) .They stated that exposure to stress induces oxidative stress and this leads to increased free radical production which cause hypertrophy in the vascular smooth muscle cells and hypertrophy of arterial walls and increased mortality . Decreased protein content due to oxidative damage has been reported by **Nikolaos et al. (2004) and Samson et al .(2005)** .

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## تأثير الضوضاء و العلاج بعقار السلبرايد على بعض المعايير الفسيولوجية والهستولوجية فى إناث الجرذان البيضاء

إيمان جمال الدين عزت هلال، فاطمة عيد و نعمة محمود طه عطية  
قسم علم الحيوان، كلية العلوم - جامعة الأزهر (بنات)

يعتبر الضوضاء من أكثر المؤثرات العصبية على الإنسان لذا تهدف هذه الدراسة إلى توضيح آثارها على بعض المعايير الفسيولوجية والهستولوجية وتمت هذه الدراسة على إناث الجرذان التى قسمت إلى أربع مجموعات (٦ \ مجموعة) وكانت كالتالى .  
المجموعة الأولى:- استخدمت كمجموعة ضابطة .  
المجموعة الثانية :- مجموعة عولجت بعقار السلبرايد فقط.  
المجموعة الثالثة :-مجموعة الجرذان التى تعرضت للضوضاء فقط يوميا لمدة ٣٠ يوما أكثر من ٩٠ديسبل  
المجموعة الرابعة : مجموعة الجرذان التى تعرضت للضوضاء وعولجت بعقار السلبرايد.  
ولقد أوضحت نتائج هذا البحث أن المعالجة بعقار السلبرايد لم يحدث أى تغير فى كل المعايير التى تم دراستها.  
أما عند التعرض للزحام فقد كانت هناك زيادة إحصائية فى كل من : وظائف الكلى-البروتين الكلى- والدهون الكلية والثلاثية والكولسترول عالى الكثافة والكولستيرول منخفض الكثافة ولقد إتضح أن هذا العقار حسن الكثير من التغيرات الناتجة عن الضوضاء .لوحظ أن تعاطى عقار السلبرايد لم يظهر أى آثار جانبية فى نسيج الكلى ولكن لوحظت زيادة فى الخلايا اللمفية أما التعرض للضوضاء فقط أظهرت تغيرات هستولوجية وكميانية عديدة بالنسيج الكلى وأظهرت المعاملة بالعقار بعد التعرض للضوضاء تحسنا ملحوظا فى كل النسيج الكلى. ولهذا ينصح باستخدام عقار السلبرايد فى البشر الذين يتعرضون للضوضاء.

