

Effects of Medicinal Plants on Some Physiological Parameters in Rats

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ABSTRACT

An experiment was conducted to study the effect of *Nigella sativa* and *Allium sativum* on some physiological parameters in rats. The study included two experiments during winter and summer seasons. Each experiment includes 25 adult male *Albino* rats with an average live body weight of 200 ± 20 g. Rats were distributed into 5 groups (5 rats each). Group (1) control, Groups (2) and (3) rats fed on *Nigella sativa* as additive to the diet at 3% and 6%, respectively. Groups (4) and (5) rats were fed on *Allium sativum* as additive to the diet at 3% and 6%, respectively. In each season (winter and summer), blood samples were collected from each group after 3, 6 and 9 weeks from the start of the experiment and centrifuged at 3000 rpm for 15 min. to obtain serum. Serum was separated and kept frozen until subsequent analyses. Finally, at the end of the experiment, rats were sacrificed to obtain the livers and kidneys for examination. Results showed that in winter season treatment of rats with 6% *Nigella sativa*, 3% *Allium sativum* or 6% *Allium sativum* prevent the lesions in liver and kidney that were shown in both the control and 3% *Nigella sativa* groups. Meanwhile in summer season treatment of rats with medicinal plant did not show any change in the liver histology as compared with the control rats and improve the lesions in kidney that were shown in the control group. Results also showed that most of serum parameters (total protein, albumin, globulin, alanin aminotransferase (ALT), aspartate aminotransferase (AST) and urea) of treatments were in normal range.

Key words: Medicinal plants, *Nigella sativa*, *Allium sativum*, physiological parameters, liver examination, kidney examination, rats.

Introduction

Plants are the green factors in our planet; they convert carbon dioxide and water to carbohydrates, and nitrogen to amino acids. Besides food, plants are considered the nature's green pharmacy, which provide drugs to maintain the good health and to restore the failed health of humans. The medical arts had its origin when mankind first began to use remedial measures to get rid of their pains, sufferings and other illnesses (Badr *et al.*, 2012).

The seeds of *Nigella sativa* sometimes known as black seed, black cumin or habatul Barakah have long been used in the Middle East as a traditional medicine for a variety of complaints, headache, cough, flatulence, as a choleric, antispasmodic and uricosuric. Furthermore, the pharmacological and toxicological studies have demonstrated that crude extract or ethanolic extract of *Nigella sativa* and some of its active constituents might have protective effect against renal ischemia-reperfusion-induced oxidative injury and nephrotoxicity and hepatotoxicity that induced by either disease or chemicals (Ali and Blunden, 2003 and Hosseinzadeh and Montahaei, 2007).

Allium sativum which is commonly called garlic belongs to the family Liliaceae and genus *Allium* (Krishnaraju *et al.* 2006). Garlic is commonly used in food and its medical properties have been well recognized since time immemorial. The traditional medical practitioners have considered garlic as an excellent medicinal plant that has a lot of therapeutic potential. Borek, (2001) reported that garlic compounds have tremendous antioxidant property which exerts actions by scavenging reactive oxygen species (ROS) enhancing cellular antioxidant enzymes and increasing glutathione in the cells.

The present study was designed to ascertain the beneficial effects of *Nigella sativa* and *Allium sativum* on the histopathological changes in liver and kidney and some serum parameters in normal rats.

Materials and Methods

This study was carried out in Animal House Laboratory. Department of Animal Production, Faculty of Agriculture, Al-Azhar University, Cairo, Egypt, which provided standard laboratory chemicals and equipment for this study.

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Experimental Animals: A total number of 50 Male *Albino* rats were obtained from El Osman Farm, Cairo, Egypt. Animals were housed in stainless steel cages under natural ambient temperature in both seasons (winter and summer) and provided with food and water ad libitum. All animals were healthy and clinically free of diseases.

Experimental design: Rats were randomly divided into 5 equal groups. Each group contained 5 rats and fed on one of the following diets:

Group 1: Control diet. Group 2: Control diet + 3% *Nigella sativa*.

Group 3: Control diet + 6% *Nigella sativa*. Group 4: Control diet + 3% *Allium sativum*. Group 5: Control diet + 6% *Allium sativum*.

Two medicinal plants were used with the diet. The medicinal plants are *Nigella sativa* (Black seeds or N.S.) and *Allium sativum* (Garlic or A.S.). In this study two levels of each medicinal plant were used (3% and 6% of the diet).

Effect of season: The experiment was carried out in winter (from 28 December 2013 to 27 February 2014) and summer (from 28 June to 28 August 2014). In both seasons blood samples were obtained from rats by withdrawing blood from the orbital venous plexuses using a capillary tube. Samples were collected every 3 weeks after the beginning of the experiment. Blood samples were taken and centrifuged at 3000 rpm for 15 min to obtain blood serum, and transferred to eppendorf tube and stored in a deep freezer until subsequent analysis.

Histopathological studies: At the end of the experiment, rats were sacrificed to obtain the livers and kidneys. Immediately after extraction, the livers and kidneys were immersed in formalin concentration 10% for two days, then washed in water, dehydrated in ascending grade of ethyl alcohol and finally cleared by xylene and embedded in melted paraffin wax. The liver and kidney blocks were sectioned at six-micron thickness and stained by eosin and hematoxylin according to Pearse, (1968).

Serum parameters: Serum total protein was determined using colorimetric method according to Burtis (1999). Serum albumin was measured using kits depending on the method according to Gindler and Westgard, (1973). Serum globulin was calculated by subtraction of albumin from total protein. Activities of alanine aminotransferase (ALT) in serum was measured by colorimetric method as described by Mathieu *et al.* (1982a). Activities of aspartate aminotransferase (AST) in serum were determined by using a colorimetric method according to Mathieu *et al.* (1982b). Serum urea was measured by colorimetric method based on the method of Tabacco *et al.* (1979).

Statistical analyses: Statistical analyses were carried out using SPSS program. One-way analysis of variance (Procedure ANOVA of SPSS) followed by Duncan's multiple range test (Duncan, 1955) at 5% level of significance to test the effect of *Nigella sativa* and *Allium sativum* after 3, 6 and 9 weeks from the experiment within each season (Winter and Summer).

Results and Discussion

Histopathological changes of the liver:

In winter the liver sections of the control and 3% *Nigella sativa* groups showed preserved lobular architecture. The portal tracts consisted of normal hepatic artery, portal vein and bile duct. The central veins, some were seen normal and some congested. The hepatocytes were normal in arrangement of cytoplasm and nuclei. Some hepatic sinusoids revealed mild congestion (Fig 1 and 2). Meanwhile in 6% *Nigella sativa*, 3% and 6% *Allium sativum* groups the liver sections showed preserved lobular architecture. The portal tracts consisted of normal hepatic artery, portal vein and bile ducts. The hepatocytes have normal cytoplasm and nuclei as well as normal hepatic sinusoids (Fig 3, 4 and 5). In summer the liver sections of the control, 3% *Nigella sativa*, 6% *Nigella sativa*, 3% *Allium sativum* and 6% *Allium sativum* groups showed preserved lobular architecture. The portal tracts consisted of hepatic artery, portal vein and bile duct. The central veins, some were normal and some were congested. The hepatocytes were normal in arrangement and cytoplasm and nuclei. Some hepatic sinusoids revealed moderate congestion (Fig 6, 7, 8, 9 and 10).

The above results revealed that during winter season the liver section in the control group showed preserved lobular architecture, the central veins showed some congestion and also some hepatic sinusoids revealed mild congestion. These results being shown in the control group during winter may be due to water or food contamination. The winter results also showed that treatment of rats with 6% *Nigella sativa*, 3% *Allium sativum* or 6% *Allium sativum* prevent the lesions in liver that appeared in the control and 3% *Nigella sativa* groups. These results may be due to the antioxidant potential effect of *Nigella sativa* and *Allium sativum*.

The above mentioned results showed that during summer season the liver section in the control group showed preserved lobular architecture, the central veins showed some congestion and also some hepatic sinusoids were mildly congested. The results also showed that treatment of rats with medicinal plant did not show any change in the liver histology as compared with the control rats. These results revealed that the lesions

in liver sections in all groups may be due to the contamination in either water, food or air and in summer medicinal plant did not have any significant effect on liver sections.

Pourbakhsh *et al.* (2014) showed that all histological findings were normal in the control group and *Nigella sativa* oil alone (0.5 ml/kg per day intraperitoneally) in the liver and they added that histological changes were observed in ethanol treated group (3 g/kg per day) in the liver tissue. Ethanol induced liver damage included severe congestion, steatosis and infiltration of inflammatory focal portal space. They also showed that the liver lesions were improved in all ethanol (3 g/kg per day) plus *Nigella sativa* oil groups (0.125, 0.25 and 0.5 ml/kg per day intraperitoneally) compared to ethanol treated group. Ince *et al.* (2012) reported that necroses of hepatic cells, with degeneration, dilatation of sinusoids and dissociated remark cordons in the livers have been observed in mice treated with cypermethrin (10 mg/kg/day). While treatment of mice with cypermethrin (10 mg/kg/day) and combination with thymoquinone at doses of 5, 10, and 20 mg/kg/day had mild necroses of hepatic cells, with degeneration, dilatation of sinusoids and dissociated remark cordons in the livers. Zaoui *et al.* (2002) showed that there were no significant histopathological modifications noted in liver in *Nigella sativa*-treated rats (2 ml/kg body weight) after 12 weeks of chronic treatment as compared with control animals.

Zhang *et al.* (2012) showed that treatment of N-nitrosodiethylamine in rats with garlic oil (40 mg/kg bw) caused a significant improvement of hepatocellular architecture as compared with N-nitrosodiethylamine group. Shaarawy *et al.* (2009) showed that the liver sections of control rats showed normal architecture, characterized by polyhedral shaped hepatocytes and cytoplasm granulated with small uniform nuclei. Hepatocytes were arranged in well-organized hepatic cords and separated by narrow blood sinusoids. While animals treated with garlic exhibited normal architecture, indicating the non-toxic effect of garlic. They also showed that the liver sections of rat injected with N-nitrosodiethylamine showed loss of lobular architecture, fibrosis and fatty infiltration. Also, the nuclei of many hepatocytes appeared malignant or have features of degenerating and dividing process, while treatment of rats receiving N-nitrosodiethylamine with garlic showed extended portal tract infiltrated with mononuclear inflammatory cells, less fibrosis, less disarrangement and degeneration of hepatocytes as compared with N-nitrosodiethylamine induced animals.

In summer medicinal plants did not show any beneficial effect on liver sections and these results may be due to that heat stress may prevent the beneficial effect of medicinal plants. Or may be due to that heat may effect on the active ingredient in the medicinal plants during summer and that prevent the beneficial effect of medicinal plants on liver sections.

Al-Zahrani *et al.* (2011) showed that the liver sections of the mice that were subjected to heat stress presented a dilatation in the hepatic sinusoids and an interstitial hemorrhage. They also showed that most of the histological changes that occurred due to the heat stress were modulated by thymoquinone supplementation, which resulted in a liver that showed a normal, decongested central vein that was surrounded by a healthy hepatic lobule structure.

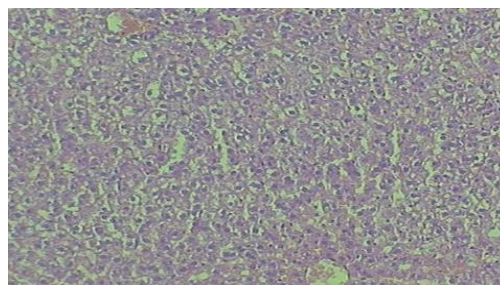


Fig. 1: Liver structure during winter season in the control group showing preserved lobular architecture. The portal tracts consisted of normal hepatic artery, portal vein and bile duct. The central veins, some were normal and some congested. The hepatocytes were normal in arrangement of cytoplasm and nuclei. Some hepatic sinusoids revealed mild congestion.

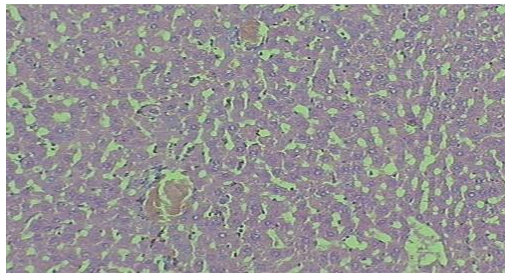


Fig. 2: Liver structure during winter season in the 3% *Nigella sativa* group showing preserved lobular architecture. The portal tracts consisted of hepatic artery, portal vein and bile duct. The central veins, some were normal and some congested. The hepatocytes were normal in arrangement of cytoplasm and nuclei. Some hepatic sinusoids revealed mild congestion.

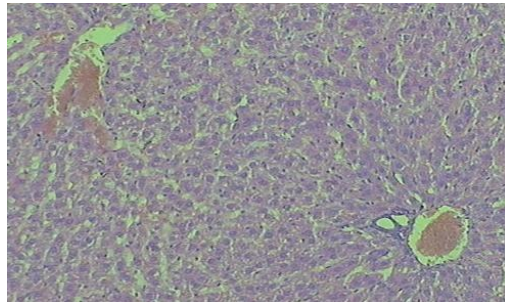


Fig. 3: Liver structure during winter season in the 6% *Nigella sativa* group showing preserved lobular architecture. The portal tracts consisted of normal hepatic artery, portal vein and bile ducts. The hepatocytes were normal cytoplasm and nuclei and normal hepatic sinusoids.

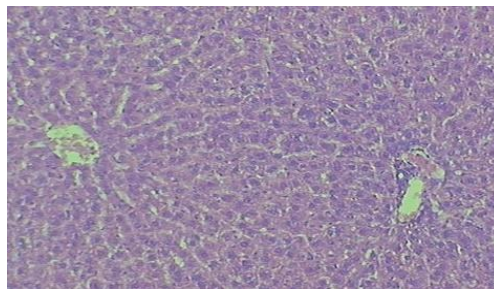


Fig. 4: Liver structure during winter season in the 3% *Allium sativum* group showing preserved lobular architecture. The portal tracts consisted of normal hepatic artery, portal vein and bile ducts. The hepatocytes were normal cytoplasm and nuclei and normal hepatic sinusoids.

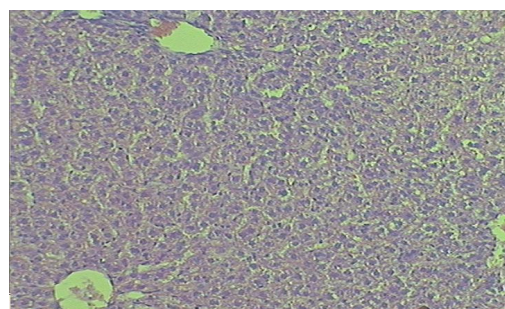


Fig. 5: Liver structure during winter season in the 6% *Allium sativum* group showing preserved lobular architecture. The portal tracts consisted of normal hepatic artery, portal vein and bile ducts. The hepatocytes were normal cytoplasm and nuclei and normal hepatic sinusoids.

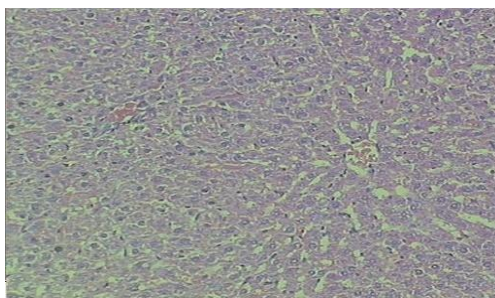


Fig. 6: Liver structure during summer season in the control group showing preserved lobular architecture. The portal tracts consisted of hepatic artery, portal vein and bile duct. The central veins, some were normal and some congested. The hepatocytes were normal in arrangement and cytoplasm and nuclei. Some hepatic sinusoids were mildly congested.

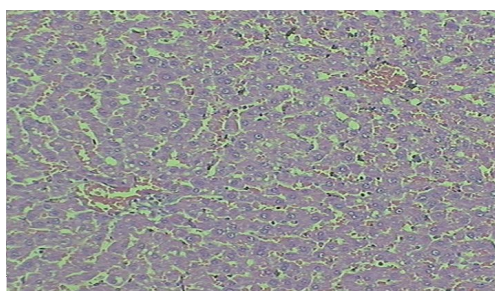


Fig. 7: Liver structure during summer season in the 3% *Nigella sativa* group showing preserved lobular architecture. The portal tracts consisted of hepatic artery, portal vein and bile duct. The central veins, some were normal and some congested. The hepatocytes were normal in arrangement and cytoplasm and nuclei. Some hepatic sinusoids revealed moderate congestion.

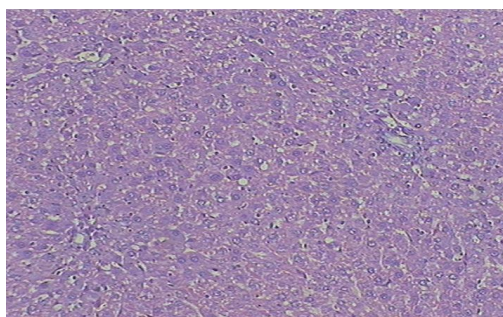


Fig. 8: Liver structure during summer season in the 6% *Nigella sativa* group showing preserved lobular architecture. The portal tracts consisted of hepatic artery, portal vein and bile duct. The central veins, some were normal and some congested. The hepatocytes were normal in arrangement and cytoplasm and nuclei. Some hepatic sinusoids revealed mild congestion.

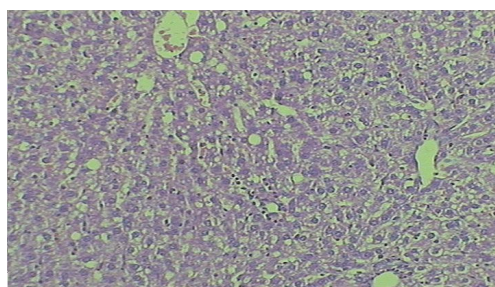


Fig. 9: Liver structure during summer season in the 3% *Allium sativum* group showing preserved lobular architecture. The portal tracts consisted of hepatic artery, portal vein and bile duct. The central veins, some were normal and some congested. The hepatocytes were normal in arrangement and cytoplasm and nuclei. Some hepatic sinusoids revealed mild congestion.

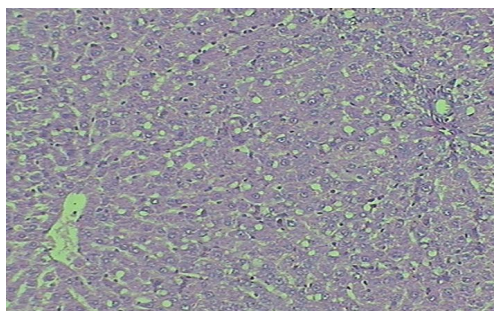


Fig. 10: Liver structure during summer season in the 6% *Allium sativum* group showing preserved lobular architecture. The portal tracts consisted of hepatic artery, portal vein and bile duct. The central veins, some were normal and some congested. The hepatocytes were normal in arrangement and cytoplasm and nuclei. Some hepatic sinusoids revealed mild congestion.

Histopathological changes of the kidney:

In winter the kidney section of the control group showed preserved architecture. The cortex revealed normal glomeruli and tubules with mild congestion of the cortical blood vessels. The medulla revealed normal tubules and mild congested blood vessels of interstitial tissue (Fig 11). While kidney section of the 6% *Nigella sativa*, 3% *Allium sativum* and 6% *Allium sativum* groups showed preserved architecture. The cortex revealed normal glomeruli and tubules with mild congestion of the cortical blood vessels. The medulla revealed normal tubules and interstitial tissue (Fig 13, 14 and 15). Meanwhile, in 3% *Nigella sativa* group kidney section showed preserved architecture. The cortex revealed normal glomeruli and tubules with minimal congestion of the cortical blood vessels. The medulla revealed normal tubules and minimal congested blood vessels of interstitial tissue (Fig 12).

In summer the kidney sections of the control group showed preserved architecture. The cortex revealed normal glomeruli and tubules with mild congestion of cortical blood vessels. The medulla revealed normal tubules and mild congested blood vessels of interstitial tissue (Fig 16). Meanwhile in 3% *Nigella sativa*, 6% *Nigella sativa*, 3% *Allium sativum* and 6% *Allium sativum* groups showed preserved architecture. The cortex revealed normal glomeruli and tubules with minimal congestion of cortical blood vessels. The medulla revealed normal tubules and minimal congested blood vessels of interstitial tissue (Fig 17, 18, 19 and 20).

The above results revealed that during winter season the kidney section in the control group showed preserved architecture, the cortex shows normal glomeruli and tubules with mild congestion of the cortical blood vessels and we also show the medulla revealed normal tubules and mild congested blood vessels of interstitial tissue. The results shown in the control group during winter may be due to contamination in water or food and the treatment of rats with 3% *Nigella sativa* improved the lesions in the tubules of the cortical blood vessels observed in the control and other treatment groups. The winter treatment of rats with 6% *Nigella sativa*, 3% *Allium sativum* or 6% *Allium sativum* prevented the lesions in the medulla of kidney of the control and 3% *Nigella sativa* groups. These results may be due to the antioxidant potential effect of *Nigella sativa* and *Allium sativum*.

The above results indicated that during summer season the kidney section in the control group showed preserved architecture, the cortex showed normal glomeruli and tubules with mild congestion of the cortical blood vessels and the medulla revealed normal tubules and mild congested blood vessels of interstitial tissue. These results may be due to contamination in water or food. Treatment of rats with medicinal plant improved the lesions in kidney appeared in the control group. These results may be due to the antioxidant potential effect of *Nigella sativa* and *Allium sativum*.

Al-Zahrani *et al.* (2011) reported that the kidney of the male, heat-stressed mice exhibited interstitial hemorrhage, scattered renal tubules and atrophy in the glomeruli. They also added that when mice subjected to heat stress were orally supplemented with thymoquinone (5 mg/kg body weight/day for 75 days) exhibited the characteristics of recovery, including a slight hemorrhage in the renal tubules and glomerulus, during the heat stress period. Dollah *et al.* (2013) found that rats treated with *Nigella sativa* (0.01 g/kg, 0.1 g/kg and 1 g/kg bw) the kidney tissue revealed a normal structure of kidney similar to control group without any tissue degeneration, inflammation, necrosis, and tubular dilation. Zaoui *et al.* (2002) showed that there were no significant histopathological modifications noted in kidneys in *Nigella sativa*-treated rats (2 ml/kg bw) after 12 weeks of chronic treatment as compared with control animals.

Shiju *et al.* (2013) found that rats supplemented with garlic extract (500 mg/kg bw) did not show any change in the kidney histology as compared with the control group. While injection of rats with streptozotocin (45 mg/kg bw intraperitoneally) kidney histology showed evidence for mesangial expansion and nodular

glomerulosclerosis with increase in the thickening of the glomerular capillary membrane. They added that there is evidence of glycosuria and proteinuria in the tubules. They also found normal kidney histology when diabetic rats were supplemented with garlic extract (500 mg/kg bw) as compared with diabetic group. Nasri *et al.* (2013) reported that treatment of rats with gentamicin (10 mg/kg) for 10 days significantly increased damage score of kidney as compared with control group, while treatment of rats with gentamicin (10 mg/kg) for 10 days followed by garlic (20 mg/kg) for 10 days or garlic (20 mg/kg) and gentamicin (10 mg/kg) for 10 days significantly attenuated the damage score of kidney when compared with gentamicin group.

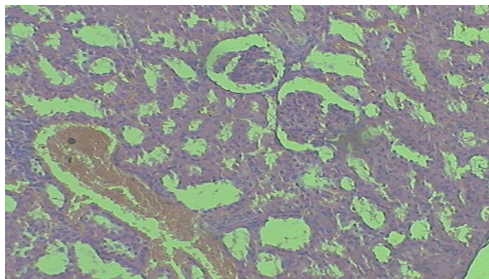


Fig. 11: Kidney structure during winter season in the control group showing preserved architecture. The cortex revealed normal glomeruli and tubules with mild congestion of the cortical blood vessels. The medulla revealed normal tubules and mild congested blood vessels of interstitial tissue.

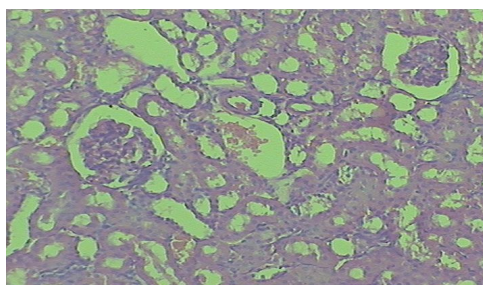


Fig. 12: Kidney structure during winter season in the 3% *Nigella sativa* group showing preserved architecture, the cortex revealed normal glomeruli and tubules with minimal congestion of the cortical blood vessels. The medulla revealed normal tubules and minimal congested blood vessels of interstitial tissue.

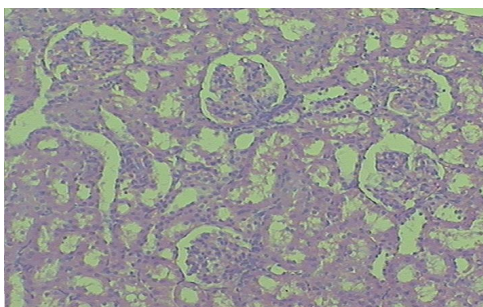


Fig. 13: Kidney structure during winter season in the 6% *Nigella sativa* group showing preserved architecture, the cortex revealed normal glomeruli and tubules with mild congestion of the cortical blood vessels. The medulla revealed normal tubules and interstitial tissue.

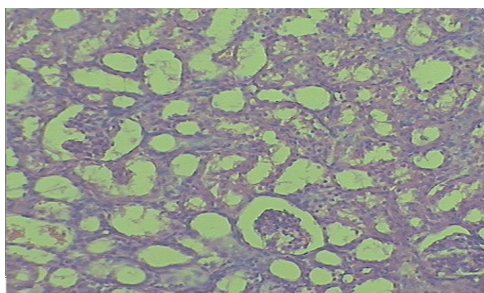


Fig. 14: Kidney structure during winter season in the 3% *Allium sativum* group showing preserved architecture, the cortex revealed normal glomeruli and tubules with mild congestion of the cortical blood vessels. The medulla revealed normal tubules and interstitial tissue.

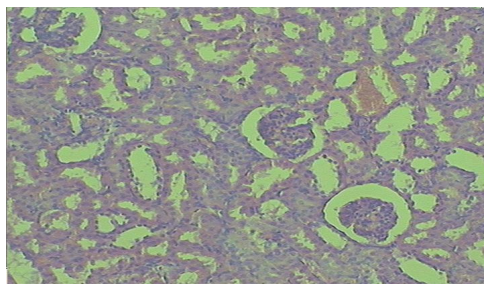


Fig. 15: Kidney structure during winter season in the 6% *Allium sativum* group showing preserved architecture, the cortex revealed normal glomeruli and tubules with mild congestion of the cortical blood vessels. The medulla revealed normal tubules and interstitial tissue.

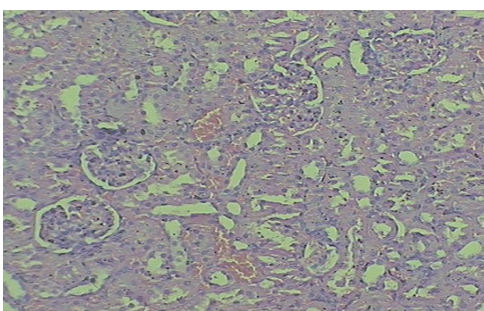


Fig. 16: Kidney structure during summer season in the control group showing preserved architecture. The cortex revealed normal glomeruli and tubules with mild congestion of cortical blood vessels. The medulla revealed normal tubules and mild congested blood vessels of interstitial tissue.

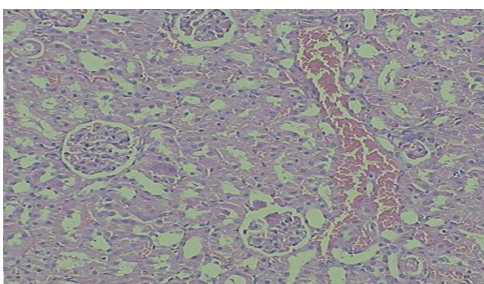


Fig. 17: Kidney structure during summer season in the 3% *Nigella sativa* group showing preserved architecture, the cortex revealed normal glomeruli and tubules with minimal congestion of cortical blood vessels. The medulla revealed normal tubules and minimal congested blood vessels of interstitial tissue.

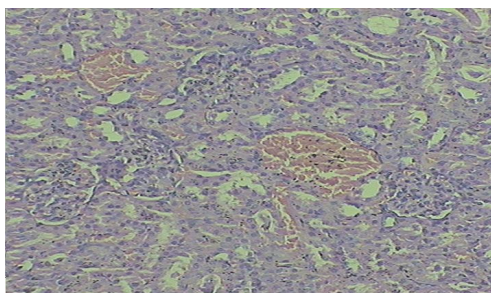


Fig. 18: Kidney structure during summer season in the 6% *Nigella sativa* group showing preserved architecture, the cortex revealed normal glomeruli and tubules with minimal congestion of cortical blood vessels. The medulla revealed normal tubules and minimal congested blood vessels of interstitial tissue.

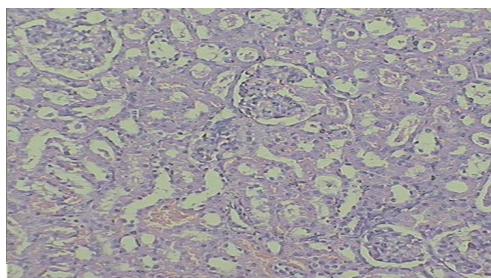


Fig. 19: Kidney structure during summer season in the 3% *Allium sativum* group showing preserved architecture, the cortex revealed normal glomeruli and tubules with minimal congestion of cortical blood vessels. The medulla revealed normal tubules and minimal congested blood vessels of interstitial tissue.

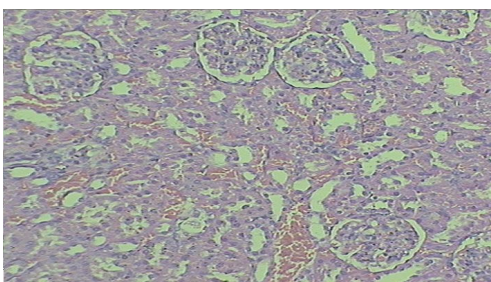


Fig. 20: Kidney structure during summer season in the 6% *Allium sativum* group showing preserved architecture, the cortex revealed normal glomeruli and tubules with minimal congestion of cortical blood vessels. The medulla revealed normal tubules and minimal congested blood vessels of interstitial tissue.

Blood serum parameters:

Table (1) shows that during winter after 3, 6 and 9 weeks from the start of the experiment medicinal plants did not show any significant effect on serum total protein as compared with the control group. During summer after 3 and 6 weeks from the start of the experiment medicinal plants did not show any significant effect on serum total protein. While after 9 weeks 3% *Nigella sativa* significantly increased serum total protein as compared with the control and other treatment groups. The significant increase in serum total protein after treatment with 3% *Nigella sativa* during summer season are in the normal range.

The above results indicated that treatment of rats with *Nigella sativa* (3% or 6% of diet) or *Allium sativum* (3% or 6% of diet) for 9 weeks during winter or summer seasons did not show any significant effect on serum total protein. These results are in accordance with those of Al-Logmani and Zari (2011) who showed that treatment of diabetic and non-diabetic rats with 5% *Nigella sativa* oil for 7 weeks did not show any significant effect on serum concentration of total protein as compared with untreated diabetic and control rats. Ghalehkandi *et al.*(2012) showed that treatment of rats with garlic aqueous extract had no significant changes in the serum

value of total protein. They also found that combinative use of garlic and chromium chloride has not effects on serum value of total protein.

On the other hand, Al-Nazawi and El-Bahr (2012) found that treatment of rats with black cumin seed 2% (*Nigella sativa*) significantly increased serum total protein level, when compared with control group. However, Amber *et al.* (2001) reported that plasma total protein was significantly decreased in New Zealand white rabbits by increasing the level of *Nigella sativa* cake (6.25, 12.5 and 25 % NSC in diets).

Table 1: Mean \pm S.E for the effect of medicinal plants on serum total protein concentrations (g/dl) during winter and summer seasons.

Season	Winter									Summer								
Time	3 weeks			6 weeks			9 weeks			3 weeks			6 weeks			9 weeks		
Groups	Mean	S.E	d.t	Mean	S.E	d.t	Mean	S.E	d.t	Mean	S.E	d.t	Mean	S.E	d.t	Mean	S.E	d.t
G1	6.95	0.32	A	7.67	0.75	A	7.49	0.77	A	6.68	0.51	A	8.29	0.57	A	7.70	0.43	B
G2	7.35	0.40	A	8.17	0.45	A	7.90	0.17	A	7.06	0.12	A	7.29	0.31	A	8.99	0.34	A
G3	7.17	0.31	A	8.82	0.28	A	8.45	0.25	A	7.81	0.35	A	7.60	0.05	A	7.72	0.44	B
G4	7.16	0.41	A	8.09	0.73	A	7.80	0.24	A	7.58	0.53	A	7.86	0.31	A	8.20	0.48	AB
G5	7.53	0.16	A	8.20	0.68	A	7.23	0.18	A	6.97	0.07	A	7.59	0.29	A	7.73	1.02	B

S.E: Standard error. d.t: Duncan s, multiple range test between groups. Means with the same letter are not significantly different.

G1: Control G2: 3% *Nigella sativa*

G3: 6% *Nigella sativa* G4: 3% *Allium sativum* G5: 6% *Allium sativum*.

Table (2) shows that during winter after 3 and 9 weeks from the start of the experiment medicinal plants did not show any significant effect on serum albumin compared with the control group. While after 6 weeks 3% *Allium sativum* significantly increased serum albumin compared with the control and other treatment groups. During summer after 6 and 9 weeks from the start of the experiment medicinal plants did not show any significant effect on serum albumin as compared with the control group. While after 3 weeks 6% *Nigella sativa* significantly increased serum albumin as compared with the control and other treatment groups. The significant increase in serum albumin after treatment with 6% *Nigella sativa* during summer season are in the normal range.

The above mentioned results indicated that during winter or summer seasons most of treatments did not show any significant effect on serum albumin levels. These results are in accordance with those found by Al-Nazawi and El-Bahr (2012) who showed that treatment of rats with 2% black cumin seed (*Nigella sativa*) the serum albumin level was unchanged significantly when compared with control group. Hussein *et al* (2004) showed that administration of garlic oil (28 mg/kg bw orally) to hyperlipidemic rats did not show any significant variations in serum albumin concentration all over the experimental periods as compared with hyperlipidemic group.

On the other hand, Nasr and Attia (1998) showed that addition of *Nigella sativa* increased blood albumin in New Zealand white rabbits. Mudie *et al.* (2014) showed that serum albumin concentration significantly decreased in rats treated with highly active antiretroviral therapy when compared with the rats in normal control group. They also showed that administration of rats with *Nigella sativa* seed extract (100, 200, 400 and 800 mg/kg) plus highly active antiretroviral therapy significantly increased serum albumin concentration when compared with rats treated with highly active antiretroviral therapy. Anwar and Meki (2003) reported that the treatment of diabetic rats with garlic oil (10 mg/kg bw) for 15 days significantly increased plasma albumin. Nasr (2014) showed that treatment of rats with aged garlic extract (250 mg/kg) + cisplatin (7.5 mg/kg) caused a significant increase in serum albumin level as compared with cisplatin-treated group.

Table 2: Mean \pm S.E for the effect of medicinal plants on serum albumin concentrations (g/dl) during winter and summer seasons.

Season	Winter									Summer								
Time	3 weeks			6 weeks			9 weeks			3 weeks			6 weeks			9 weeks		
Groups	Mean	S.E	d.t	Mean	S.E	d.t	Mean	S.E	d.t	Mean	S.E	d.t	Mean	S.E	d.t	Mean	S.E	d.t
G1	3.82	0.22	A	3.92	0.35	C	4.91	0.70	A	3.51	0.32	B	4.37	0.36	A	4.48	0.05	A
G2	3.90	0.42	A	4.16	0.12	BC	4.91	0.48	A	4.13	0.18	AB	3.85	0.28	A	4.83	0.17	A
G3	3.64	0.18	A	5.08	0.26	AB	4.87	0.17	A	4.52	0.16	A	3.87	0.29	A	4.23	0.36	A
G4	4.07	0.14	A	5.28	0.53	A	4.27	0.48	A	4.22	0.13	AB	4.00	0.13	A	4.36	0.07	A
G5	3.95	0.17	A	4.20	0.14	BC	4.14	0.18	A	3.52	0.34	B	3.88	0.12	A	4.63	0.22	A

S.E: Standard error. d.t: Duncan s, multiple range test between groups. Means with the same letter are not significantly different.

G1: Control G2: 3% *Nigella sativa*

G3: 6% *Nigella sativa* G4: 3% *Allium sativum* G5: 6% *Allium sativum*.

Table (3) shows that during winter and summer seasons after 3, 6 and 9 weeks from the start of the experiment medicinal plants did not show any significant effect on serum globulin as compared with the control group.

The above results indicated that treatment of rats with *Nigella sativa* (3% or 6% of diet) or *Allium sativum* (3% or 6% of diet) for 9 weeks during winter or summer seasons did not show any significant effect on serum

globulin. These results are in accordance with those of Ghalehkandiet *al.* (2012) whoshowed that treatment of rats with garlic aqueous extract had no significant changes in the serum value of globulin. They also found that combinative use of garlic and CrCl3 has no effects on serum globulin value.

On the other hand, Al-Gaby (1998) reported that when rat's diet supplemented with 25 % *Nigella sativa* (black cumin cake) serum globulin was significantly increased. Al-Nazawi and El-Bahr (2012) showed that treatment of rats with black cumin seed 2% (*Nigella sativa*) significantly increased serum globulin level compared with control group. Hussein *et al.* (2004) showed that administration of garlic oil (28 mg/kg. body wt. orally) to hyperlipidemic rats significantly increased serum total globulin level after 4 weeks as compared with hyperlipidemic group.

Table 3: Mean \pm S.E for the effect of medicinal plants on serum globulin concentrations (g/dl) during winter and summer seasons.

Season	Winter									Summer								
Time	3 weeks			6 weeks			9 weeks			3 weeks			6 weeks			9 weeks		
Groups	Mean	S.E	d.t	Mean	S.E	d.t	Mean	S.E	d.t	Mean	S.E	d.t	Mean	S.E	d.t	Mean	S.E	d.t
G1	3.13	0.11	A	3.75	0.66	A	2.58	0.38	A	3.18	0.61	A	3.92	0.22	A	3.22	0.20	A
G2	3.45	0.62	A	4.01	0.14	A	2.99	0.63	A	2.93	0.30	A	3.45	0.04	A	4.16	0.28	A
G3	3.53	0.13	A	3.74	0.18	A	3.58	0.39	A	3.29	0.32	A	3.74	0.26	A	3.49	0.25	A
G4	3.09	0.43	A	2.80	0.43	A	3.52	0.25	A	3.35	0.40	A	3.86	0.26	A	3.84	0.34	A
G5	3.58	0.12	A	4.00	0.53	A	3.10	0.08	A	3.45	0.37	A	3.71	0.41	A	3.10	0.46	A

S.E: Standard error. d.t: Duncan s, multiple range test between groups. Means with the same letter are not significantly different.

G1: Control G2: 3% *Nigella sativa*

G3: 6% *Nigella sativa* G4: 3% *Allium sativum*

G5: 6% *Allium sativum*.

Table (4) shows that during winter after 3 and 6 weeks from the start of the experiment 6% *Nigella sativa* significantly increased serum ALT as compared with the control and other treatment groups, while after 9 weeks' medicinal plants significantly decreased serum ALT as compared with the control group. During summer after 3 weeks from the start of the experiment 6% *Nigella sativa*, 3% and 6% *Allium sativum* significantly decreased serum ALT as compared with the control and 3% *Nigella sativa* groups, while after 6 weeks' medicinal plants significantly decreased serum ALT as compared with the control group. While after 9 weeks 3% *Allium sativum* significantly decreased serum ALT as compared with the control and other treatment groups.

The results in table (4) show that serum ALT activity were ranged between 5 to 20.33 and these activities are in the normal range.

Badary *et al.* (1998) studied the effects of acute and subchronic administration of thymoquinone (the main constituent of the volatile oil of *Nigella sativa*) in male Swiss *Albino* mice. They found that treatment by thymoquinone increased significantly the enzyme activities of alanine aminotransferase (ALT). Al-Jishi and Hozaifa (2003) showed that *Nigella sativa* seed powder (180 mg/kg rat/day) increased ALT activity in rats. Sulaiman *et al.* (2014) revealed that administration of rats with aqueous extract of *Allium sativum* significantly increased the activity of ALT in serum when compared with control group. Develi *et al.* (2014) showed that treatment of rats with bing ethanol application (5 g/kg) every 12h three times caused significant increases in plasma transaminase activity (ALT). While treatment of rats with *Nigella sativa* oil (5 ml/kg) significantly decreased plasma transaminase activity (ALT). El-Demerdash *et al.* (2005) found that when rats injected subcutaneously with a single dose of alloxan (120 mg/kg bw) significantly increased plasma ALTas compared with the control group. While treatment of diabetic rats with garlic juice (1 ml/100g bw/day) significantly decreased ALT activities in the liver tissue as compared with the control group. Samson *et al.* (2012) recorded that treatment of rats with aqueous extract of garlic or combined aqueous extract of onion and garlic (200, 400 and 600 mg/kg/day) significantly decreased serum ALT when compared with control group.

Table 4: Mean \pm S.E for the effect of medicinal plants on serum ALT concentrations (U/L) during winter and summer seasons.

Season	Winter									Summer								
Time	3 weeks			6 weeks			9 weeks			3 weeks			6 weeks			9 weeks		
Groups	Mean	S.E	d.t	Mean	S.E	d.t	Mean	S.E	d.t	Mean	S.E	d.t	Mean	S.E	d.t	Mean	S.E	d.t
G1	9.00	0.58	C	10.67	0.33	B	11.33	0.33	A	17.33	0.88	A	20.33	0.33	A	18.33	1.45	A
G2	12.00	0.00	B	8.67	0.33	B	5.67	0.33	C	17.33	0.33	A	13.67	1.20	BC	19.00	0.58	A
G3	18.00	1.00	A	14.00	0.58	A	8.67	0.67	B	11.33	0.88	B	16.00	0.58	B	19.00	0.58	A
G4	7.33	0.88	C	10.33	1.45	B	5.33	0.67	C	10.00	0.58	B	12.33	0.67	C	11.00	1.16	B
G5	12.00	0.58	B	10.00	0.58	B	5.00	1.00	C	11.33	0.88	B	14.00	1.16	BC	20.33	2.19	A

S.E: Standard error. d.t: Duncan s, multiple range test between groups. Means with the same letter are not significantly different.

G1: Control G2: 3% *Nigella sativa*

G3: 6% *Nigella sativa* G4: 3% *Allium sativum*

G5: 6% *Allium sativum*.

Table (5) shows that during winter season after 3 weeks from the start of the experiment all treatments significantly decreased serum AST activity compared with the control rats except treatment with 6% *Nigella*

sativa which did not show any significant effect in this respect, while after 6 weeks from treatment all medicinal plant significantly decreased serum AST activity except treatment with 6% *Allium sativum* which did not show any significant effect in this respect compared with the control and other treatment groups. Meanwhile, after 9 weeks from treatment all medicinal plant did not show any significant effect on serum AST activity except treatment with 6% *Nigella sativa* significantly decrease serum AST activity compared with the control and other treatment groups. During summer after 3, 6 and 9 weeks from the start of the experiment medicinal plants significantly decreased serum AST compared with the control group.

The above results indicate that during winter or summer seasons treatment of rats with *Nigella sativa* (3% or 6% of diet) or *Allium sativum* (3% or 6% of diet) for 3, 6 and 9 weeks significantly reduced serum AST activity as compared with the control except in winter after 3 weeks' treatment with 6% *Nigella sativa* and after 6 weeks' treatment with 6% *Allium sativum* did not show any significant effect on serum AST activities. The significant decreased of serum AST after treatment with *Nigella sativa* or *Allium sativum* are in accordance with those found by El-Demerdash *et al.* (2005) who treated diabetic rats with garlic juice (1 ml/100g bw/day). Ha *et al.* (2015) showed that treatment of rats with high-fat with 1.5 % black garlic extract caused a significant decrease in plasma AST level as compared to the high-fat (20% fat) group. Mohammed (2010) showed that treatment of rabbits with aluminum chloride (sub lethal dose 200 mg/kg bw) plus *Nigella sativa* (10 g/liter) significantly increased serum ALT when compared with *Nigella sativa* (10 g/liter) and control groups. He added that treatment of rabbits with *Nigella sativa* (10 g/liter) significantly decreased serum ALT compared with aluminum chloride treated group. Bashandy (1996) reported that administration of *Nigella sativa* oil (daily dose of 0.27 g/100g) to senile rats decreased serum GOT (aspartate aminotransferase).

On the other hand, Sulaiman *et al.* (2014) revealed that administration of rats with aqueous extract of *Allium sativum* significantly increased the activity of AST in serum when compared with control group. Mohammed (2010) showed that treatment of rabbits with aluminum chloride (sub lethal dose 200 mg/kg bw) plus *Nigella sativa* (10 g/liter) significantly increased serum AST when compared with *Nigella sativa* (10 g/liter) and control groups.

Table 5: Mean \pm S.E for the effect of medicinal plants on serum AST concentrations (U/L) during winter and summer seasons.

Season Time	Winter									Summer								
	3 weeks			6 weeks			9 weeks			3 weeks			6 weeks			9 weeks		
Groups	Mean	S.E	d.t	Mean	S.E	d.t	Mean	S.E	d.t	Mean	S.E	d.t	Mean	S.E	d.t	Mean	S.E	d.t
G1	94.33	6.64	A	126.33	2.96	A	76.33	4.41	A	100.00	5.77	A	108.67	1.86	A	112.67	4.06	A
G2	67.67	0.67	B	92.67	7.22	BC	81.00	4.93	A	79.33	4.70	B	82.33	3.18	B	92.00	1.73	B
G3	83.33	6.69	A	73.00	12.12	C	55.33	3.33	B	76.33	0.88	B	78.00	2.65	B	63.33	5.24	C
G4	56.67	2.91	B	104.00	1.16	B	72.00	1.53	A	59.33	2.03	C	63.67	2.03	C	48.00	3.46	D
G5	59.33	2.33	B	125.33	2.33	A	81.67	2.60	A	79.33	3.18	B	58.33	1.20	C	65.67	2.03	C

S.E: Standard error. d.t: Duncan s, multiple range test between groups. Means with the same letter are not significantly different. G1:

Control G2: 3% *Nigella sativa*

G3: 6% *Nigella sativa* G4: 3% *Allium sativum*

G5: 6% *Allium sativum*.

Table (6) shows that during winter after 3 weeks from the start of the experiment all medicinal plant treatment groups did not show any significant effect on serum urea levels except those treated with 3% *Nigella sativa* which significantly increased serum urea as compared with the control group. After 6 weeks from the start of the experiment, treatment with 3% *Nigella sativa* and 6% *Allium sativum* significantly increased serum urea, while treatment with 6% *Nigella sativa* significantly decreased serum urea compared with the control group. Meanwhile, after 9 weeks all medicinal plant did not show any significant effect on serum urea compared with the control group. During summer after 3 weeks from the start of the experiment 6% *Nigella sativa* and 3% *Allium sativum* significantly increased serum urea as compared with the control group. While after 6 weeks from the start of the experiment all medicinal plant did not show any significant effect on serum urea as compared with the control group. Meanwhile, after 9 weeks all medicinal plant did not show any significant effect on serum urea except treatment with 3% *Allium sativum* that significantly decreased serum urea as compared with the control group.

The above results indicated that during winter after 3 or 6 weeks from treatment with 3% *Nigella sativa* and 6% *Allium sativum* caused an increase in serum urea, while 6% *Nigella sativa* after 6 weeks from treatment significantly decreased serum urea. Meanwhile in summer after 3 or 6 weeks from treatment 3% *Nigella sativa* decreased serum urea but this effect was not significant, while after 3 weeks 6% *Nigella sativa* and 3% *Allium sativum* significantly increased serum urea. After 9 weeks 3% *Allium sativum* in summer season significantly decreased serum urea.

El-Demerdash *et al.* (2005) revealed that when rats injected subcutaneously with a single dose of alloxan (120 mg/kg bw) significantly increased plasma urea as compared with control group. While treatment of diabetic rats with garlic juice (1 ml/100g bw/day) significantly decreased plasma urea when compared with the diabetic group. Ghorbel *et al.* (2015) showed that treatment of rats with iron chloride (FeCl₂) at a dose of 150

mg/100ml of drinking water caused a significant increase in serum urea level as compared with control group. However, when rats treated with FeCl₂ and garlic respectively at doses of 150 mg/100ml of drinking water and 5 g/100g of dampen standard diet serum urea level reached to normal value of control rats. Dollah *et al.* (2013) showed that treatment of rats with *Nigella sativa* (0.1 g/kg bw) caused a significant reduction in serum urea concentration as compared with control group and rats treated with *Nigella sativa* (0.01 g/kg bw), while treatment of rats with *Nigella sativa* (0.01 g/kg bw) increased serum urea level when compared with control group. Hosseinian *et al.* (2015) showed that treatment of rats with cisplatin (6 mg/kg bw) demonstrated a significant raise in serum urea concentration when compared with control animals. They also showed that treatment of rats with *Nigella sativa* extract (200 mg/kg bw) had significantly decreased compared with cisplatin group.

On the other hand, Oluwole (2001) found that treatment of rats with 100 and 200 mg garlic/day significantly increased serum urea after 15 and 30 days' post treatment. Badary *et al.* (1998) studied the effects of acute and subchronic administration of thymoquinone (the main constituent of the volatile oil of *Nigella sativa*) in male Swiss albino mice. They found that treatment by thymoquinone significantly increased plasma concentration of urea. Mohammed (2010) showed that treatment of rabbits with aluminum chloride (sub lethal dose 200 mg/kg bw) + *Nigella sativa* (10 g/liter) or *Nigella sativa* (10 g/liter) significantly increased serum urea as compared with control group.

Table 6: Mean \pm S.E for the effect of medicinal plants on serum urea concentrations (mg/dl) during winter and summer seasons.

Season	Winter									Summer								
	3 weeks			6 weeks			9 weeks			3 weeks			6 weeks			9 weeks		
Time	Mean	S.E	d.t	mean	S.E	d.t	mean	S.E	d.t	mean	S.E	d.t	mean	S.E	d.t	mean	S.E	d.t
G1	47.00	3.06	B	76.67	4.10	B	58.67	2.33	AB	58.00	2.65	BC	57.00	3.46	AB	53.00	1.73	A
G2	74.00	12.70	A	92.00	2.31	A	60.33	4.26	AB	52.33	3.18	C	51.67	4.33	B	53.33	1.70	A
G3	49.67	2.73	B	58.67	1.20	C	47.67	2.03	B	82.33	3.48	A	61.33	1.45	AB	44.33	3.18	AB
G4	45.00	1.16	B	76.00	3.46	B	63.33	11.29	AB	75.67	2.33	A	66.67	3.84	A	39.67	0.67	B
G5	63.00	3.61	AB	99.00	2.08	A	69.00	6.08	A	63.67	1.76	B	65.67	2.40	A	47.00	2.00	AB

S.E: Standard error. d.t: Duncan s, multiple range test between groups. Means with the same letter are not significantly different.

G1: Control G2: 3% *Nigella sativa*

G3: 6% *Nigella sativa* G4: 3% *Allium sativum* G5: 6% *Allium sativum*.

Conclusion

From the above mentioned results, it could be concluded that providing levels of 6% *Nigella sativa*, 3% *Allium sativum* or 6% *Allium sativum* during winter season are effective to maintain the normal histopathological structure for liver and kidney. Meanwhile, during summer season, more of studies we needed to investigate the effect of treatment with *Nigella sativa* and *Allium sativum* on the histopathological structure of liver and kidney and more of studies we shall needed to detect the reasons that lead to lesions of liver and kidney structures in the control group.

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