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PROTECTIVE EFFECT OF SOME MEDICINAL PLANTS ON BLOOD PARAMETERS, KIDNEY AND LIVER FUNCTIONS AND HISTO-PATHOGICAL FEATURES OF KIDNEY IN RATS

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SUMMARY

The study was undertaken in the animal house belonging to the Animal Production Department, Faculty of Agriculture, Al-Azhar University. Twenty four adult male albino rats with an average live body weight of 130 gm were allocated to 4 equal groups (6 rats each): group 1 (G1) served as the control group and was orally given 1 ml of distilled water, group 2 (G2) was orally given 1 ml Cymbopogon proximus (CP, halfa barr) suspension, group 3 (G3) was orally given 1 ml Ammi visnaga (AV, Khella) suspension and group 4 (G4) was orally given administrated 1 ml Ambrosia maritime (AM, deamsissa) suspension. Feeding and drinking water were offered ad-libitum during the experimental period. Two experiments were carried out during hot season in summer (August and September, 2009). The first experiment was designed to investigate the effect of medicinal plants (CP, AV and AM) after 60 days from the start of the treatments on kidney function and histological structure. The second experiment was designed to test the effect of medicinal plants on diurnal variations of blood plasma parameters within each treatment at the end of the experiment. In the first experiment, blood samples were collected and kidney were studied,whereos in the second experiment, blood samples were collected in heparinized tubes three times daily from all animals within each group at 8 am, 4 pm and 12 pm.. The aim of the study was to investigate the effect of using Cymbopogon proximus (Halfa barr, CP), Ammi visnaga (Khella, AV) and Ambrosia maritime (Deamsissa, AM) on kidney structure and function of albino rats.

Results indicate that the kidney histopathological sections of the control and CP groups showed normal renal glomeruli and tubules. On the other renal section showed minimal degenerative changes in renal glomeruli in AV group with normal tubules and mild degenerative changes of renal glomeruli in the form of proeifuation of glomerular epithelium and mild atrophy in some glomeruli in AM group.Oral administration of medicinal plants had no significant effect on plasma creatinine, urea nitrogen, total protein, albumin, globulin, albumin /globulin, ALT, AST. Meanwhile, AV significantly increased plasma glucose to be higher than that in other groups.

It could be concluded that CP is safe to be used as an effective remedy for renal spasms and diabetes treatment without any side effects on kidney function. Also, it could be recommended that AV could be used for treatment of kidney stone but the duration of treatment have to be no longer than two weeks. Meanwhile, kidney function must be considered during any treatment with AM which is mainly used for its hypoglycemic effect.

Keywords: Rat, medicinal plants, blood, metabolities enzymes, kidney, liver, histopathology

INTRODUCTION

The vegetation on the earth is aperennial and renewable source of food and energy which is necessary for the survival of most organisms. Plants are the green factors of our planet; they convert carbon dioxide and water to carbohydrates; and nitrogen to amino acids. Besides food, plants are considered to be the nature's green pharmacy, which provide drugs to maintain the good health and to restore the failing health of humans. The medicinal arts had its origin when mankind first began to use remedial measures to get rid of their pains, sufferings and other illnesses, by using healing potions prepared from plants. Thus, from the tribal medicines and folk medicines, we have reached the modern era of sophisticated synthetically made drugs.The medicines of the ancient civilization and cultures were mostly associated with plants.

Mansour *et al*. (2002) reported that the administration of *lupinus termis*, *CP* or *Zygophyllum coccineum* suspensions to the diabetic rats could restore plasma glucose, urea, creatinine, total protein and albumin to their normal levels after 4 weeks of treatment. They concluded that these herb suspensions are capable of ameliorating the impaired diabetic kidney function in addition to its hypoglycemic control. Al-Sayeda *et al*. (2002) showed that treatment with *CP* suspensions restored the plasma glucose level in alloxan diabetic rats. They also showed that treatments with *CP*

suspensions resulted in improvements in plasma total lipids, triglyceride and total cholesterol.

Ibrahim *et al*. (2004a) showed that feeding 2% *AV* for 3 weeks had no changes in serum AST, cholesterol and total lipids, while feeding on 2% *AV* for 6 or 9 weeks increased serum AST, cholesterol and decreased serum total lipid. Jouad *et al* . (2002) revealed that the aqueous extract of *AV* at 20 mg/kg significantly reduced blood glucose in normal rats 6 hours after a single oral administration and nine days after repeated oral administration. This hypoglycemic effect is more pronounced in streptozotocin diabetic rats.

Ahmed and Khater (2001) fond that when rats were treated with acetaminophen alone they developed significant hepato-cellular damage as was evident from a significant increased in the serum levels of AST, and ALT when compared with the controls. Pretreatment of rats with *AM* extract at doses of 100 and 200 mg/kg markedly reduced the elevated serum levels of these hepatospecific enzymes. They concluded that *AM* seems to preserve the structural integrity of the hepato-cellular membranes as evident by the significant reduction in the acetaminophen induced rise in serum enzymes in rats. The reversal of increased serum enzymes in acetaminophen – induced liver damage by *AM* may be due to the prevention of leakage of the intracellular enzymes by its membrane stabilizing activity. Ibrahem *et al* . (2004b) tested the effects of aqueous and ethanolic extracts of *AM* on the glucose level in streptozotocin induced diabetic rats. The extracts showed a highly significant hypoglycemic effect on the experimental animals, after 10 days. All the diabetic rats exhibited normal glucose level and AST, and ALT enzymes returned to normal values after treatment with *Ambrosia marritime*.

The objective of this study was to investigate the effect of *CP, AV* and *AM* administration on kidney structure and function of albino rats.

MATERIALS AND METHODS

The study was undertaken in Department of Animal Production, Faculty of Agriculture, Al-Azhar University, Cairo.

Experimental Animals:

The albino rats used in this study were obtained from Egyptian Organization for Biological Products and Vaccines, Cairo, Egypt and raised in the animal house. Animals were housed in cages where the mean ambient temperature ranged from 27 and to 31 ºC. The photoperiod was approximately a 12-hour light /dark cycle. The standard laboratory chow and tap water were provided *ad libitum*. All animals were healthy and clinically free from diseases.

Experimental design:

The following parts of three medicinal plants were used in the present study: whole plant of *AM*, bark of *CP* and seed of *AV*. Plants were obtained from the local market in Cairo– powders and were suspended in boiled distilled water (100 g of medicinal plant were added into 300 ml boiled water).

The study included 24 adult male albino rats, with an average live body weight of 130 g (ranged from 110 – 150 g). Animals were randomly divided into four equal groups (6 rats each), as the following: G1-Control group orally administered with 1ml distilled water/ animal/day. Whereas the other three groups G2,G3 and G4 were orally odministed with 1ml *CP, AV* and *AM* suspension/animal/day (333 mg/100 g BW/day), respectively .Ad libitum feed and drinking water were offered.

Two experiments were oyecuted for two months in summer (August and September 2009). The first experiment was designed to investigate the effect of feeding medicinal plants (*CP, AV* and *AM*) for 60 days. The second experiment was designed to test the effect of the plant extracts on diurnal variations of blood parameters within each treatment at the end of the experiment. In the first experiment, blood samples were collected and kidney sections were investigated meanwhile, in second experiment, blood samples were collected three times daily from the 6 animals from each group at 8 a.m., 4 p.m. and 12 p.m. At the end of the experiment, rats were sacrificed to obtain the kidneys. Immediately after extraction, the kidneys was immersed in formalin 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 kidney block was sectioned at six-micron cut and stained by eosin and heamatoxylin according to Pearse (1968).

Blood sampling and analyses:

Blood samples were obtained from rats by withdrawing blood from the orbital venous plexuses using a capillary tube. Then centrifuged at 3000 rpm for 15 min to obtain plasma which was thens transferred to Ependorff tubes and stored at – 20ºC until subsequent analyses.

Plasma creatinine was measured by colorimetric method based on Murray (1984). Plasma urea-nitrogen concentration was determined by using enzymatic colorimetric

method according to Tabacco *et al.* (1979). Plasma total protein was determined using colorimetric method according to Henry (1964). Plasma albumin was measured using Diamond Kits according to Dumas and Biggs (1972). Plasma globulin was calculated by subtraction of albumin from total protein. The glucose concentration was determined by glucose oxidase method (Trinder,1969). Plasma ALT was determined by using a colorimetric method according to Reitmena and frankel (1957). Plasma AST was determined by using a quantitative colorimetric method according to Henry (1974). Plasma total lipids was measured by colorimetric method based on the method of Zollner *et al*. (1962).

Statistical analyses:

Data were collected and statistically analyzed by the analysis of variance using ANOVA procedure of SAS program (SAS, 1996) at the 0.05 probability level. Duncan's Multiple Range Test (P=0.05) was used to test the effect of treetment *(control, Cymbopogon proximus (Halfa barr), Ammi visnaga (Khella)* and *Ambrosia maritime (Deamsissa)* at the end of the experiment as well as test the effect of diurnal variations within each group.

RESULTS AND DISCUSSION

Histopathological changes of the kidney:

The kidney strctur of the control and *CP* groups showed normal renal glomeruli and tubules (Figs 1and 2). Renal fauture showed minimal degenerative changes in renal glomeruli in the *AV* group with normal tubules and mild degenerative changes of renal glomeruli in the form of proeifuation of glomerular epithelium and mild atrophy in some glomeruli in the *AM* group(Figs 3and 4). No side effects of *CP* on kidney function have been reported in the literature which is in constancte with the present results. Consequently, *CP* is safe to be used as an effective remedy for renal spasms (Abou-Shoer *et al*., 2011) and diabetes treatment. Al-Sayeda *et al.* (2002) and Mansour *et al.* (2002) found that suspension of *CP* restored the plasma glucose of alloxan induced diabetic rats to the normal level due to increased insulin levels (Eskander and Won Jun, 1995).

Regarding the effect of *AM* on renal histopathology, similar results had been reported by Abuelgasim *et al.* (2007) who found that oral administration of *Ambrosia maritime* (*AM* group) caused degeneration of the renal tubules. Also, Mansour *et al.* (2007) found few changes in renal tissues of rats treated with *AM* extract. So, the effect of AM on kidney function must be considered during any treatment with AM which is mainly used in folk medicine for its hypoglycemic effect (Ibrahim *et al*., 2004b). Owing to the effect of *AV*. Vanachayangkul, *et al*. ((2011) found that the histopathological examination of the kidneys revealed that oral administration of *AV* extract for 14 days had no significant effect on kidney histopathology. However, it did significantly reduced the incidence of calcium oxalate (CaOx) crystal deposition. In addition, *AV* significantly increased urinary excretion of citrate along with a decrease of oxalate excretion. The main beneficial effects of *AV* in human medicine is its use in kidney stone treatment. Tilgner (2000) reported that *AV* is used in kidney stone treatment due to its strong antispasmodic action on the ureters thereby allowing the passage of kidney stones. Khan *et al.* (2001) revealed that the antilithiatic effect of *AV* is mainly because of highly potent diuretic activity and amelioration of uraemia and hyperbilirubinemia by seeds of *AV*. The slight changes in kidney histopathology in *AV* group in the present study may be due to the shoster duration of the treatment (two months) compared with 2 weeks as the in Vanachayangkul *et al.* (2011) study. So, it is recommended that *AV* can be used for treatment of kidney stone but the duration of treatment should not be longer than two weeks.

Blood plasma parameters:

Table (1) shows that oral administration of medicinal plants had no significant effect on plasma creatinine, urea total protein, albumin, globulin, A/G ratio, ALT, AST. Meanwhile, *AV* significantly increased plasma glucose to be higher than that in other groups which is in contradiction with previous results. Where, Jouad *et al*. (2002) revealed that administration with *AV* aqueous extract at 20 mg/kg had a significant hypoglycemic effect in normal and streptozotocin diabetic rats. This contradiction may be due to the different doses used, duration of treatment between the present work and that in the literature. Also, it may be due to the inhibitory effect of *AV* treatment on insulin secretion or to the effect of *AV* on gluconeogensis causing the increase in plasma glucose and insignificant decrease in total lipids (Table 1). studies are needed to investigate the effect of dose and duration of *AV* administration on plasma glucose. On the other hand, *AM* treatment caused insignificant decrease in plasma glucose level (Table 1) which is in agreement with Ibrahem *et al*. (2004b) who found that the *Ambrosia marritima* extracts showed a highly significant hypoglycemic effect on the streptozotocin induced diabetic rats after ten days. The insignificant effect of *CP* on plasma glucose is in contrast with the findings of Al Sayeda *et al*.

(2002) and Mansour *et al*. (2002) who works on alloxan diabetic rats indicates that *CP* has a hypoglycemic effect on diabetic rats only, while in normal rats *CP* has no significant effect on plasma glucose. Similar conclusions had been reported by Ibrahim *et al*. (2004b) who found that the addition of *AM* extract significantly decreased serum glucose in all of the streptozotocin diabetic rats, while, its hypoglycemic effect was not observed in normal rats. They concluded that the hypoglycemic effects may be exerted through the inhibition of glucose absorption, increase sensitivity of receptors to insulin, insulin as inhibiting effect, stimulation of β-cells of pancreas to secret insulin or stimulation of peripheral tissues uptake of glucose.

Diurnal effect:

Table (2) shows that although there was a significant diurnal variation in plasma parameters which differ in different groups but the mean plasma parameters level at different times in different groups were within the clinical normal range, except plasma glucose level indicating that these diurnal changes were clinically insignificant and no significant diurnal changes in kidney function had been occurred due to medicinal plants treatments. Plasma glucose was significantly higher at day time (at 8:00 am) than at night (at 12:00 pm in control, *CP* and *AV* groups and at 4:00 pm in *AM* group) may be due to eating time and increasing activities during at 8:00 am. (Badr 2002).

CONCLUSION

Cymbopogon proximus (halfa barr) is safe to be used as an effective remedy for renal spasms and diabetes treatment without any adverse side effects on kidney function. Also, it is recommended that *Ammi visnaga* could be used for treatment of kidney stones but the duration of treatment should be no longer than two weeks. Meanwhile, kidney function must be considered during any treatment with *Ambrosia maritime* which is mainly used for its hypoglycemic effect.

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Table 1. The effect of medicinal plants on different plasma parameters

Parameter	G1			G2			G3			G4		
	Mean	S.E	dt	Mean	S.E	dt	Mean	S.E	dt	Mean	S.E	dt
Creatinine (mg/dl)	**0.58**	**0.035**	**a**	**0.57**	**0.038**	**a**	**0.55**	**0.019**	**a**	**0.50**	**0.025**	**a**
Urea (mg/dl)	**49.83**	**2.040**	**a**	**45.47**	**1.929**	**a**	**43.71**	**2.037**	**a**	**45.01**	**1.954**	**a**
Total protein (g/dl)	**6.28**	**0.254**	**a**	**6.34**	**0.155**	**a**	**6.26**	**0.186**	**a**	**5.83**	**0.135**	**a**
Albumin (g/dl)	**3.17**	**0.120**	**a**	**3.67**	**0.285**	**a**	**3.47**	**0.033**	**a**	**3.23**	**0.393**	**a**
Globulin (g/dl)	**3.11**	**0.157**	**a**	**2.67**	**0.299**	**a**	**2.79**	**0.132**	**a**	**2.60**	**0.215**	**a**
A/G ratio	**1.01**	**0.529**	**a**	**1.37**	**0.180**	**a**	**1.24**	**0.176**	**a**	**1.24**	**0.416**	**a**
Glucose (mg/dl)	**104.71**	**5.521**	**b**	**105.19**	**7.669**	**b**	**125.54**	**6.133**	**a**	**93.11**	**6.305**	**b**
ALT (u/l)	**8.33**	**0.870**	**a**	**9.06**	**0.891**	**a**	**10.89**	**1.695**	**a**	**10.78**	**1.307**	**a**
AST (u/l)	**22.28**	**4.142**	**a**	**20.61**	**5.166**	**a**	**19.11**	**5.958**	**a**	**20.51**	**4.272**	**a**
Total lipids (mg/dl)	**252.12**	**13.959**	**a**	**255.58**	**18.873**	**a**	**244.95**	**9.761**	**a**	**265.67**	**12.030**	**a**

S.E. = Standard error

dt : Duncan's Multiple Range Test between groups . Means within each row with similar letters are not significantly different at $p \leq 0.05$.

G1=Control *G3=Ammi visnaga*

G2=Cymbopogon proximus *G4=Ambrosia maritime*

Table 2. The effect of medicinal plants on plasma 60 days from the beginning of the experiment

Parameters		G1			G2			G3			G4		
		Mean	S.E	dt	Mean	S.E	dt	Mean	S.E	dt	Mean	S.E	dt
Creatinine (mg/dl)	8:00am	0.57	0.02	AB	0.57	0.03	AB	0.51	0.02	B	0.56	0.02	A
	4:00pm	0.62	0.08	A	0.61	0.08	A	0.54	0.04	AB	0.53	0.04	AB
	12:00pm	0.54	0.08	B	0.53	0.09	B	0.58	0.02	A	0.42	0.02	B
Urea (mg/dl)	8:00am	52.03	4.50	A	45.47	1.43	AB	40.90	3.33	B	45.43	3.08	AB
	4:00pm	49.33	2.77	AB	40.87	1.28	B	41.57	4.24	AB	40.20	0.29	B
	12:00pm	48.13	4.24	B	50.07	4.45	A	48.66	1.48	A	49.40	3.87	A
Total protein (g/dl)	8:00am	6.60	0.21	A	6.43	0.26	AB	5.80	0.15	B	5.93	0.18	AB
	4:00pm	6.53	0.68	A	6.50	0.35	A	6.20	0.06	AB	6.06	0.32	A
	12:00pm	5.70	0.10	B	6.10	0.23	B	6.77	0.39	A	5.50	0.00	B
Albumin (g/dl)	8:00am	4.53	0.22	A	3.70	0.27	B	4.03	0.03	AB	4.13	0.23	A
	4:00pm	4.46	0.44	A	4.40	0.46	A	3.90	0.15	B	3.76	0.32	B
	12:00pm	3.90	0.15	B	4.13	0.29	AB	4.57	0.07	A	3.67	0.32	B
Gobulin (g/dl)	8:00am	2.07	0.41	A	2.73	0.33	A	1.77	0.15	B	1.80	0.27	B
	4:00pm	2.07	0.29	A	2.10	0.62	AB	2.30	0.20	AB	2.30	0.55	A
	12:00pm	1.80	0.12	B	1.97	0.47	B	2.20	0.06	A	1.83	0.32	B
A/G ratio	8:00am	2.18	0.53	A	1.35	0.18	B	2.27	0.18	A	2.29	0.42	A
	4:00pm	2.18	0.22	B	2.09	0.97	A	1.69	0.25	B	1.63	0.77	B
	12:00pm	2.16	0.21	B	2.09	0.46	AB	2.07	0.00	B	2.00	0.58	AB
Glucose (mg/dl)	8:00am	120.60	5.55	A	129.45	5.44	A	134.58	13.30	A	108.10	9.72	A
	4:00pm	106.27	7.28	AB	106.23	4.03	AB	123.60	1.67	B	73.93	2.40	B
	12:00pm	87.27	1.53	B	79.90	6.73	B	118.40	14.26	B	97.30	8.48	A
ALT (u/l)	8:00am	8.67	2.33	A	8.67	2.05	AB	12.33	0.44	A	11.17	1.17	AB
	4:00pm	7.67	1.59	B	8.17	1.48	B	9.00	5.53	B	13.67	2.91	A
	12:00pm	8.67	0.88	A	10.33	1.36	A	11.33	8.08	AB	7.50	1.04	B
AST (u/l)	8:00am	15.50	4.25	B	25.00	2.08	AB	13.50	4.75	AB	27.20	11.37	A
	4:00pm	27.17	10.94	A	27.50	14.79	A	34.50	14.87	A	13.33	0.88	B
	12:00pm	24.17	5.60	AB	9.33	0.60	B	9.33	0.60	B	21.00	6.37	AB
Total lipids (mg/dl)	8:00am	298.17	20.58	A	245.60	13.28	AB	247.06	0.38	AB	302.50	18.12	A
	4:00pm	231.20	12.20	AB	233.73	28.02	B	212.77	4.79	B	244.80	19.60	B
	12:00pm	227.00	13.08	B	287.40	50.18	A	275.03	12.15	A	249.70	0.69	AB

S.E. = Standard error

dt : Duncan's Multiple Range Test between times. Means within each column and parameter with similar letters are not significantly different at $p \leq 0.05$.

G1=Control *G3=Ammi visnaga*

G2=Cymbopogon proximus *G4=Ambrosia maritime*

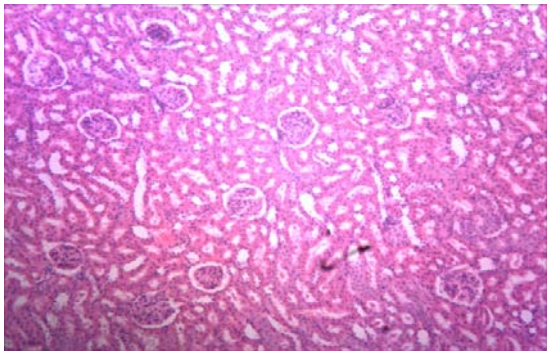

Fig. (1): Kidney structure in the ***control*** group showing normal renal glomeruli and tubules (X100).

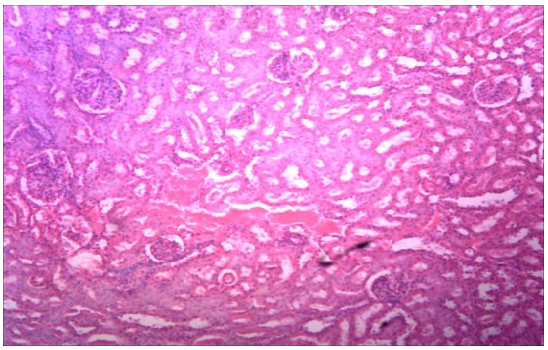

Fig. (2): Kidney structure in *the* ***Cymbopogon proximus*** group showing normal renal glomeruli and tubules (X100).

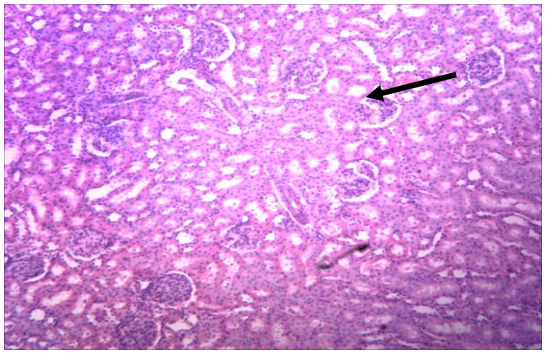

Fig. (3): Kidney structure in the ***Ammi visnaga*** group showing minimal degenerative changes of renal glomeruli and normal tubules (X100).

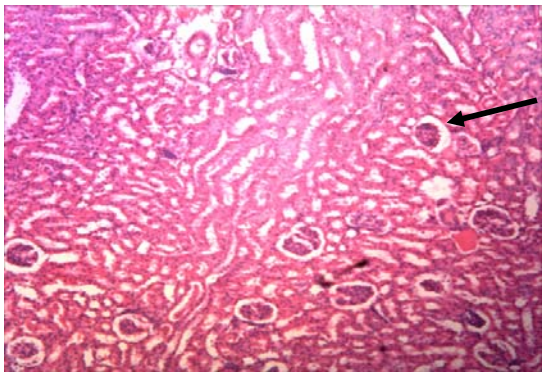

Fig. (4): Kidney structure in the ***Ambrosia marritima*** group showing mild atrophic changes of renal glomeruli (X100).

التاثيرالوقائى لبعض النباتات الطبيةعلى بعض مقاييس الدم ووظائف الكبد و الكلى وفحص امراض النسيج المميزة فى كلية الفئران

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أجريت هذه التجربة بمعامل بحوث قسم الإنتاج الحيوانى بكلية الزراعة جامعة الازهر بالقاهرة. تم تقسيم 24 فأر البينو ذكر بالغ (متوسط وزن الجسم ١٣٠ جم) إلى أربعة مجاميع متساوية (٦ فئران فى كل مجموعة): المجموعة الأولى إستخدمت كمجموعة مقارنة حيث تم تجريع الفئران ١ مل ماء مقطر، أما المجموعات التالية الاخرى يتم تجريع الفئران ١ مل مستخلص من كل من الحلفابر و بذر الخلة و الدمسيسة وقد كان الغذاء والماء متاحان طوال فترة التجربة. تم اجراء التجربة اثناء موسم الصيف لمدة شهرين (شهرى اغسطس وسبتمبر عام ٢٠٠٩). وقد اشتملت الدراسة تجربتين حيث تم تصميم التجربة الاولى لدراسة تأثير تجريع مستخلص النباتات الطبية (الحلفابر و بذر الخلة والدمسيسة) لمدة ٦٠ يوما على وظائف الكلية وتركيبها الهستولوجى. بينما تم تصميم التجربة الثانية لدراسة تأثير تجريع هذه النباتات على التغيرات اليومية فى بعض مكونات بلازما الدم على نفس الفئران. فى التجربة الاولى تم سحب عينات الدم وعمل قطاعات عرضية فى الكلية فى نهاية التجربة (بعد المعاملة لمدة ٦٠ يوما) بينما تم فى التجربة الثانية سحب عينات دم من الفئران فى نهاية التجربة ثلاث مرات: الساعة ٨ صباحا والساعة ٤ عصرا والساعة ١٢ بعد منتصف الليل. تم فصل بلازما الدم وحفظه على درجة -٢٠° م حتى إجراء التحليلات.

أظهرت النتائج ما يلى:

١- كان التركيب النسيجى للكلى طبيعيا فى المجموعة المقارنة والمجموعة الاولى (المعاملة بمستخلص الحلفابر) بينما حدث تغيرات طفيفة فى الكبيبات الكلوية دون التأثير على قنيات الكلى فى المجموعة الثانية (المعاملة بمستخلص بذر الخلة) بينما حدثت تغيرات متوسطة فى كبيبات الكلى (فى النسيج الطلائى) وضمور متوسط فى بعض القنيات الكلوية فى المجموعة الثالثة (المعاملة بمستخلص نبات الدمسيسة).

٢- لم يؤدى التجريع بمستخلص هذه النباتات لمدة ٦٠ يوما الى تأثيرات معنوية فى مكونات بلازما الدم (تركيز الكرياتينين- اليوريا – البروتينات الكلية - الالبيومين – الجلوبيولين – نسبة الالبيومين الى الجلوبيولين – انزيمات الكبد) بينما ادت المعاملة بمستخلص بذر الخلة الى زيادة معنوية فى تركيز سكر الجلوكوز فى بلازما الدم.

الخلاصة و التوصيات :

يستنتج من النتائج السابقة انه يمكن استخدام مستخلص الحلفابر لعلاج تقلصات الكلى ومرض البول السكرى دون حدوث تأثيرات ضارة على الكلى. كذالك يمكن استخدام مستخلص بذر الخلة لعلاج حصوات الكلى الا انه يجب ان يؤخذ فى الاعتبار طول فترة المعاملة حيث تؤدى المعاملة الى بعض التأثيرات الضارة الخفيفه اذا زادت المدة عن اسبوعين . بينما يجب ان يؤخذ فى الاعتبار وظائف الكلى والاثار الجانبية على نسيج الكلى فى حالات استخدام مستخلص الدمسيسة لخفض سكر الدم.