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Toxicological Study of Ethanol Extract of Lavandula Stoechas on Kidney of Wistar Rat

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ABSTRACT

Introduction/Aim: Herbal products are medicinal agents obtained from plants. They are believed to have lesser tendency for side effect in spite of their numerous possible health benefits. Lavender (Lavandula stoechas L.) is a medicinal plant largely used for different medicinal purposes. The aim of this study is to determine the toxicological effect of Lavandula stoechas on the kidney of Wistar rats.

Method: Animals of either sex were selected. Group 1 received distilled water (10 ml/kg), while group 2, 3 and 4 received Lavandula stoechas 50, 100 and 200 mg/kg respectively. Animals were kept in standard cages and given access to the extract, water and food orally for 28 days, after which they were weighed and sacrificed. Blood was collected by cardiac puncture and taken immediately for analysis.

Result: There was significant ($P<0.05$) decrease in RBC, HGB, MCV, while there was no change in the level of neutrophiles, basophiles, eosinophiles and platelets.Lavandula stoechas, significantly ($p<0.05$) caused decreased K^+ level at 100 and 200 mg/kg respectively. While there was significant ($p<0.05$) increase of Na^+ at 200 mg/kg dose. Level of Creatinine, chloride and urea were not significantly ($p<0.05$) affected across doses administered. Histological study reveals slight tubular distortion.

Conclusion: The result of the study showed that the plant could have slight effect on the kidney which suggests that the plant should be use with caution when taken for a sustained period of time. Histological study reveals slight tubular distortion.

Key: Lavandula stoechas, blood, rats, kidney

Introduction

The use of plants for healing purposes predates human history and forms the origin of modern medicine. Many conventional drugs such as aspirin (willow bark), digoxin (foxglove), quinine (cinchona bark), and morphine (opium poppy) originated from plant sources[1-3]. Globally, use of herbal medicinal products has increased tremendously. Medicinal plants have been discovered and used in traditional medicine practices since prehistoric times. Plants synthesize hundreds of chemical compounds for functions including defence against insects, fungi, diseases, and herbivorousmammals3,4. Numerous phytochemicals with potential or established biological activity have been identified[6,7]. However, since a single plant contains widely diverse phytochemicals, the effects of using a whole plant as medicine are uncertain. Furthermore, the phytochemical content and pharmacological actions, of many plants having medicinal potential remain unassessed by rigorous scientific research to define efficacy and safety[8,9]. Medicinal plants are widely used in non-industrialized societies, mainly because they are readily available and cheaper than modern medicine[10]

However, the rationale for the utilization of medicinal plants has rested largely on long-term clinical experience with little or no scientific data on their efficacy and safety[11,12]. Medicinal herbs have their use as medicament based simply on a traditional folk use that has been perpetuated along several generations[13,14]. With the upsurge in the use of herbal medicines a thorough scientific investigation of these plants is imperative, based on the need to validate their folkloric usage[15,16]. Herbs are supposed to be safe but many unsafe and fatal side effects have been reported[17,18]. These could be direct toxic effects, allergic reactions, effects from contaminants and/or interactions with drugs and other herbs. Phytotherapeutic products are many times, mistakenly regarded as less toxic because they are 'natural'. Nevertheless, those products contain bioactive principles with potential to cause adverse effects[19-23].

Lavender (Lavandula stoechas), a member of the Labiatae family, is used for a variety of cosmetic and therapeutic purposes in herbal medicine[24-26]. Inhalation of essential oils of lavender reduced cholesterol plaques in atherosclerotic disease in rabbits, but showed no effect on serum cholesterol

levels[27,28]. Lavander showed a hypolipidemic effect in rats[29]. In addition, lavender aromatherapy has displayed vasodilatory effects and enhanced coronary blood flow in human[30]. Extract of lavender flower protected isolated rat hearts against ischemic reperfusion (IR) injury[31,32]. In a study, lavender oil showed neuroprotective activity and antioxidant properties in an experimental model of stroke[33]. In a very recent study, treatment with essential oil of lavender after MI reduced ischemic injury in rats[34]. This study aimed to investigate the sub-acute toxicity study on the effects of different doses of lavender plant on liver of wister rats.

Material and Method

Male and female wistar rats were obtained from Bingham University, Animal House. They were maintained on standard animal pellets and given water ad libitum. Permission and approval for animal studies were obtained from the College of Health Sciences Animal Ethics Committee of Bingham University.

Plant collection

Leaves of Lavandula stoechaswere collected from its natural habitat from nearby Karu village, Nasarawa State, Nigeria. The plant was authenticated from Department of Botany, Bingham University, Nasarawa State Nigeria.

Plant extraction

The flowers were shadow dried for two weeks. The dried plant material was further reduced into small pieces and pulverized. The powdered material was macerated in 70% ethanol. The liquid filtrates were concentrated and evaporated to dryness at 40°C invacuum using rotary evaporator. The ethanol extract was stored at -4°C until used.

Animal study

Twenty-four (24) rats of either sex (174-257g) were selected and randomized into four groups of six rats per group. Group 1 served as the control and received normal saline (10ml/kg) while the rats in groups 2, 3 and 4 were giving 50, 100, and 200 mg/kg of Lavandula stoechasextract respectively. The weights of the rats were recorded at the beginning of the experiment and at weekly intervals. The first day of dosing was taken as D0 while the day of sacrifice was designated as D29.

Haematological analysis

The rats were sacrificed on the 29th day of experiment. Blood samples were collected via cardiac puncture. One portion of the blood was collected into sample bottles containing EDTA for hematological analysis such as Hemoglobin concentration, white blood cell counts (WBC), differentials (neutrophils, eosinophils, basophils, lymphocyte and monocyte), red blood cell count (RBC), platelets and hemoglobin (Hb) concentration using automated Haematology machine (Cell-Dyn, Abbott, USA).

Chempathology analysis

Second portion of the blood was collected into plain bottle, allowed to clot and centrifuged at 300rpm for 10 minutes. The serum collected was used to estimate biochemical parameters.

Histological study

The heart of the animals were surgically removed and weighed and a part of each was fixed in 10% formaldehyde for histological processes.

Statistical analysis

Data were expressed as the Mean ±Standard Error of the Mean (SEM). Data were analyzed statistically using one-way Analysis of Variance (ANOVA) followed by Dunnett's post hoc test for multiple comparisons between the control and treated groups. Values of $P \leq 0.05$ were considered significant.

Results

Effect of 28 days oral administration of Lavandula stoechason hematological parameters in rats.

Lavandula stoechascaused significant ($p<0.05$) decrease in the level of red blood cell, hemoglobin, platelet at 100 mg/kg dose and significantly ($p<0.05$) caused an increase in mean corpuscular hemoglobin concentration in the rats at the dose level of 50 mg/kg compared to the control. The level of basophiles, neutrophiles, eosinophils and lymphocytes were however not significantly ($p<0.05$) affected by mean corpuscular hemoglobin concentration (Table 1).

Effect of 28 days oral administration of Lavandula stoechason renal indices and electrolytes in Wistar rats.

There was significant (P<0.05) decrease in RBC, HGB, MCV, while there was no change in the level of neutrophiles, basophiles, eosinophiles and platelets.Lavandula stoechas, significantly (p<0.05) caused decreased K^+ level at 100 and 200 mg/kg respectively. While there was significant (p<0.05) increase of Na^+ at 200 mg/kg dose. Level of Creatinine, chloride and urea were not significantly (p<0.05) affected across doses administered. Histological study reveals slight tubular distortion.

Histopathological Investigations of the effect of 28 days oral administration of Lavandula stoechason renal indices and electrolytes in Wistar rats.

The kidney showed slight tubular distortion and glomerular necrosis at 200 mg/kg and 400 mg/kg. There was also, Slight tubular necrosis with lymphocyte hyperplasia at 100 mg/kg. normal renal histological features were observed in the control group.

Table 1: Effect of 28 days oral administration of ethanol leaf extract of *Lavandula angustifolia*onhematological parameters in wistar rats.

		Treatment (mg/kg)		
Hematological parameters	DW(10ml/kg)	50	100	200
WBC (×10^9/L)	8.17±0.77	6.74±1.42	3.70±0.67*	7.20±1.85
RBC (×10^12/L)	8.30±0.35	8.65±0.664	6.17±0.55*	7.74±0.25
HGB (g/dL)	15.90±0.56	15.24±0.66	11.36±0.87*	14.58±0.36
HCT (g/dL)	55.18±2.02	56.61±3.76	34.67±3.19*	53.40±1.80
MCV (fL)	66.67±0.94	65.44±1.435	57.17±0.30*	69.60±1.72
MCH (pg)	19.16±0.16	17.80±1.019	18.83±0.37	18.80±0.22
MCHC (g/dL)	29.15±0.16	27.43±1.23	32.51±0.60*	27.10±0.67
PLT (×10^9/L)	620.83±52.81	567.00±96.48	252.00±50.34*	670.45±55.78*
LYM (%)	86.81±4.61	85.00±4.13	82.83±5.82	86.41±3.14
NEUT (×10^9/L)	10.81±3.64	10.82±3.67	15.40±5.61	11.00±3.23
EOSI (×10^9/L)	1.50±0.32	2.40±0.78	1.800±0.44	1.25±0.21
BASO (×10^9/L)	1.00±0.28	2.00±0.54	2.50±1.50	3.30±2.20

Data presented as Mean ± SEM: n = 6, Oneway ANOVA, followed by Dunnett's post hoc for multiple comparison *significantly different from the distilled water (DW) control at p<0.05. DW = distilled water (WBC = white blood cells, RBC = red blood cells, HGB = hemoglobin, HCT = hematocrit, MCV = mean corpuscular volume, MCH = mean corpuscular hemoglobin, MCHC = mean corpuscular hemoglobin concentration, PLT = platelet, LYM = lymphocyte, NEUT = neutrophils, EOSI = eosinophils, BASO = basophils).

Table 4.4: Effect of 28 days oral administration of ethanol leaf extract of Lavandula stoechas on hematological parameters in wistar rats.

Renal indices and electrolytes (mmol/L)	DW(10ml/kg)	LS (50)	Treatment (mg/kg) LS (100)	LS (200)
Potassium	7.00±0.55	7.60±0.70	5.30±0.48*	5.8±0.20 *
Sodium	158.00±2.91	168.20±2.91	169.00±1.90*	164.250±1.89
Chloride	101.30±5.831	99.71±6.611	111.23±2.45	100.53±3.21
Urea	9.43±0.29	9.54±0.55	8.90±0.25	8.75±0.52
Creatinine	63.44±9.63	80.22±12.41*	55.11±16.932	73.71±6.10

Data presented as Mean ± SEM: n = 6, One Way ANOVA, followed by Dunnett's post hoc for multiple comparison *significantly different from the distilled water (DW) control at p <0.05. SHBP = Safi® herbal blood purifier, DW = distilled water.

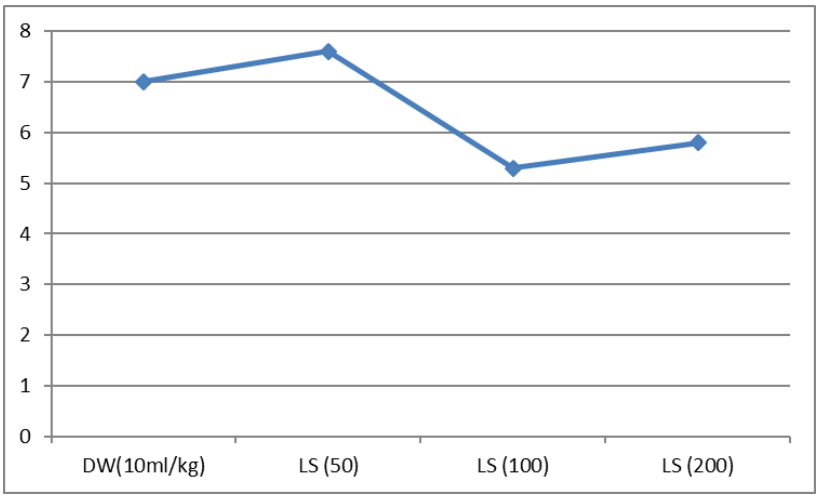

Fig 1: Graph showing effect of the ethanol leaf extract of Lavandula stoechasserum potassium level in rats

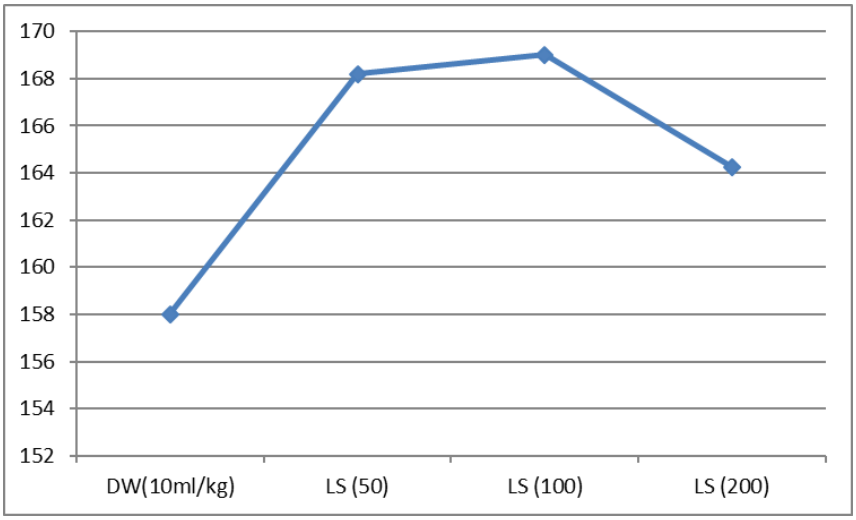

Fig 1: graph showing effect of the ethanol leaf extract of Lavandula stoechasserum sodium level in rats

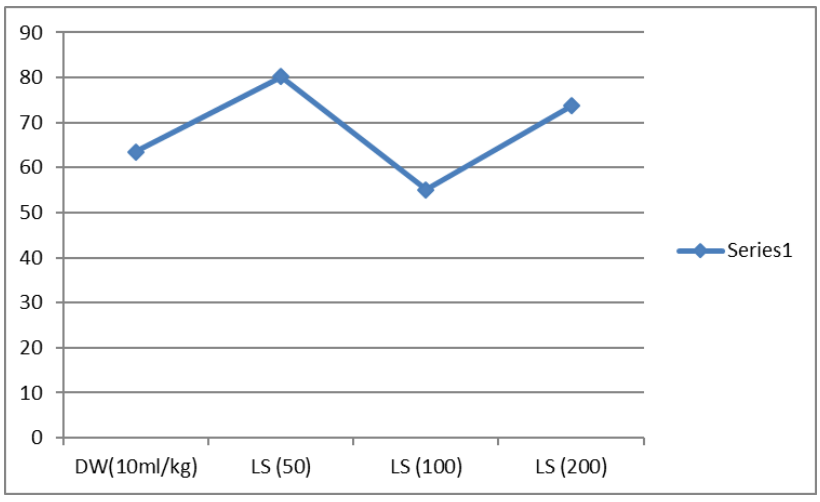

Fig 1: graph showing effect of the ethanol leaf extract of Lavandula stoechasserum creatinine level in rats

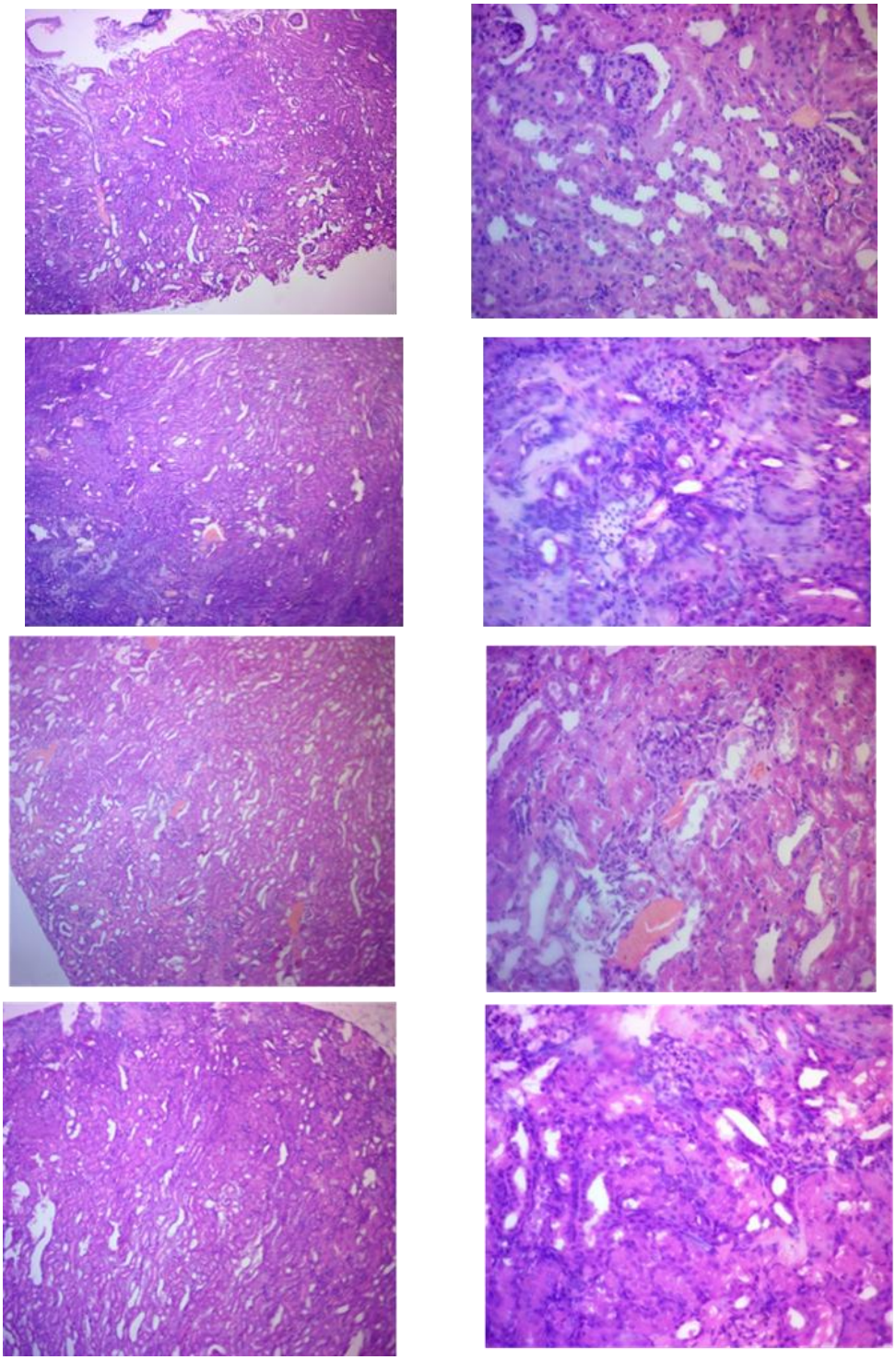

Figure 4: Histological sections of Kidneys of rats treated with Normal saline 10 ml/kg (1), LS 50 mg/kg (2), LS 100 mg/kg bw (3) and LS 200 mg/kg at magnification A (x100) and B(x400)) stained with H&E Technique.

Discussion

The globally harmonized system (GHS) defines sub-acute toxicity test as specific target organ/system toxicity arising from 28-days repeated exposure to chemicals in rodents[35,36]. Sub-acute toxicity testing is used to evaluate primarily effects on various organ systems, and to establish a no observed effect level[37-39]. The end points consist of an evaluation of clinical observation, blood analysis whole body gross necropsy and microscopic examination of all organs and tissues (histopathology)[40,41].Sub-acute toxicity testing is used to asses toxicity in targets species, it gives idea for the relative toxicity of chemicals such that it can be classified as slight, moderate, highly toxic and practically non-toxic. It's also provides information on the mechanism of

toxic action of chemicals and provides basis for basis for choosing doses for efficacy studies, also provides basis for choosing doses to be used for long term toxicity studies[42,43].

Herbal plants has been used for various medicinal and health benefits. Medicinal plants are often consumed locally without a graded dose or expected duration of use[44,45]. This can precipitate unexpected side effects on the tissue, organ or body system[46]. In this study the effect of the plant on the heart and vascular parameters were evaluated. Ethanol extract ofLavandula stoechasresulted in significant (*p<0.05) decrease in the red blood cell, hemoglobin and platelet when compared to the control group of rats. This indicated that the plant may either suppress the production of red blood cells, decrease the lifespan of red blood cells or causes problems with how the body uses iron. A low red blood count, or anemia, can cause feelings of fatigue and weakness. When there is lower red blood count than is normal, the body has to work harder to get enough oxygen to the cells. A low red blood cell (RBC) count can cause a variety of symptoms and health complications[47-50]. Hemoglobin is essential for transferring oxygen in your blood from the lungs to the tissues. Myoglobin, in muscle cells, accepts, stores, transports and releases oxygen[51,52]. Also, the level of basophiles, neutrophiles, eosinophils and lymphocytes were not affected by the extract. This reveals that the plant may not affect the body immune. It could also suggest that the plant may have immunomodulatory property.

The study also showed that Lavandula stoechas caused increase in serum Potassium ion and decrease in serum sodium ion, while other parameters remain relatively unchanged. This may be due to disruptive effect of the plant. An increase creatinine level can be observe in some kidney diseases, due to loss of normal excretory function of the creatinine[53-57], when there is a muscular cells damage or following an incompatable medication interfering with the normal functioning of the kidney[58-59]. Creatinine, is mostly derived from endogenous sources by tissue creatinine breakdown[60]. The extract did not affect creatinine level which suggest that it does not affect glomerular filtration rate and therefore has noclinical significance in inducing or treatment of kidney related diseases. Thus serum urea concentration is often considered a more reliable renal function predictor than serum creatinine[61,62]. In this study, serum urea was unaffected suggesting that the plant may not cause damage to the kidney.

The histopathological analysis, showed that in all groups after 28 days administration of ethanol extract of Lavandula stoechasthe kidney there was slight changes at the cellular level in comparison to control. This resonates with other parameters that the leaves of the plant slightly have nephrotoxic effect.

Conclusion

Result from biochemical parameters and histological study showed that Lavandula stoechaspossesses chemical constituent that may slightly alter anatomical and physiological property of the kidney which suggests that caution should be taken while consumed for sustained period of time.

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