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Toxicological study of ethanol extract of Lavandula stoechas on Liver of Wistar rat.

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ABSTRACT

Aim/Introduction: Plants have been used for several ailments. Some of these claims have been established while some yet to be authenticated. 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 Liver of Wister 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. The histological hepatotoxic potential of the plant was studied using haematotoxylin and eosin (H&E) staining technique.

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 significantly caused ($p<0.05$) increase of ALP and BILD at 100 mg/kg dose. Level of other parameters were not significantly ($p<0.05$) affected across doses administered. Histological study reveals slight tubular distortion.

Conclusion: Though the plant is relatively safe, result of the study reveals that the plant could have slight effect on the liver 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, liver

I. INTRODUCTION

Over the past decade, there has been an increased global interest in traditional systems of medicine and herbal medicinal products. In part, this surge has been due to the rare or non-existent access to modern medicine in developing countries as well as the acceptance of herbal medicines by large populations of people in developed nations[1-3]. In the latter countries, complementary and alternative medicine (CAM), often used concomitantly with conventional medicine[4]. Kaufman et al[5] reported that as many as 16% of prescription drug users consume herbal supplements[6]. 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[7-8]. 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 herbivorous mammals[9,10]. Numerous phytochemicals with potential or established biological activity have been identified. 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. Medicinal plants are widely used in non-industrialized societies, mainly

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because they are readily available and cheaper than modern medicines[11,12]

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[12-14]. Medicinal herbs have their use as medicament based simply on a traditional folk use that has been perpetuated along several generations. 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]. Herbs are supposed to be safe but many unsafe and fatal side effects have been reported[16,17]. These could be direct toxic effects, allergic reactions, effects from contaminants and/or interactions with drugs and other herbs[18,19]. 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[20-23].

Lavender (Lavandula stoechas), a member of the Labiatae family, is used for a variety of cosmetic and therapeutic purposes in herbal medicine[24]. Inhalation of essential oils of lavender reduced cholesterol plaques in atherosclerotic disease in rabbits, but showed no effect on serum cholesterol levels[25]. Lavander showed a hypolipidemic effect in rats[26]. In addition, lavender aromatherapy has displayed vasodilatory effects and enhanced coronary blood flow in human[27]. Extract of lavender flower protected isolated rat hearts against ischemic reperfusion (IR) injury[28]. In our recent study, lavender oil showed neuroprotective activity and antioxidant properties in an experimental model of stroke[29]. In a very recent study, treatment with essential oil of lavender after MI reduced ischemic injury in rats[30]. This study aimed to investigate the sub-acute toxicity study on the effects of different doses of lavender plant on liver of wistar rats.

II. MATERIAL AND METHOD

Male and female wister 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 stoechas were 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 in vacuum 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 stoechas extract 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

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control and treated groups. Values of P≤ 0.05 were considered significant.

III. RESULTS

Effect of 28 days oral administration of Lavandula stoechas on hematological parameters in rats

Lavandula stoechas caused 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 stoechas on hepatic indices in rats.

Lavandula stoechas, significantly significantly caused ($p<0.05$) increase of ALP and BILD at 100 mg/kg dose. Level of other parameters were not significantly ($p<0.05$) affected across doses administered.

Effect of 28 days oral administration of ethanol leaf extract of Lavandula stoechas on histology Liver of rats.

The liver showed vascular congestion, slight hepatic necrosis with slight sinusoidal congestion and lymphocyte hyperplasia at 100 mg/kg and 200 mg/kg, Sinusoidal congestion at 100 mg/kg and Moderate hepatic necrosis and vascular congestion at the control (10ml/kg) (Fig. 4).

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

Hematological parameters	DW(10ml/kg)	Treatment (mg/kg) LS (50)	LS (100)	LS (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, One way 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 3: Effect of 28 days oral administration of Ocimum canum on hepatic indices in wistar rats.

Hepatic indices	DW(10ml/kg)	Treatment (mg/kg) LS (50)	LS (100)	LS (200)
ALB (g/L)	38.53±1.76	44.20±1.00	35.20±1.71	43.22±1.33
ALP (IU/L)	113.200±6.729	152.000±8.19	370.00±43.72*	125.500±6.34
ALT (IU/L)	62.80±3.42	70.00±10.18	94.20±10.43	87.50±1.98
AST (IU/L)	299.40±9.90	297.33±7.62	175.20±3.79	233.00±1.77
BILD (mol/L)	0.32±0.073	0.26±0.71*	0.60±0.18*	0.61±0.13
BILT (mol/L)	2.34±0.51	2.92±0.25	3.46±0.19*	2.77±0.16
TP (g/L)	69.60±3.08	66.07±2.71	61.33±5.11	82.25±2.11

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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. DW = distilled water (ALB = albumin, ALP = alanine phosphatase, ALT = alanine transaminase, BILD = unconjugated bilirubin, BILT = conjugated bilirubin, TP = total protein).

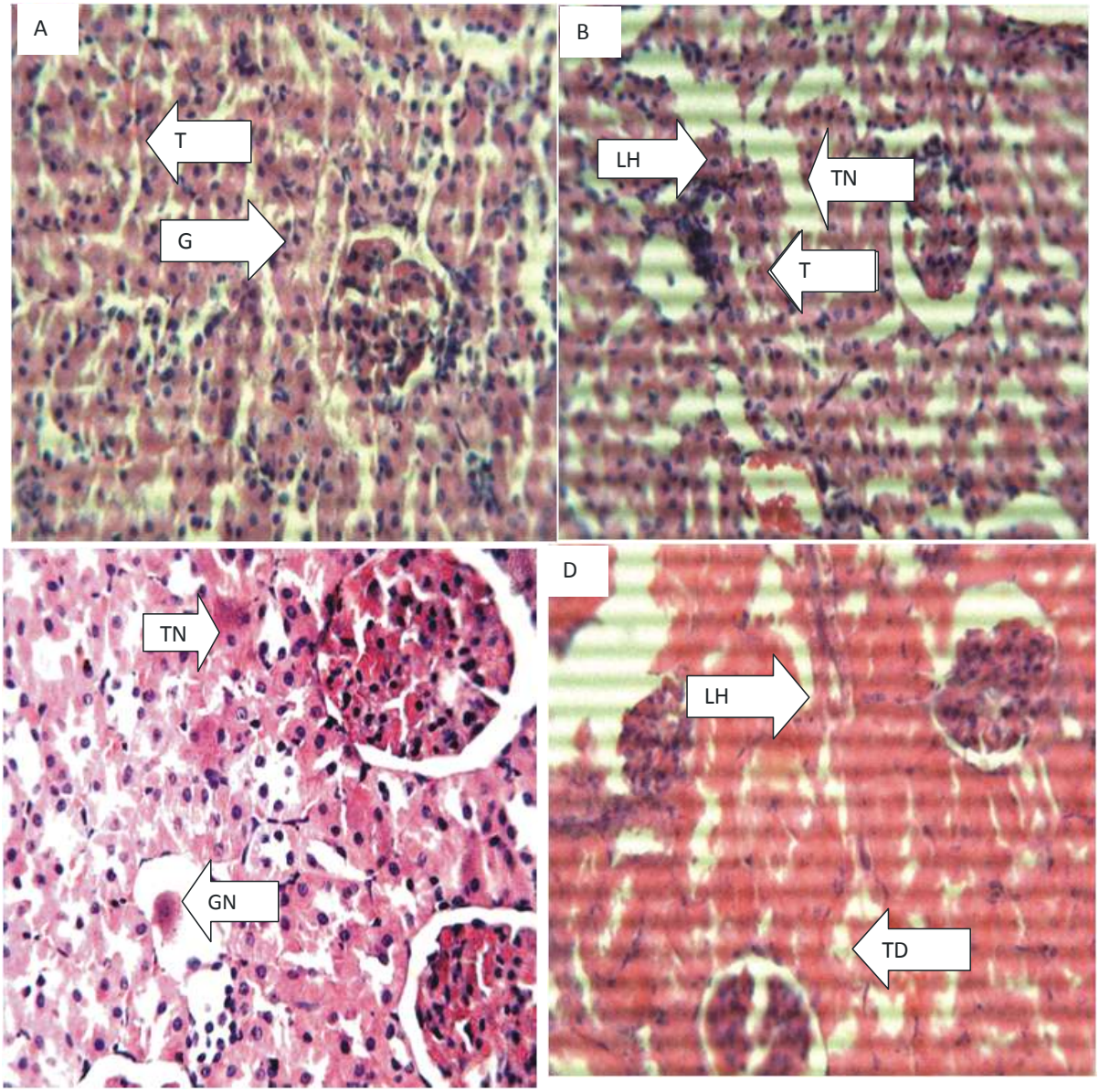

Figure 4:. figure of the liver (Hematoxylin and eosin. H and E ×100). (a) Control group, shows normal hepatocyte (H). (b) LS 50 mg/kg, (c) LS 100 mg/kg, (d) LS 200 mg/kg.

IV. DISCUSSION

Herbal medicine has been an essential component of oriental medicine (OM)[31,32], which has existed for over two thousand years[33]. The herbal medicines include dietary supplements that contain herbs either single or in mixtures. They are also called botanicals for their scents, flavour and/or therapeutic properties[34]. Herbal drugs are readily available in the market from health food stores without prescriptions and are widely used all over the world[35-38]. Over the past decade, there has been an increased global interest in traditional systems of medicine and herbal medicinal products. In part, this surge has been due to the rare or non-existent access to modern medicine in developing countries as well as the acceptance of herbal medicines by large populations of people in developed nations[39-45]. Hematological parameters

are useful indices that can be employed to assess the toxic potentials of plant extracts in living systems[46-50]. They can also be used to explain blood relating functions of chemical compound/plant extract. 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[51-54]. This can precipitate unexpected side effects on the tissue, organ or body system. In this study the effect of the plant on the heart and vascular parameters were evaluated[55-59]. Ethanol extract of Lavandula stoechas resulted 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 a person has a lower red blood count than is normal, their 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. Hemoglobin is essential for transferring oxygen in the blood from the lungs to the tissues. Myoglobin, in muscle cells, accepts, stores, transports and releases oxygen[61-63]. 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.

Liver function was assessed by assaying the activities and levels of serum ALT, AST, ALP, bilirubin (total and direct), total cholesterol, total protein and albumin which are originally present in the cytoplasm[43,64]. When there is hepatopathy, these enzymes and molecules leak into the blood stream which serves as an indicator for the liver damage[34,64]. The most commonly used indicators of liver (hepatocellular) damage are alanine aminotransferase (ALT) and aspartate aminotransferase (AST). The ALT is felt to be a more specific indicator of liver inflammation as AST is also found in other organs such as the heart and skeletal muscle[45,46]. The normal levels of serum ALT, AST and total protein and albumin levels as observed in extract administered rats is indicative of the plant possessing little to no effect in inducing liver injury. Alkaline phosphatase estimation is the most frequently used test to detect obstruction in the biliary system. Bilirubin is the main bile pigment in humans which, when elevated causes the yellow discoloration of the skin called jaundice. Bilirubin is formed primarily from the breakdown of a substance called heme found in red blood cells. It is taken up from the blood, processed, and then secreted into the bile by the liver. There is normally a small amount of bilirubin in the blood in healthy individuals (<17µmol/L). Conditions which cause increased formation of bilirubin, such as destruction of red blood cells, or decrease in its removal from the blood stream as in liver dysfunction, may result in an slight increase in the level of bilirubin in the blood[65,66]. Findings from the study revealed that there was significant increase in the level of ALP, BILD and BILT. These indicate that the plant extract may cause mild biliary obstruction, destruction of red blood cells and/or decrease in RBC removal from the blood stream. Slight hepatic necrosis with other normal hepatic features in histopathological study shows agreement with other parameters.

V. CONCLUSION

Though the plant is relatively safe, result of the study reveals that the plant could have slight effect on the liver which suggests that the plant should be use with caution when taken for a sustained period of time. Histological study reveals slight tubular distortion.

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