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Research Article

Evaluation of Biochemical Parameters of Ethanolic Extract of *Lepidium meyenii* in Male Wistar Rats

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ABSTRACT

The effects of ethanolic extract of *Lepidium meyenii* on some biochemical parameters were investigated with the purpose of *in vivo* safety evaluation of the extract. Forty male Wistar rats were grouped into five groups of eight animals each. Group A served as the control and received distilled water throughout the period of administration while groups B, C, D, and E received 25, 50, 75, and 100 mg/kg body weight of ethanolic extract of *L. meyenii* respectively for seven and fourteen days. After seven days of the administration, four animals from each of the groups were sacrificed and the rest were sacrificed after fourteen days, and biochemical alterations were monitored. The effects after the seven-day administration revealed that there was no significant ($p > 0.05$) difference in organ-body weight percentage, liver functional indices, kidney functional indices and the activity of some cytosolic and membrane-bound enzymes studied but following the fourteen-day administration, a significant difference ($p < 0.05$) were observed with increase in organ-body weight percentage of selected organs, increase in serum activity of the enzymes: ALT, AST, ALP; and aberrant variation in the kidney functional indices studied at the 50, 75 and 100 mg/kg body weight showing selective toxicity of the extract. Inconclusive results were obtained in the analysis of the seminal parameters for both the seven- and fourteen-day administration while similar effects on hematological parameters were observed for both the seven- and fourteen-day administration. This study showed that the extract may be hepatotoxic and nephrotoxic when administered beyond seven days in male Wistar rats especially at 100 mg/kg body weight.

Keywords: Cytosolic, Haematology, Hepatotoxic, Membrane, Nephrotoxic

Introduction

Traditional medicine is fundamentally based on health knowledge and beliefs about herbs, spiritual remedies, manual techniques, and exercises in order to maintain well-being and handle or prevent diseases [4, 7]. A medicinal plant is a plant that is used to maintain good health, to be administered for a specific condition, or both, whether in modern medicine or traditional medicine [34, 3]. Medicinal edible plants and plant-derived foods have nutritional and therapeutic benefits due to the synthesis of bioactive compounds, which are responsible for pharmacological activities and nutritional value [9, 11]. Extracts from plants have been reported to have a wide range of biological activities, which include antioxidant [24], anti-inflammatory and antimicrobial [16], cytotoxic [27, 19], and immunomodulatory activities [31]. Despite the profound therapeutic advantages posses-

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sed by some of the plants, some constituents of medicinal plants have been shown to be potentially toxic, carcinogenic and teratogenic [29]. Plants in folk medicine should therefore, be evaluated for safety or toxicity and necessary recommendations made on their use.

Lepidium meyenii commonly known as maca, is a species indigenous to the Central Andes of Peru as well as Nigeria which has been cultivated traditionally as a food crop and for its medicinal properties. Maca has a rosette of frilly leaves of 12–20 leaves like in radish and grows in the harsh climate of Central Andes in Peru, where there are strong winds and the highest temperature is 12ºC [26, 6]. *L. meyenii* is called Isu baka in yoruba language in Nigeria. Maca is the only domesticated Brassicaceae cultivated for food in the Andes [20]. Maca has been advertised as a 'superfood' and as the 'Peruvian Viagra' and the 'Peruvian Ginseng' referring to the attributed health claims of increasing vitality and longevity, enhancing fertility and libido and alleviating menopausal symptoms in women [22, 32, 10].

A wide range of studies on maca, both clinical trials and *in vivo* and *in vitro* assays, have been carried out over the years to examine these health claims [8]. However, there are few reports on the biochemical alterations of these plants in literature. With the alleged biological properties of *L. meyenii*, its toxicity should be examined. This study was conducted to investigate the biochemical alterations that are likely to be experienced following exposure to an ethanolic extract of *L. meyenii*.

Material and Methods

Plant material and authentication

Fresh *L. meyenii* roots were purchased from an herb seller in Oje market in Ibadan, Oyo State. It was authenticated at the Herbarium unit, Department of Plant Biology, Faculty of Life Sciences, University of Ilorin where a voucher number: UIL/001/1352, was given.

Experimental animals

Forty male Wistar rats (*Rattus novergicus*) weighing between 128 and 179 g, were obtained from the animal house unit, Department of Biochemistry, University of Ilorin, Ilorin, Kwara State. The rats were housed in clean polypropylene cages placed in well-ventilated housing conditions under humid tropical conditions. They were maintained on Vital Finisher Feed (Grand Cereals Ltd, Plateau, Nigeria) and tap water *ad libitum*. All the animals received humane care according to the criteria outlined in the 'Guide for the Care and Use of Laboratory Animals prepared by the National Academy of Science and published by the National Institute of Health [33].

Assay kits and chemical reagents

The assay kits for Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Alkaline Phosphatase (ALP), Gamma Glutamyl transferase (GGT) are products of Randox Laboratories Ltd. Ardmore, Diamond Road, Crumlin, County Antrim. All other reagents used in addition to those used in the determination of protein concentration were of analytical grade and were prepared in glass apparatus using distilled water and suitable solvents.

Preparation of extract

The *L. meyenii* roots were carefully peeled, washed, sliced into pieces, oven dried at 40 ºC and later milled into a fine powder before extraction. Powdered plant material (300g) was extracted in 500 ml of ethanol for 48hours at room temperature with frequent stirring. The extract was filtered through a sieve, handkerchief and Whattman no. 1 filter paper before it was concentrated using a water bath at 40 ºC (DK-420, China). This was later reconstituted in distilled water to give the required doses of 25, 50,75 and 100 mg/kg respectively.

Grouping of experimental animals

The animals were weighed and grouped according to their body weights into five groups of eight rats each. Group A (Control) received orally, 0.6 ml of distilled water for seven and fourteen days while Groups B, C, D and E were treated like the control except they received 25, 50 75 and 100 mg/kg body weight of the plant extract. The extract and distilled water were administered daily between 0700 – 0730 h using plastic oropharyngeal cannula.

Preparation of serum

The method described by Yakubu *et al.* [40], was adopted for the preparation of the serum. Briefly, under ether anaesthesia, the neck area of the rats was quickly shaved to expose the jugular veins. The veins after being slightly displaced (to avoid contamination with interstitial fluid) were

cut with sterile blade and an aliquot of the blood was collected into EDTA bottles for analysis of haematological parameters. The remaining blood samples collected in non- heparinized bottles were allowed to clot for 10 minutes at room temperature then centrifuged at 3000 rpm for 10 minutes using a tabletop centrifuge (80-1, China) in order to separate the serum from the clotted blood. The serum was separated into labelled bottles using a Pasteur's pipette and used within 48 h of preparation for the various biochemical assays. The liver, kidney and heart were thereafter harvested from the animals and weighed for the determination of the organ-body weight percentage before homogenized to carry out biochemical analysis.

Determination of biochemical parameters

The method described by Ashafa *et al.* [5] was adopted in the calculation of organ-body weight percentage. Albumin, globulin, bilirubin (total and direct), total protein, electrolytes such as sodium ion, potassium ion and chloride ion, creatinine, urea, alkaline phosphatase, creatine kinase, gamma glutamyl transferase, alanine and aspartate aminotransferases were determined in the serum using assay kits from Randox Laboratories, Crumlin, County Antrim, Northern Ireland on Versa-Max ELISA Microplate Reader, California, United States. The index of sperm motility and morphology was evaluated using the method descrybed by Sonmez *et al.* [35] while the sperm count was evaluated using the method described by Verma *et al.* [38]. The SYSMEX-K21 (Japan) was used for the determination of haematological parameters.

Statistical analysis

Data were expressed as the mean± SEM of at least two [2] determinations. Statistical analysis was performed using One-way Analysis of Variance (ANOVA) and Duncan Multiple Range Test (DMRT). The data were considered statistically significant at $P < 0.05$.

Results and Discussion

Effects of oral exposure of the ethanolic extract of L. meyenii on organ-body weight percentage of male wistar rats

Following the seven-day administration, the ethanolic extract induced a significant increase ($p < 0.05$) in the organ-weight percentage of the heart in the animals administered with 25 and 50 mg/kg body weight of the extract when compared with the control and other groups which showed no significant variation as shown in Table 1. While after the fourteen-day administration period, the ethanolic extract of *L. meyenii* induced a significant increase on the organ-body weight percentage of the liver in animals that were administered with 25 mg/kg body weight of the extract while a significant decrease was observed in animals administered with the 100 mg/kg body weight of the extract when compared with the control and the other groups which were not significantly altered (Table 2). There was a significant decrease ($p < 0.05$) in the percentage for the kidney in the group administered with the 100 mg/kg body weight of the extract when compared to the control and the other groups. There was significant increase in the heart of groups administered with the 25, 75, and 100 mg/kg body weight of the extract when compared with the control.

Plants are widely used to treat diseases in non-industrialized societies, not just because they are cheaper than the modern medicinal counterparts but also because they exhibit similar therapeutic

Table 1. Effects of seven days oral exposure of the ethanolic extract of *L. meyenii* on organ-body weight percentage of male wistar rats

	Percentage (%)		
Doses (mg/kg body weight)	Liver	Kidney	Heart
Control	2.86 ± 0.12^{a}	0.62 ± 0.03^{a}	0.39 ± 0.06^{a}
25	3.19 ± 0.13^{b}	0.60 ± 0.02^{a}	0.35 ± 0.02^{a}
50	3.02 ± 0.03^{b}	0.61 ± 0.02^{a}	0.35 ± 0.01^{a}
75	3.12 ± 0.18^{a}	0.62 ± 0.02^{a}	0.32 ± 0.03^{a}
100	3.10 ± 0.15^{a}	0.67 ± 0.05^{a}	0.32 ± 0.01^{a}

Values are mean of 4 replicates ± SEM, data carrying different superscripts for each parameter are significantly ($P < 0.05$) different

Table 2. Effects of fourteen days oral exposure of the ethanolic extract of *L. meyenii* on organ-body weight percentage of male wistar rats

	Percentage (%)		
Doses (mg/kg body weight)	**Liver**	**Kidney**	**Heart**
Control	3.07 ± 0.24^{a}	0.59 ± 0.01^{a}	0.27 ± 0.02^{a}
25	3.52 ± 0.12^{b}	0.59 ± 0.03^{a}	0.34 ± 0.03^{b}
50	3.14 ± 0.27^{a}	0.60 ± 0.02^{a}	0.30 ± 0.01^{a}
75	3.29 ± 0.06^{a}	0.63 ± 0.03^{a}	0.32 ± 0.02^{b}
100	2.84 ± 0.00^{c}	0.50 ± 0.00^{b}	0.32 ± 0.00^{b}

Values are mean of 4 replicates ± SEM, data carrying different superscripts for each parameter are significantly ($P < 0.05$) different

effects [15]. Herbal medicine is used by up to 80 % of the population in developing countries [13]. Despite the widespread use, few scientific studies have been undertaken to ascertain the safety and efficacy of traditional remedies [13].

In this study, the extract did not significantly alter the organ-body weight percentages of the liver and kidney. The phenolic compounds present in the ethanolic extract of *L. meyenii* which have anti-inflammatory properties [37] are likely to be related to lack of increase in organ-body weight percentages observed in the experimental animals.

Effects of oral exposure of the ethanolic extract of L. meyenii on haematological indices of male wistar rats

After seven days, the ethanolic extract of *L. meyenii* induced a significant increase ($p < 0.05$) in the amount of white blood cells (WBC) and red blood cells (RBC) in the animals administered with 75 and 100 mg/kg body weight of the extract while the other groups had no significant variation when compared to the control (Table 3). The extract induced significant increase ($p < 0.05$) in the concentration of haemoglobin (HGB), mean corpuscular haemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) in the animals administered with 50, 75 and 100 mg/kg body weight of the ethanolic extract while the 25 mg/kg test group showed no significant variation when compared with the control. Significant increase ($p < 0.05$) in the haematocrit (HCT) was observed in all the test groups when compared to the control. The mean corpuscular volume (MCV) increased significantly ($p < 0.05$) in the 50 and 75 mg/kg body weight test groups. The platelet (PLT) count of the animals administered with the 25 mg/kg body weight of the ethanolic extract was significantly decreased ($p < 0.05$) when compared with the control and other groups. The amount of lymphocytes (LYM) was observed to have reduced significantly ($p < 0.05$) in the 50 mg/kg

Table 3. Effects of seven days oral exposure of the ethanolic extract of *L.meyenii* on haematological indices of male wistar rats

Parameters	Control	25 mg/kg bwt	50 mg/kg bwt	75 mg/kg bwt	100 mg/kg bwt
WBC($x10^3/\mu L$)	9.35 ± 0.85^{a}	10.50 ± 2.50^{a}	11.35 ± 1.45^{a}	13.25 ± 0.85^{b}	14.40 ± 2.90^{b}
RBC($x10^6\mu L$)	7.39 ± 0.04^{a}	7.25 ± 0.25^{a}	7.37 ± 0.09^{a}	8.08 ± 0.61^{b}	7.59 ± 0.14^{b}
HGB(g/dl)	11.20 ± 0.00^{a}	11.40 ± 0.30^{a}	12.35 ± 0.05^{b}	13.10 ± 0.60^{b}	12.45 ± 0.35^{b}
HCT(%)	37.50 ± 0.10^{a}	38.40 ± 0.10^{b}	40.10 ± 0.90^{b}	42.55 ± 3.15^{b}	39.75 ± 0.65^{b}
MCV(fL)	50.75 ± 0.45^{a}	53.05 ± 1.95^{a}	54.40 ± 0.90^{b}	52.65 ± 0.05^{c}	52.40 ± 1.80^{a}
MCH (pg)	15.15 ± 0.05^{a}	15.75 ± 0.95^{a}	16.75 ± 0.15^{b}	16.25 ± 0.45^{b}	16.45 ± 0.75^{b}
MCHC(g/dl)	29.85 ± 0.05^{a}	29.70 ± 0.70^{a}	30.80 ± 0.60^{b}	30.85 ± 0.85^{b}	31.30 ± 0.40^{b}
PLT($x10^{3/}\mu L$)	802.00 ± 37.00^{a}	685.50 ± 43.50^{b}	770.50 ± 74.50^{a}	805.50 ± 126.5^{a}	795.00 ± 23.00^{a}
LYM(%)	$96.\ 15 \pm 0.75^{a}$	90.50 ± 5.00^{a}	89.10 ± 0.00^{b}	94.60 ± 1.50^{a}	96.90 ± 0.00^{a}

Values are mean of 4 replicates ± SEM, data carrying different superscripts for each parameter are significantly ($P < 0.05$) different

Table 4. Effects of fourteen days oral exposure of ethanolic extract of *L. meyenii* on haematological idices of male wistar rats

Parameters	Control	25 mg/kg bwt	50 mg/kg bwt	75 mg/kg bwt	100 mg/kg bwt
WBC ($\times10^3$/µL)	10.65 ± 1.65^a	13.15 ± 3.75^a	12.60 ± 2.10^a	12.50 ± 4.00^b	11.00 ± 0.00^a
RBC ($\times10^6$µL)	7.13 ± 0.37^a	6.42 ± 0.40^a	7.70 ± 0.01^b	7.28 ± 0.66^a	7.06 ± 0.00^a
HGB (g/dl)	11.20 ± 0.60^a	9.70 ± 1.70^a	12.20 ± 0.20^b	12.45 ± 0.75^a	11.50 ± 0.00^a
HCT (%)	36.80 ± 2.70^a	33.50 ± 1.80^a	40.15 ± 1.25^a	39.75 ± 3.45^a	36.40 ± 0.00^a
MCV (fL)	51.55 ± 1.15^a	52.25 ± 0.45^a	52.15 ± 1.65^a	54.65 ± 0.15^b	51.60 ± 0.00^a
MCH (pg)	15.70 ± 0.00^a	15.00 ± 1.70^a	15.85 ± 0.25^a	17.15 ± 0.55^b	16.30 ± 0.00^b
MCHC (g/dl)	30.50 ± 0.60^a	28.75 ± 3.55^a	30.40 ± 0.40^a	31.40 ± 0.80^a	31.60 ± 0.00^b
PLT ($\times10^{3/}$µL)	632.50 ± 104.50^a	423.50 ± 112.50^a	714.0 ± 56.00^a	611.50 ± 11.50^a	677.00 ± 0.00^a
LYM (%)	96.65 ± 0.25^a	77.25 ± 2.25^b	97.10 ± 0.00^c	93.75 ± 1.15^d	96.90 ± 0.00^a

Values are mean of 4 replicates ± SEM, data carrying different superscripts for each parameter are significantly ($P < 0.05$) different

body weight test group as shown in Table 3.

Following the fourteen-day administration, the ethanolic extract induced significant increase in WBC and MCV in the animals administered with the 75 mg/kg body weight of the extract when compared to the control group while there was no significant variation in the other groups (Table 4). Significant increase ($p < 0.05$) in RBC and HGB was observed in the animals administered with the 50 mg/kg of the extract when compared to the control and the other groups which had no significant difference. No significant variation was observed in the HCT and PLT amounts of all test groups administered with the ethanolic extract of *L. meyenii* when compared to the control. The extract induced a significant increase ($p < 0.05$) in MCH of animals administered with 75 and 100 mg/kg body weight of the ethanolic extract when compared to the control. A significant increase ($p < 0.05$) in the MCHC was observed in the animals administered 100 mg/kg body weight of the extract when compared with the control. The LYM count was significantly decreased ($p < 0.05$) in the groups administered with 25 and 75 mg/kg body weight of the extract while there was a significant increase in the group administered with 100 mg/kg body weight of the extract when compared to the control as shown in Table 4.

The increase in white blood cells by the extract of *L. meyenii* at higher doses may indicate a boost in the immune system [41]. Hence, at high concentrations it has the potential of inducing white blood cell generation. The increase in red blood cell count, haemoglobin concentration, haematocrit, mean corpuscular volume, mean corpuscular haemoglobin and mean corpuscular haemoglobin concentration might be indicative of the haemoprotective potential of the extract due to the observed potential ability of the extract to protect the functional and structural integrity of haemoglobin as well as stimulate bone marrow production of red blood cells. The reduction in platelet counts in rats administered with the 25mg/kg body weight dose could be associated with thrombocytopenia [1]. It can thus be inferred that at lower doses, the ethanolic extract may not have marked effect on the haematological parameters of experimental animals, while higher doses of about 100 mg/kg body weight increase some of the hematological parameters of male Wistar rats, which agrees with a study from Fei *et al.* [18] that extracts of *L. meyenii* plant increased some haematological parameters of male rats.

Effects of oral exposure of the ethanolic extract of L. meyenii on alanine aminotransferase (alt) activity of male wistar rats

The ethanolic extract of *L. meyenii* induced no significant ($p > 0.05$) differences in the specific activity of alanine aminotransferase in the serum of the animals treated with the 25, 50 and 75 mg/kg body weight of the extract when compared with the control, however, there was a significant decrease ($p < 0.05$) in the activity of ALT in the 100mg/kg body weight test group when compared to the control and the other groups (Figure 1). There were no significant variations ($p > 0.05$) in the activity of ALT in the kidney and liver at all doses when compared to the control.

The ethanolic extract of *L. meyenii* induced significant increase ($p < 0.05$) in the activity of ALT in the serum of the experimental animals

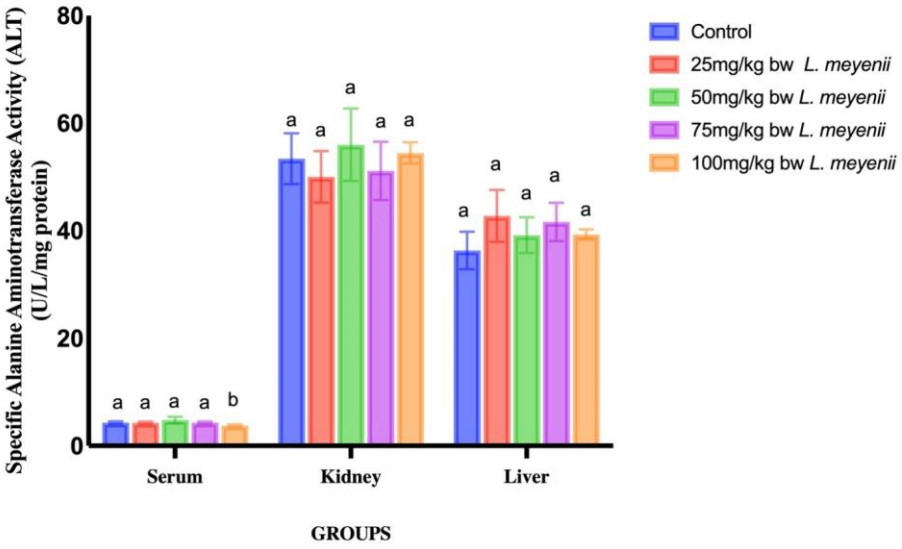

Figure 1. Specific Alanine Aminotransferase (ALT) activity in the serum and isolated organs of male Wistar rats administered with the ethanolic extract of *L. meyenii* after seven days

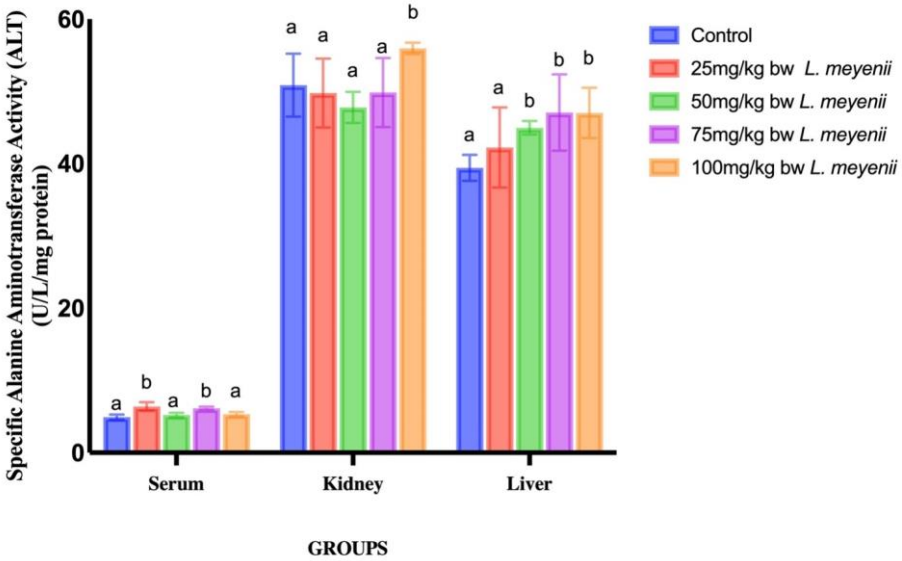

Figure 2. Specific Alanine Aminotransferase (ALT) activity in the serum and isolated organs of male Wistar rats administered with the ethanolic extract of *L. meyenii* after fourteen days

Note: Values are mean of 4 replicates ± SEM, bars carrying different superscripts for each parameter are significantly ($P < 0.05$) different

administered the 25 and 75 mg/kg body weight of the extract when compared to the control while both the 50 mg/kg and 100 mg/kg body weight test groups showed no variation ($p > 0.05$) against the control (Figure 2). The activity in the kidney was significantly increased in the 100 mg/kg body weight test group alone, when compared to the control while the 25, 50 and 75 mg/kg body weight groups showed no significant variation when compared with the control. In the liver, the extract induced significant increase in the activity of ALT in the 50, 75 and 100 mg/kg body weight test groups when compared to the control while the 25 mg/kg body weight test grouped showed no significant variation ($p > 0.05$) when compared to the control as depicted in Figure 2.

The decrease in serum alanine aminotransferase (ALT) activity at the 100 mg/kg body weight dose and no significant variation in activity in the organs studied (liver and kidney) at all the doses after a seven-day administration period implied the extract did not cause cellular damage which

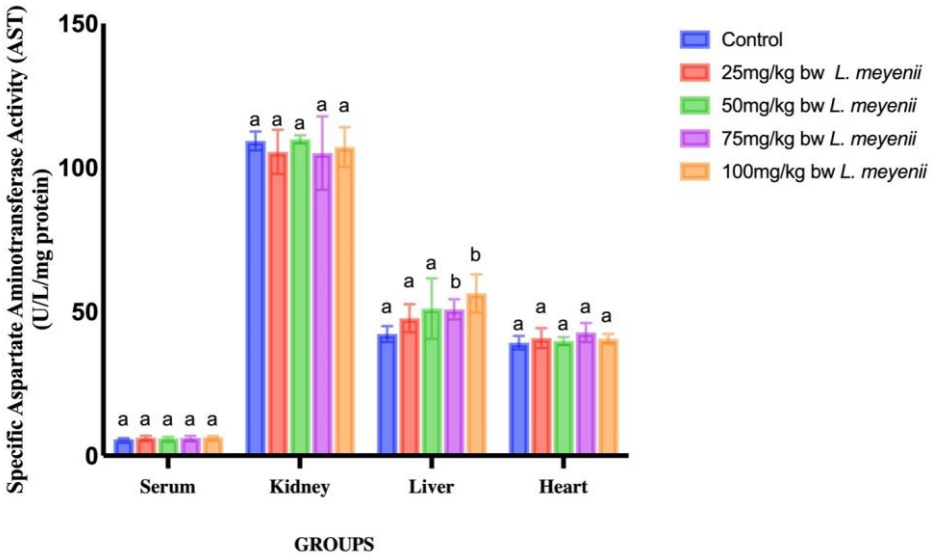

Figure 3. Specific Aspartate Aminotransferase (AST) activity in the serum and isolated organs of male Wistar rats administered with the ethanolic extract of *L. meyenii* after seven days

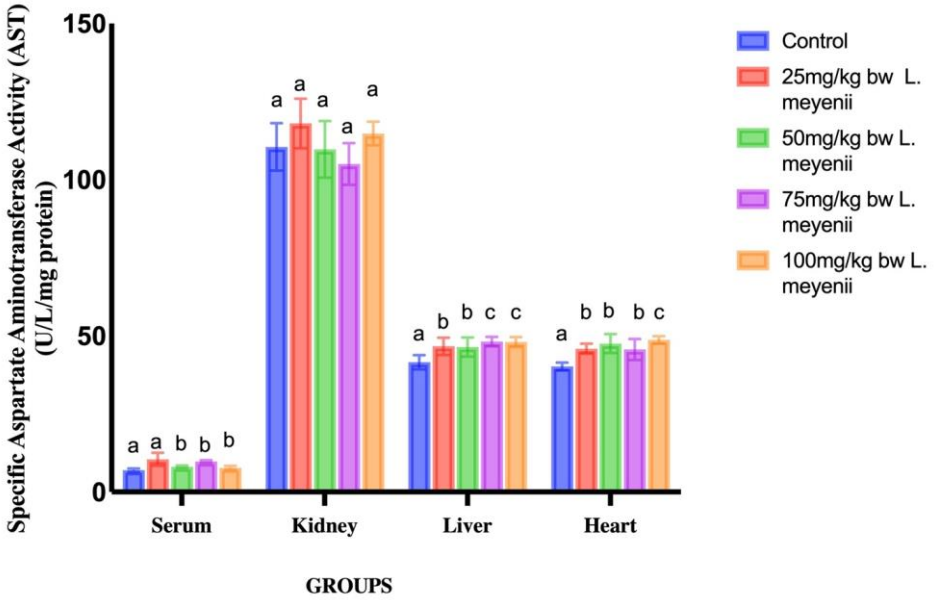

Figure 4. Specific Aspartate Aminotransferase (AST) activity in the serum and isolated organs of male Wistar rats administered with the ethanolic extract of *L. meyenii* after fourteen days

Note: Values are mean of 4 replicates ± SEM, bars carrying different superscripts for each parameter are significantly ($P < 0.05$) different

agrees with a study carried out by Gregory *et al.* [21] where the observed activity of ALT in the serum was seen to be lower than in the organs at normal physiological states.

After a fourteen-day administration period, increased ALT activity in the kidney at the 100 mg/kg body weight dose and increased ALT activity in the liver at the 50, 75 and 100 mg/kg body weight doses may be suggestive of the extract's potential in stimulating expression and synthesis of ALT, thus possessing nephroprotective and hepatoprotective properties, however, elevated serum activity at the 25 and 75 mg/kg body weight dose is suggestive of enzyme leakage due to cellular damage. The hepatoprotective properties of the saponins and flavonoids present in the ethanolic extract may have contributed to the observed activity which is in line with reports by Qu *et al.* [30] where saponins from *Actinida valvata* dun root reversed carbon tetrachloride-induced liver damage in mice.

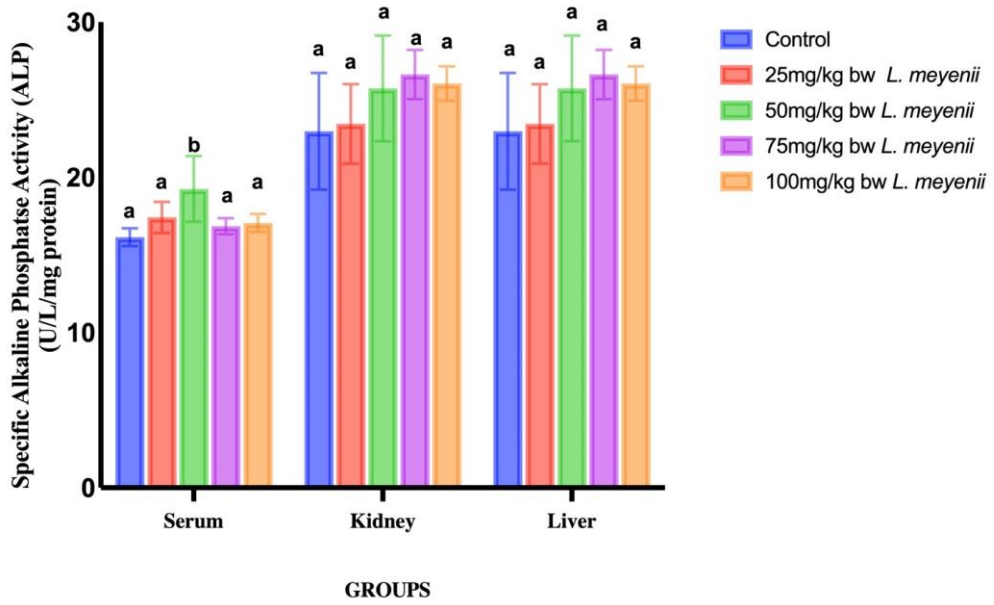

Figure 5. Specific Alkaline Phosphatase (ALP) activity in the serum and isolated organs of male Wistar rats administered with the ethanolic extract of *Lepidium meyenii* after seven days

Note: Values are mean of 4 replicates ± SEM, bars carrying different superscripts for each parameter are significantly ($P < 0.05$) different

Effects of oral exposure of the ethanolic extract of L. meyenii on aspartate aminotransferase (ast) activity of male wistar rats

The ethanolic extract of *L. meyenii* induced no significant variations ($p > 0.05$) in the activity of aspartate aminotransferase in all test groups when compared with the control in the serum, kidney and heart (Figure 3). In the liver, the extract induced significant increase ($p < 0.05$) in the activity of AST in the 75 and 100 mg/kg body weight test groups when compared to the control while the 25 and 50 mg/kg body weight test groups showed no significant variations against the control as depicted in Figure 3.

The ethanolic extract of *L. meyenii* induced no significant variation in the serum activity of AST in the 25 mg/kg test group however, the 50, 75 and 100 mg/kg body weight test groups showed statistical increases ($p < 0.05$) when compared to the control (Figure 4). The activity of AST in the kidney showed no significant variation ($p > 0.05$) when compared to the control at all doses. The extract induced significant increase in the activity in all doses when compared to the control in the liver and heart in a somewhat similar manner as shown in Figure 4.

No variations in the activity of aspartate aminotransferase in the serum, kidney and heart but increase in activity in the liver at the 75 and 100 mg/kg body weight dose after a seven-day administration period further supports the observed findings of the hepatoprotective potential of the ethanolic extract of *L. meyenii*. The increased activity of AST in the serum at the 50, 75 and 100 mg/kg body weight doses after a fourteen-day administration period implied cellular damage to the plasma membrane of the rats' organs. Such tissue damage also suggests that the extract is not completely safe at doses higher than 25 mg/kg body weight. Therefore, it can be inferred that at elevated doses and prolonged oral use of the ethanolic extract of *L. meyenii* may pose a threat to good health.

Effects of oral exposure of the ethanolic extract of L. meyenii on alkaline phosphatase (alp) activity of male wistar rats

The ethanolic extract of *L. meyenii* induced no significant variation ($p > 0.05$) on the serum activity of alkaline phosphatase when compared with the control in all but the 50 mg/kg body weight test group where there was a significant increase ($p < 0.05$) when compared to the control (Figure 5). The extract induced no significant variations ($p >$

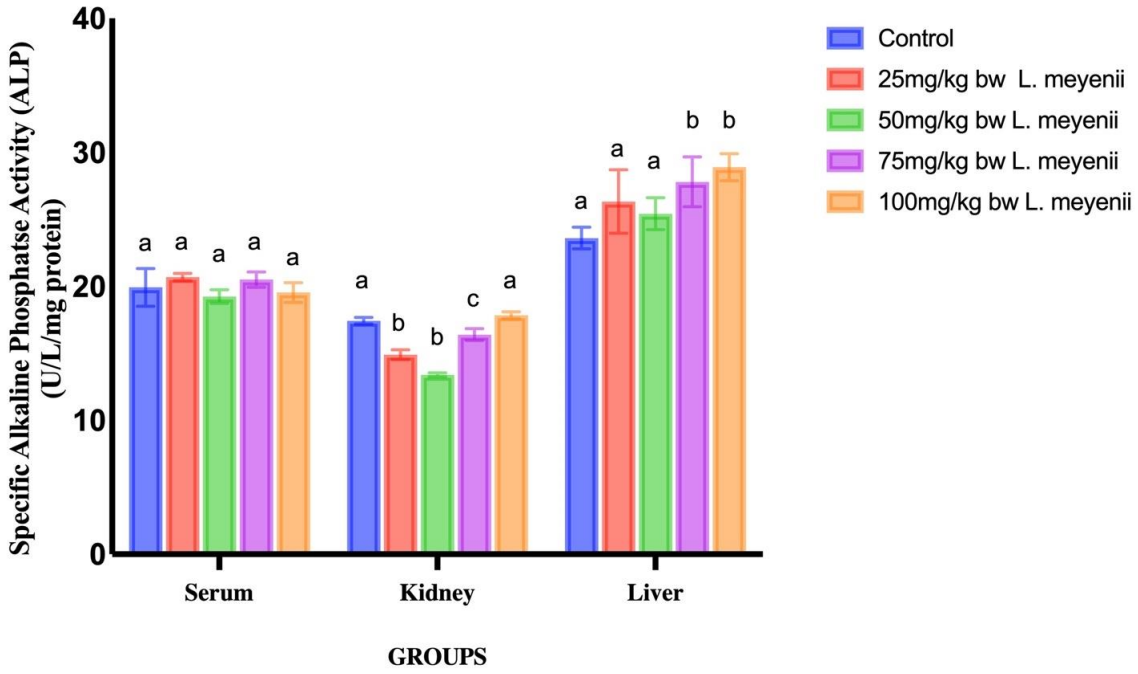

Figure 6. Specific Alkaline Phosphatase (ALP) activity in the serum and isolated organs of male Wistar rats administered with the ethanolic extract of *L. meyenii* after fourteen days

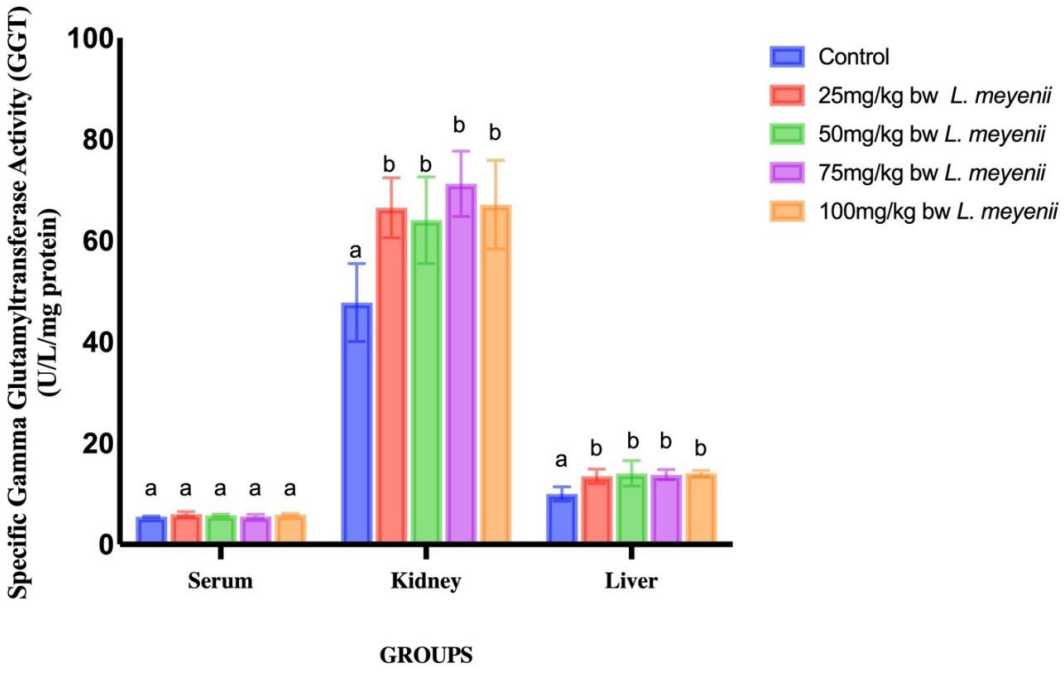

Figure 7. Specific Gamma Glutamyltransferase (GGT) activity in the serum and isolated organs of male Wistar rats administered with the ethanolic extract of *L. meyenii* after seven days

Note: Values are mean of 4 replicates ± SEM, bars carrying different superscripts for each parameter are significantly ($P < 0.05$) different

0.05) in the activity of ALP in the liver and kidney of the experimental animals at all doses when compared to the control as shown in Figure 5.

The activity of ALP in the serum showed no significant variation ($p > 0.05$) in the experimental animals administered with the ethanolic extract of *L. meyenii* at all doses when compared to the control (Figure 6). The activity in the kidney was

significantly decreased ($p < 0.05$) in the 25, 50 and 75 mg/kg body weight test groups when compared to the control while the activity of ALP in the kidney of animals administered the 100 mg/kg body weight of the extract showed no significant variation. The activity of ALP in the liver increased significantly ($p < 0.05$) in the groups administered the 75 and 100 mg/kg body weight of the extract when compared to the control while the 25 and 50 mg/kg body weight test groups showed no significant variation when compared to the control (Figure 6).

After the fourteen-day administration period, no variation in alkaline phosphatase activity was observed when compared to the control in the serum but a significant decrease was observed in the kidney at the 25, 50 and 75 mg/kg body weight groups which may be attributed to the extract impairing or preventing the synthesis or expression of the enzyme. An increase in activity was observed in the liver at the 75 and 100 mg/kg body weight which may be due to increased functional activity of the liver probably leading to *de novo* synthesis of enzyme molecules [40].

Effects of oral exposure of the ethanolic extract of L. meyenii on gamma glutamyltransferase (GGT) activity of male wistar rats

The ethanolic extract of *L. meyenii* induced no significant variation ($p > 0.05$) on the serum activity of gamma glutamyltransferase when compared to the control (Figure 7). The activity of GGT in
the kidney and liver showed significant increase in the animals administered the 25, 50, 75 and 100 mg/kg body weight of the ethanolic extract when compared to the control as depicted in Figure 7.

Figure 8 shows the activity of GGT in the serum and kidney with no significant variation ($p > 0.05$) in the animals administered the 25, 50 and 75 mg/kg body weight of the ethanolic extract of *L. meyenii* when compared to the control while the 100 mg/kg body weight test group showed significant increase ($p < 0.05$) in activity when compared to the control. The activity of GGT in the liver showed no significant variation ($p > 0.05$) when compared to the control (Figure 8).

In this study, following the seven-day administration, no variation was observed in the serum activity of GGT when compared to the control, however, there was significant increase in activity of the enzyme in the liver and kidney. The activity of the GGT was however elevated in the serum after a fourteen-day administration at the 100 mg/kg body weight group when compared with the control, a similar increase was observed in the kidney, but no variation was seen in the liver. It can thus be assumed that at higher doses, the potential of toxicity of the extract increases.

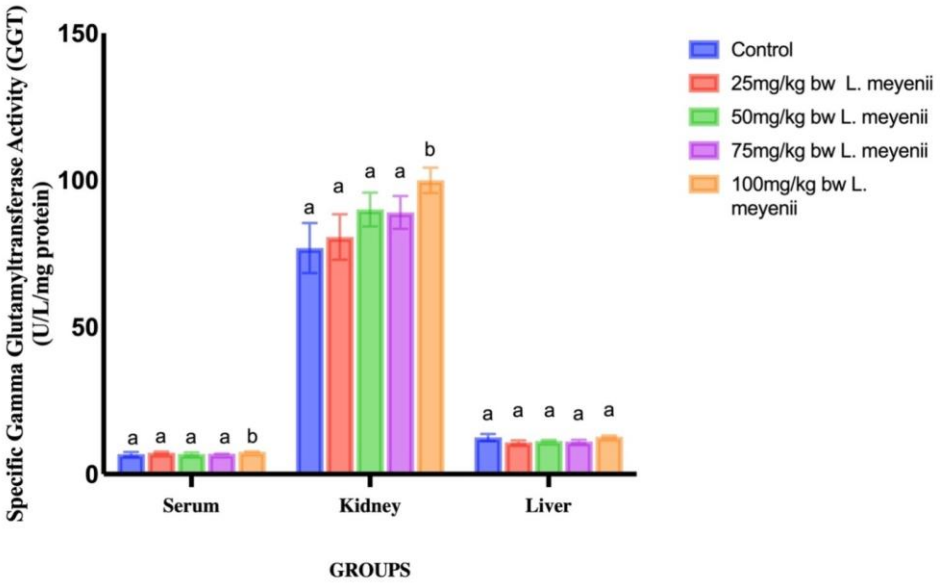

Figure 8. Specific Gamma Glutamyltransferase(GGT) activity in the serum and isolated organs of male Wistar rats administered with the ethanolic extract of *L. meyenii* after fourteen days

Note: Values are mean of 4 replicates ± SEM, bars carrying different superscripts for each parameter are significantly ($P < 0.05$) different

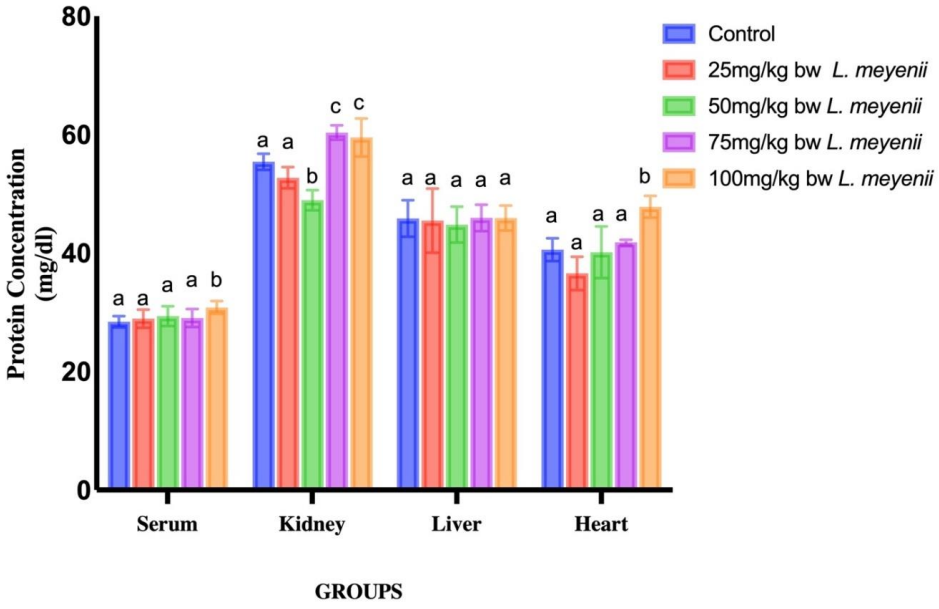

Figure 9. Protein Concentrations in the serum and isolated organs of male Wistar rats administered with the ethanolic extract of *L. meyenii* after seven days

Note: Values are mean of 4 replicates ± SEM, bars carrying different superscripts for each parameter are significantly ($P < 0.05$) different

Effects of oral exposure of the ethanolic extract of L. meyenii on protein concentrations of male wistar rats

The ethanolic extract of *L. meyenii* induced no significant variation ($p > 0.05$) in the serum and heart protein concentrations of the animals administered the 25, 50 and 75 mg/kg body weight of the extract when compared to the control while the 100 mg/kg body weight test group showed a significant increase ($p < 0.05$) when compared to the control (Figure 9). In the kidney, the protein concentration showed no significant variation in the 25 mg/kg body weight test group when compared to the control, there was however a significant decrease ($p < 0.05$) in concentration of protein in the group administered the 50 mg/kg body weight of extract when compared to the control; both the 75 mg/kg and 100 mg/kg body weight test groups showed significant increase ($p < 0.05$) in protein concentration when compared to the control and other groups (Figure 9). The protein concentration in the liver showed no significant variation ($p > 0.05$) in all the test groups when compared with the control.

Figure 10 shows the protein concentration in the serum with significant decrease ($p < 0.05$) when compared with the control in the test groups administered the 50, 75 and 100 mg/kg body weight of the ethanolic extract while the group administered 25 mg/kg body weight of the extract showed no significant variation ($p > 0.05$) when compared with the control. In the kidney, there was a significant increase ($p < 0.05$) observed in 100 mg/kg body weight test group when compared with the control while the others showed no significant variation ($p > 0.05$) when compared with the control. The protein concentration in the liver showed a significant decrease in the animals administered 25, 50 and 75 mg/kg body weight of the extract when compared to the control while an increase was observed in the 100 mg/kg body weight test group when compared to the control (Figure 10). In the heart, the concentrations showed significant increase in the 75 and 100 mg/kg body weight test groups, with no significant difference in the 25 and 50 mg/kg body weight test group as shown in Figure 10.

In this study, the serum and heart protein concentrations were elevated in the 100 mg/kg body weight group when compared to the control while the concentration in the kidney decreased in the 25 mg/kg body weight group but increased in the 75 and 100 mg/kg body weight groups when compared to the control. There were no variations in the liver indicating the ability of the liver to synthesize proteins was not compromised after a seven-day administration period. Serum total protein level may increase in cases of dehydration and

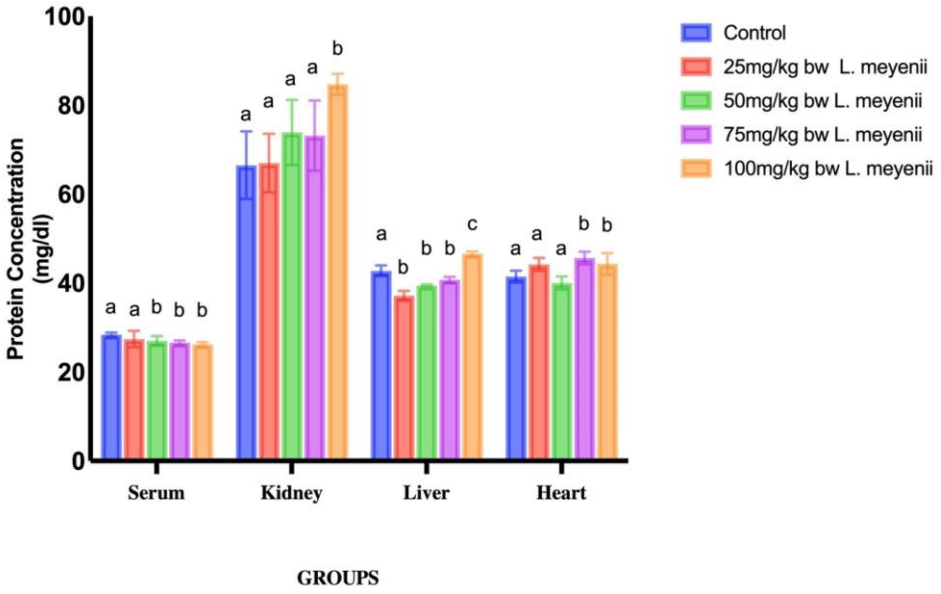

Figure 10. Protein Concentrations in the serum and isolated organs of male Wistar rats administered with the ethanolic extract of *Lepidium meyenii* after fourteen days

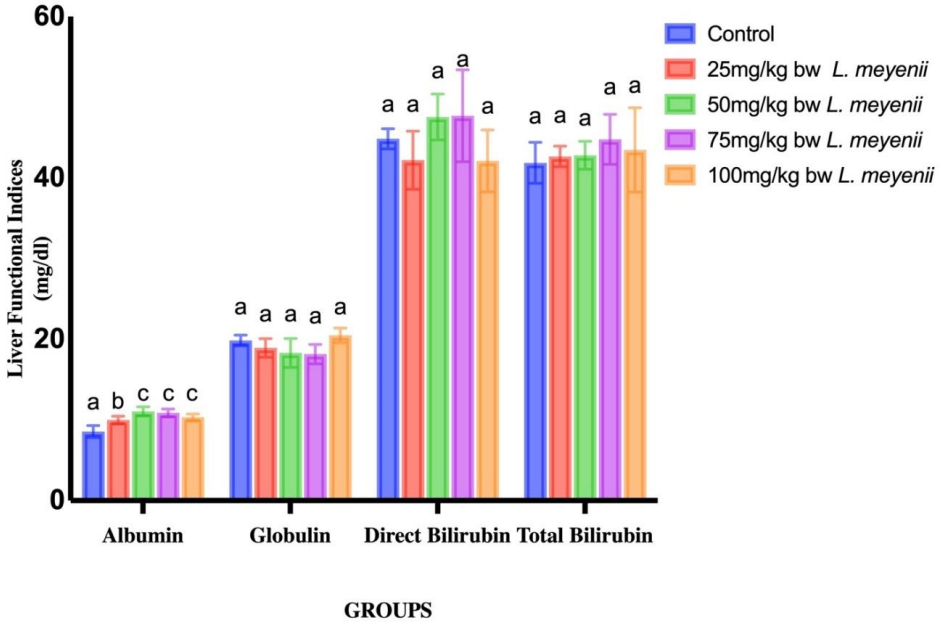

Figure 11. Liver Functional Indices of Male Wistar Rats administered with the ethanolic extract of *L. meyenii* after seven days

Note: Values are mean of 4 replicates ± SEM, bars carrying different superscripts for each parameter are significantly ($P < 0.05$) different

infections causing increase in immunoglobin concentration [2]. However, after a fourteen-day administration period, the serum protein levels were significantly decreased in all the test groups when compared with the control with a similar decrease observed in the liver at all but the 100 mg/kg test group which indicates the onset of incapability of hepatocytes to synthesize proteins, over hydration, malabsorption, liver disease and hypogammaglobulinaemia [2].

Effects of oral exposure of the ethanolic extract of L. meyenii on liver functional indices of male wistar rats

The ethanolic extract of *L. meyenii* induced no significant variation ($p > 0.05$) in the concentra-

tions of globulin, direct and total bilirubin in the animals administered the 25, 50, 75 and 100 mg/kg body weight of the extract when compared to the control (Figure 11). The albumin concentration in the groups administered the 25, 50, 75, and 100 mg/kg body weight of the extract showed significant increase ($p < 0.05$) when compared to the control as depicted in Figure 11.

The extract induced no significant variations in the albumin and globulin concentrations of all the test groups when compared with the control group (Figure 12). The total bilirubin concentrations increased ($p < 0.05$) in all but the 100 mg/kg body weight test group where it showed no significant variation from the control group. The extract induced no significant variation ($p > 0.05$) in the concentration of direct bilirubin of the animals administered the 25, 50 and 75 mg/kg body weight of the extract while there was a statistical increase ($p < 0.05$) in the concentration of the group administered the 100 mg/kg body weight of the extract as depicted in Figure 12.

In this study, after a seven-day administration period, all doses of the extract increased albumin concentration when compared with the control. The increased albumin concentrations may not be a sign of impaired liver function as albumin may also be increased in states of dehydration and the mere presence of the extract may be a factor in the increase in albumin as it is increased in the presence of certain drugs. All doses of the extract did not show a significant variation in the globulin, direct and total bilirubin concentration in the liver. After the fourteen-day administration period, there was no significant variation in concentrations of albumin and globulin when compared with the control. There was a significant increase in the concentration of total bilirubin at the 25, 50 and 75 mg/kg body weight test groups when compared with the control as well as an increase in direct bilirubin at the 100 mg/kg body weight. The increase in the concentration of bilirubin may be attributed to a compromise in liver function.

Effects of oral exposure of the ethanolic extract of L. meyenii on kidney functional indices of male wistar rats

The ethanolic extract of *L. meyenii* induced a significant increase ($p < 0.05$) in chloride ion concentrations of the animals administered with the 50 mg/kg body weight of the extract when compared with the control while the other test groups showed no significant difference. The sodium and potassium ion concentrations showed no

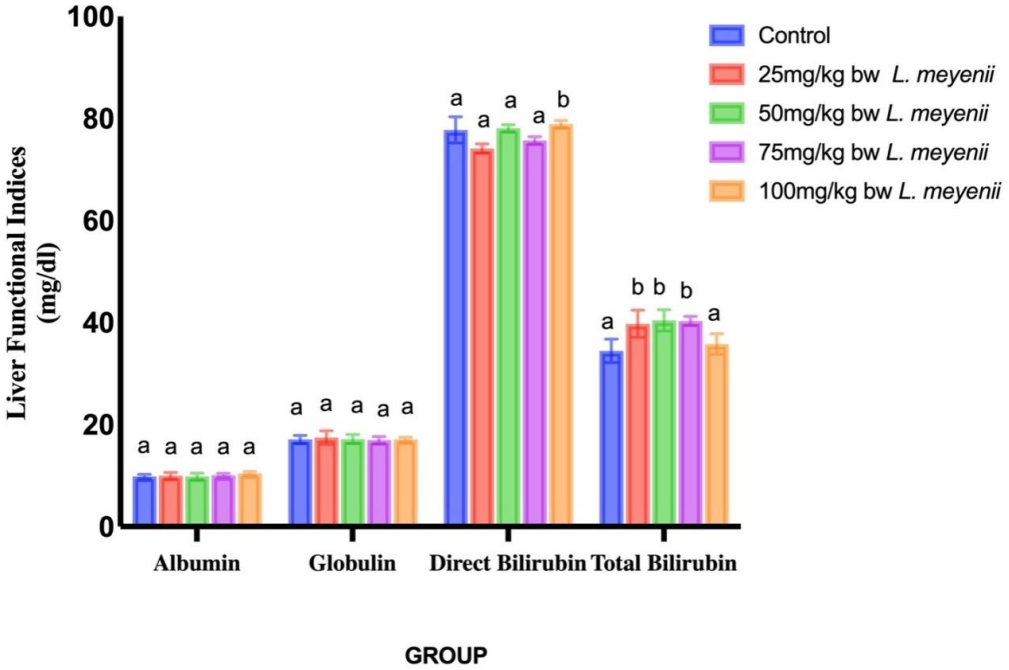

Figure 12. Liver Functional Indices of Male Wistar Rats administered with the ethanolic extract of *Lepidium meyenii* after fourteen days

Note: Values are mean of 4 replicates ± SEM, bars carrying different superscripts for each parameter are significantly ($P < 0.05$) different

significant differences ($p > 0.05$) across all test groups when compared to the control (Table 5). The urea concentrations of the animals administered with 50 mg/kg body weight of the extract showed a significant decrease in concentration when compared while the other groups showed no variation. The creatinine concentrations in the animals administered the 75 and 100 mg/kg body weight of the extract showed significant decreases in concentrations when compared with the control as shown in Table 5.

The ethanolic extract induced a significant decrease ($p < 0.05$) in chloride ion concentrations in the animals administered the 75 and 100 mg/kg of the extract, while the others showed no significant variation when compared to the control (Table 6). The sodium ion concentrations of the animals administered with the 25, 50 and 100 mg/kg body

Table 5. Effects of seven days oral exposure of the ethanolic extract of *L. meyenii* on kidney functional indices of male wistar rats

	Concentration (mg/dl)				
Parameter	Control	25mg/kg bw	50mg/kg bw	75mg/kg bw	100mg/kg bw
Chloride	22.31 ± 0.53^{a}	22.26 ± 0.63^{a}	25.13 ± 1.57^{b}	22.70 ± 0.76^{a}	22.78 ± 0.15^{a}
Sodium	60.84 ± 2.56^{a}	56.86 ± 0.85^{a}	59.30 ± 0.89^{a}	61.37 ± 0.78^{a}	61.05 ± 0.86^{a}
Potassium	7.12 ± 0.57^{a}	7.57 ± 0.84^{a}	7.06 ± 0.58^{a}	7.21 ± 0.31^{a}	7.53 ± 0.23^{a}
Urea	173.14 ± 9.14^{a}	182.45 ± 4.22^{a}	160.28 ± 0.94^{b}	167.02 ± 7.63^{a}	158.25 ± 12.28^{a}
Creatinine	2.95 ± 0.34^{a}	3.04 ± 0.11^{a}	2.70 ± 0.18^{a}	1.97 ± 0.38^{b}	1.97 ± 0.38^{b}

Table 6. Effects of fourteen days oral exposure of the ethanolic extract of *L. meyenii* on kidney functional indices of male wistar rats

	Concentration (mg/dl)				
Parameter	Control	25mg/kg bw	50mg/kg bw	75mg/kg bw	100mg/kg bw
Chloride	25.94 ± 0.85^{a}	25.11 ± 1.23^{a}	23.68 ± 1.05^{a}	24.92 ± 0.98^{a}	22.71 ± 0.89^{b}
Sodium	62.01 ± 0.89^{a}	56.54 ± 0.62^{b}	58.72 ± 1.01^{c}	61.10 ± 0.78^{a}	59.41 ± 1.45^{c}
Potassium	6.51 ± 0.24^{a}	7.68 ± 0.42^{b}	7.57 ± 0.42^{b}	7.04 ± 0.34^{b}	6.38 ± 0.35^{a}
Urea	142.82 ± 5.22^{a}	148.14 ± 4.50^{a}	159.72 ± 4.83^{b}	150.07 ± 2.73^{c}	149.47 ± 3.18^{a}
Creatinine	1.82 ± 0.00^{a}	1.69 ± 0.07^{b}	1.42 ± 0.20^{c}	1.48 ± 0.13^{c}	1.56 ± 0.13^{c}

Table 7. Effects of seven days oral exposure of the ethanolic extract of *L. meyenii* on creatine kinase (myocardial band) of male wistar rats

	Concentration (mg/dl)	
Doses	Heart	Serum
Control	53.07 ± 3.39^{a}	3.23 ± 0.10^{a}
25 mg/kg body weight	50.98 ± 3.49^{a}	3.05 ± 0.30^{a}
50 mg/kg body weight	60.43 ± 1.60^{b}	2.99 ± 0.21^{a}
75 mg/kg body weight	55.64 ± 2.27^{a}	2.96 ± 0.21^{a}
100 mg/kg body weight	52.67 ± 4.61^{a}	3.09 ± 0.17^{a}

Table 8. Effects of fourteen days oral exposure of the ethanolic extract of *L. meyenii* on creatine kinase (myocardial band) of male wistar rats

	Concentration (mg/dl)	
Doses	Heart	Serum
Control	53.78 ± 2.83^{a}	3.30 ± 0.12^{a}
25 mg/kg body weight	58.42 ± 1.17^{b}	3.62 ± 0.18^{b}
50 mg/kg body weight	55.40 ± 2.58^{a}	3.66 ± 0.14^{b}
75 mg/kg body weight	59.32 ± 0.82^{b}	3.62 ± 0.21^{b}
100 mg/kg body weight	59.44 ± 1.65^{b}	3.44 ± 0.11^{b}

Note: Values are mean of 4 replicates ± SEM, data carrying different superscripts for each parameter are significantly ($P < 0.05$) different

weight of the extract were significantly decreased ($p < 0.05$) while the 100 mg/kg test group showed no significant variation when compared control. Significant increase in the potassium ion concentration was observed in all but the 100 mg/kg body weight test group, which had no significant variation when compared with the control. The concentration of urea was significantly increased ($p < 0.05$) in the animals administered with 75 and 100 mg/kg body weight of the ethanolic extract while the others had no significant variation when compared with the control (Table 6). Creatinine concentrations showed significant decrease in the animals administered with 25, 50, 75 and 100 mg/kg body weight of the ethanolic extract when compared with the control.

The increase in the concentration of urea at the higher doses investigated might be attributed to increased protein catabolism. This is an indication of the nephrotoxic activity of the extract as it adversely affected the tubular and glomerular function of the male rats. The findings of this study agree with that reported by Yakubu *et al*. on *Fadogia agrestis* stem [42]. Elevation in the concentration of potassium ion as well as the reduction in concentration of creatinine, sodium and chloride ion indicates that tubular dysfunction had developed following the administration of higher doses of the extract. This finding agrees with previous reports by Yakubu *et al.* [42].

Effects of Oral exposure of the ethanolic extract of L. meyenii on creatine kinase-myocardial band (ck-mb) of male wistar rats

In the heart, the ethanolic extract of *L. meyenii* induced a significant increase ($p < 0.05$) in the activity of CK-MB in animals administered the 50 mg/kg body weight of the extract while the other test groups showed no significant differences when compared to the control group (Table 7). In the serum, the activity of CK-MB showed no significant variation when compared with the control group in all test groups. In the heart, the ethanolic extract induced a significant increase in the activity of CK-MB in all but the 50 mg/kg body weight test group which had no significant variation when compared with the control. In the serum, the activity of creatine kinase was observed to have significant increase when compared with the control group in all test groups. This is shown in Table 8.

It can be inferred that high doses of the extract could possibly cause poor cardiac function as observed from the result. After the seven-day administration, the lack of elevation in the serum does not support the thought of leakage of the enzyme into the serum. This is in line with what was reported by Dianat *et al.* [17] where serum levels of CK-MB remain unchanged after exposure to losartan and vanilic acid on ischaemia induced reperfusion. There was significant elevation of serum activity of CK-MB in all groups and in the heart of all but the group administered the 50 mg/kg body weight of extract following the fourteen-day administration of the ethanolic extract of *L. meyeni*, thereby indicating leakage of the enzyme into the blood, which may have stemmed from significant disruption and damage of the cardiomyocyte membrane integrity and its associated risk of resulting in acute myocardial injury development [23].

Effects of oral exposure of the ethanolic extract of L. meyenii on seminal indices of male wistar rats

Table 9 shows the results obtained from the semen analysis of the experimental animals following the seven-day oral administration of different doses of the ethanolic extract of *L. meyenii*. The semen motility showed no significant variation ($p> 0.05$) between the test groups when compared to the control. A similar trend was also observed in the percentage of dead cells, sluggish cells, cell morphology and sperm cells with severed heads (Table 9). There was no significant difference ($p> 0.05$) in the sperm cells with curved heads in the groups administered with 25 and 50 mg/kg body weight dose of the extract, while it increased in the groups administered75 and 100 mg/kg body weight of the extract. There was no significant difference ($p> 0.05$) in the number of sperm cells with bent necks in all but the group administered the 50 mg/kg body weight dose of the extract where it was significantly decreased ($p< 0.05$) when compared to the control. There was a significant increase ($p< 0.05$) in the number of sperm cells with headless tail following the administration of 25 and 75 mg/kg body weight of extract, while 50 and 100 mg/kg body weight showed no significant difference ($p> 0.05$). The total sperm cell counts significantly decreased ($p< 0.05$) in animals administered 25, 50, and 75 mg/kg body weight dose of the extract, while 100 mg/kg body weight of the extract significantly increased the total sperm cell count as shown in Table 10.

Table 9. Effects of seven days oral exposure of the ethanolic extract of *L. meyenii* on seminal indices of male wistar rats

Parameter	Control	25mg/kg	50mg/kg	75mg/kg	100mg/kg
Motility (%)	35.00 ± 15.00^{a}	15.00 ± 15.00^{a}	55.00 ± 5.00^{a}	20.00 ± 10.00^{a}	50.00 ± 10.00^{a}
Dead Cells (%)	50.00 ± 20.00^{a}	60.00 ± 40.00^{a}	20.00 ± 0.00^{a}	50.00 ± 30.00^{a}	35.00 ± 5.00^{a}
Sluggish Cells (%)	20.00 ± 10.00^{a}	25.00 ± 25.00^{a}	25.00 ± 5.00^{a}	30.00 ± 20.00^{a}	15.00 ± 5.00^{a}
Morphology (%)	35.00 ± 15.00^{a}	35.00 ± 5.00^{a}	50.00 ± 0.00^{a}	35.00 ± 5.00^{a}	45.00 ± 5.00^{a}
Headless Tail	2.50 ± 0.50^{a}	4.50 ± 0.50^{b}	3.00 ± 1.00^{a}	7.00 ± 0.00^{b}	5.50 ± 2.50^{a}
Severed Head	5.50 ± 0.50^{a}	5.00 ± 2.00^{a}	3.50 ± 0.50^{a}	4.50 ± 0.50^{a}	8.50 ± 3.50^{a}
Bent Neck	5.00 ± 1.00^{a}	4.50 ± 0.50^{a}	2.50 ± 0.50^{b}	4.50 ± 1.50^{a}	5.50 ± 2.50^{a}
Curved Head	3.00 ± 0.00^{a}	2.00 ± 2.00^{a}	2.50 ± 0.50^{a}	7.50 ± 0.50^{b}	6.00 ± 4.00^{b}
Total Cells ($\times 10^6$/ml)	60.00 ± 0.00^{a}	23.50 ±16.50^{b}	35.00 ± 5.00^{b}	35.00 ± 15.00^{b}	65.00 ± 5.00^{c}

Table 10. Effects of fourteen days oral exposure of the ethanolic extract of *L. meyenii* on seminal indices of male wistar rats

Parameter	Control	25mg/kg bw	50mg/kg bw	75mg/kg bw	100mg/kg bw
Motility (%)	60.00 ± 0.00^{a}	20.00 ± 20.00^{b}	20.00 ± 0.00^{b}	60.00 ± 10.00^{a}	50.00 ± 20.00^{a}
Dead Cells (%)	10.00 ± 0.00^{a}	25.00 ± 15.00^{a}	60.00 ± 0.00^{b}	15.00 ± 5.00^{a}	35.00 ± 25.00^{a}
Sluggish Cells (%)	30.00 ± 0.00^{a}	10.00 ± 10.00^{c}	45.00 ± 5.00^{b}	20.00 ± 0.00^{c}	15.00 ± 5.00^{c}
Morphology (%)	50.00 ± 0.00^{a}	35.00 ± 5.00^{b}	4.00 ± 0.00^{c}	50.00 ± 0.00^{a}	45.00 ± 5.00^{a}
Headless Tail	3.00 ± 0.00^{a}	3.50 ± 0.50^{ab}	4.00 ± 0.00^{b}	5.00 ± 0.00^{c}	5.00 ± 0.00^{c}
Severed Head	5.00 ± 0.00^{a}	4.50 ± 0.50^{a}	5.50 ± 0.50^{a}	6.00 ± 2.00^{a}	6.50 ± 1.50^{a}
Bent Neck	4.00 ± 0.00^{a}	8 .00± 2.00^{b}	4.00 ± 0.00^{a}	2.50 ± 0.50^{a}	5.00 ± 1.00^{ab}
Curved Head	4.00 ± 0.00^{a}	10.00 ± 0.00^{b}	5.00 ± 1.00^{a}	5.00 ± 0.00^{c}	4.50 ± 1.00^{a}
Total Cells ($\times 10^6$/ml)	40.00 ± 0.00^{a}	50.00 ± 10.00^{a}	45.00 ± 25.00^{a}	62.50 ± 2.50^{b}	45.00 ± 25.00^{a}

Note: Values are mean of 4 replicates ± SEM, data carrying different superscripts for each parameter are significantly ($P < 0.05$) different

Administration of ethanolic extracts of *L. meyenii* after fourteen days produced significant decrease ($p<0.05$) in in the motility and morphology of sperm cells at doses of 50 mg/kg body weight when compared with the control. There was also a significant increase ($p<0.05$) in the level of sluggish cells, headless tail and dead cells in the sperm cells of male Wistar rats administered with ethanolic extracts of *L. meyenii* at doses of 50mg/kg body weight when compared with the control. Also, there was significant increase ($p<0.05$) in the number of curved tails and bent neck in rats administered with doses of 25 mg/kg body weight when compared with the control (Table 10). There was no significant difference in the level of sluggish cells ($p>0.05$) at all doses when compared with the control.

It was observed that after the seven-day administration, all the doses of the ethanolic extract of *L. meyenii* administered had no significant effect on parameters like motility, sluggish cells, and dead cells. However, variations were observed in the various morphological characteristics of the sperm cells following the administration of different doses of the extract. But data gotten from the results were not sufficient to get precise information on the impact of the ethanolic extract of *L. meyenii* on semen parameters. Meanwhile, data was able to account for the effect of total cell count of sperm cells as animals administered with 100 mg/kg body weight dose of the extract had the highest sperm count which agrees with what was reported by Chung *et al.* [14] that epididymal sperm count significantly increased in animals treated with 1.0 g/kg of maca extract.

However, after the fourteen-day administration period, the highest abnormalities and the lowest motility was observed in groups administered doses higher than 50 mg/kg of the extract, this was also true in the number of dead cells highlighting

the potential toxicity of *L. meyenii* on semen parameters beyond a certain dose and an extensive use.

Conclusion

Exposure of the animals to the extract altered the indices tested within the acceptable limits expected by referenced literature leading to the conclusion that following a seven-day administration, the extract of *Lepidium meyenii* may be safe. It is thus recommended that the acceptable doses are between 25 and 75 mg/kg body weight and administration should not exceed seven days. The fourteen-day exposure may be toxic to the experimental animals as there were casualties recorded of three animals in the 100 mg/kg body weight group at days 8, 13 and 14 respectively. From the results, administration of the extract should not exceed seven days in order to ensure that the animals are safe.

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