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Evaluation of Hypoglycemic and Antihypertensive Effect of Lepidium sativum in Elderly

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Abstract

Background: Lepidium sativum, widely recognized as Chandrasura, is an annual herbaceous plant. Characterized by its smooth, hairless (glabrous) structure, it typically reaches heights of 15 to 45 centimeters[1]. Its seeds are notable for their lack of aroma and their distinctly pungent, mucilaginous flavor.[2].

Lepidium sativum seeds are known to contain a variety of phytochemicals, such as phenolic compounds, terpenoids, alkaloids, flavonoids, and organosulfur compounds.

It also contains phytosterols and their derivatives, which are known to possess antioxidant potential, anti-cancer, anti-inflammatory, cardio-protective activity, and antihypertensive [3].

Objective: To evaluate the safety & efficacy of Lepidium Sativum seeds in lowering blood pressure in hypertensive elderly.

Design: This prospective, observational study was conducted at Beni Suef University Hospital, involving hypertensive patients aged 50 years and older. Participants were categorized into two groups: a control group (Group I) of healthy volunteers and a hypertensive group (Group II). Each group comprised 20 participants (n=20), with a balanced distribution of male and female subjects. Group II received a specified dose of Lepidium sativum seeds for an 8-week treatment period.

Results: This study demonstrated a statistically significant decrease in both systolic and diastolic blood pressure among hypertensive patients who consumed Lepidium sativum seeds for eight weeks. Additionally, a significant improvement in serum lipid profiles was observed in the treatment group compared to the healthy control group, with notable reductions in triglycerides, cholesterol, and LDL and an increase in HDL ($p \leq 0.05$).

Conclusion: Our data supports previous suggestions from various research that Lepidium Sativum seed intake possesses both hypotensive and lipid profile-improving effects.

Keywords: Lepidium Sativum seed, hypertensive patients, lipid profile, phenolic compound

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Introduction:

Hypertension is a leading cause of cardiovascular diseases and mortality.[4] Its prevalence is expected to rise due to modern unhealthy lifestyles.[5]

Hypertension is the main cause of heart disease and strokes[6]. Many hypertensive patients are either unidentified or untreated, especially in poor health systems. Effective management of hypertension remains a significant public health concern [7]. Furthermore, hypertension is a major contributing factor to the development of various renal diseases and, ultimately, renal

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failure [8]

Hypertension imposes substantial economic burdens, both directly and indirectly. Direct costs, encompassing medical expenditures, include pharmaceuticals, healthcare services, and medical devices utilized in the prevention, diagnosis, and management of hypertension and its associated complications. [9].

Lepidium Sativum seeds are a medicinal Plant and have many pharmacological properties. So, it can be used to improve health benefits.

Research consistently demonstrates the safety profile of Lepidium sativum, revealing that significant doses are well-tolerated and devoid of toxic side effects..

The antihypertensive and diuretic effects of the aqueous extract of L. Sativum were studied both in normotensive and spontaneously hypertensive. Daily oral administration of the aqueous extract (20 mg/kg for 3 weeks) exhibited a significant decrease in blood pressure in spontaneously hypertensive rats, while in normotensive rats, no significant change was noted during the period of treatment [10].

Different studies suggested that the plant's diuretic effect may depend on the presence of phytochemicals such as flavonoids, saponins, steroids or organic acids[11]. In line with this, they illustrated that the aqueous and methanolic extracts of L. sativum dose-dependently augmented urine secretion in rat models.

They suggested that L. sativum extracts' diuretic activity is possibly induced by individual or synergistic effects of flavonoids and steroids, which in turn leads to increased local blood flow and vasodilation or inhibition of water and anion tubular reabsorption [11]. In addition to excessive urine production, increased sodium and water excretion contribute to L. sativum's antihypertensive effect[11]. Maghrani et al[10] investigated the diuretic and antihypertensive properties of the aqueous extract of L. sativum in normotensive and spontaneously hypertensive rats(SHR). Oral administration of the extract caused a substantial drop in blood pressure as well as the increase of urinary exertion of sodium, potassium, and chlorides in SHR rats.

This research sought to determine the magnitude of Lepidium sativum's blood pressure-lowering effects in humans and to evaluate its safety for clinical application in hypertensive patient management.

This study was conducted to assess the impact of Lepidium sativum seed consumption on blood pressure, lipid profiles, and relevant clinical parameters within a cohort of hypertensive patients.

Materials And Methods:

Source of chemicals: Commercially sourced enzyme kits were utilized for the determination of total cholesterol, triglycerides, HDL cholesterol, and other relevant clinical analytes. All chemical reagents were obtained from (Spectrum Diagnostics Cairo, Egypt, and

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MDSS GmbH, Schiffgraben 41, 30175 Hannover, Germany).

Experimental design: A prospective, observational study was conducted involving hypertensive patients aged 50 years and older, recruited from Beni Suef University Hospital. Participants were categorized into two groups: a control group (Group I) consisting of healthy volunteers, and a hypertensive group (Group II) comprising patients with a pre-existing diagnosis of hypertension.

Each group includes 20 individuals (n=20) divided into (male and female) subjects.

Participants in both the control and hypertensive groups received Lepidium sativum seeds for an 8-week treatment period. Specifically, a twice-daily dose was administered with meals, once in the morning and once in the evening. All participants were provided with lifestyle counseling regarding hypertension management. Blood pressure was assessed at baseline and weekly throughout the 8-week study. Blood glucose, lipid profiles, and renal and hepatic function tests were conducted at baseline and at the conclusion of the treatment period. Any adverse effects were monitored and documented throughout the study.

Study population: The study consisted of 40 subjects aged between >50 and less than 75 years old with untreated blood pressure. Stage II Hypertensive patients (patients with systolic blood pressure (SBP) ≥ 140 mm Hg or diastolic blood pressure (DBP) ≥ 90 mm Hg) according to new ACC and American Heart Association (AHA) guidelines 2017.

All the patients gave written informed consent before their inclusion in the study.

Biochemical measures: Fasting blood samples were collected following a minimum of 12 hours of abstinence from food and drink.

Blood samples for liver and kidney function tests, as well as lipid profile analysis, were collected in additive-free tubes and allowed to clot at room temperature for 30 minutes. Serum separation was achieved via centrifugation at 3000 rpm for 10 minutes, and samples were stored at -20°C until analysis. Alanine aminotransferase (ALT), aspartate aminotransferase (AST), urea, creatinine, total cholesterol (TC), triglycerides (TG), and high-density lipoprotein (HDL) were determined using commercially available enzyme kits. Low-density lipoprotein (LDL) was calculated using the Friedewald equation: LDL = TC - HDL - TG/5 (Friedewald et al., 1972). Blood pressure was measured using a cuff and an analog sphygmomanometer after a 15-minute rest period. Three blood pressure readings were obtained for each participant, and the average was recorded.

Statistical methods: All analyses were done using SPSS statistical software package version 25 (IBM) and graphics utilizing Tableau. All continuous data were expressed as mean ± SD, categorical data were expressed as frequency in tables. P-value < 0.05 is considered significant i.e. 95% confidence interval is used. All key variables were varied through standard deviations or reasonable ranges. The analysis was performed using Tableau.

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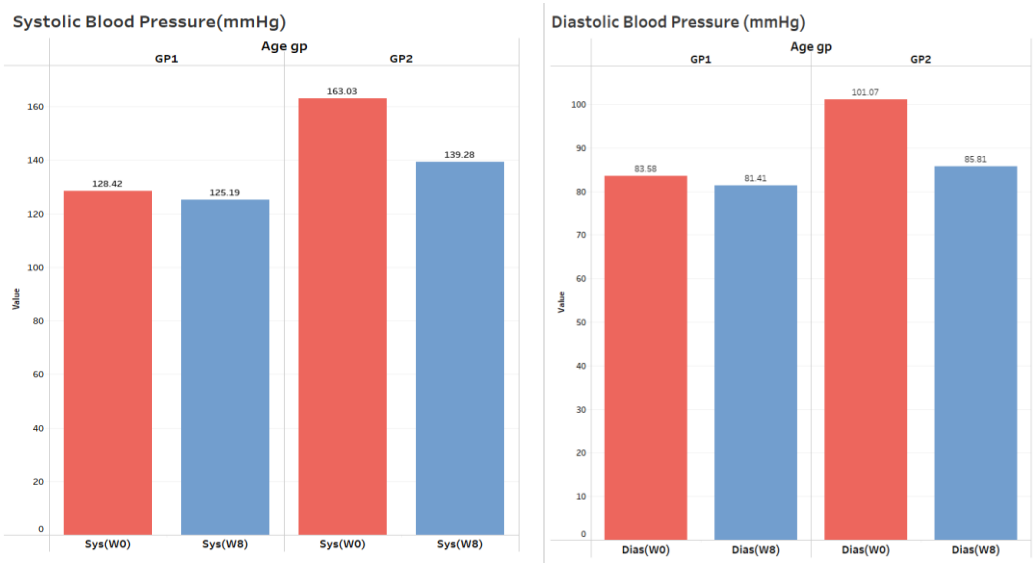
Results:

Effect of Lepidium Sativum seeds on hypertension:

Significant variations in blood pressure occurred throughout the 8-week study. The mean change in systolic blood pressure (Sys) was a decrease of 3.23 mmHg in the control group (Group 1), a decrease of 23.75 mmHg in the hypertensive group (Group 2), and an overall decrease of 7 mmHg after the 8-week intervention.(Fig.1.a).

The average difference diastolic BP (dias.) in these groups also reached a maximum, amounting to 2.17 mmHg in control healthy group (Gp.1), up to 16.06 mmHg in the hypertensive group (Gp.2), up to 6.31 mmHg after the whole 8 weeks of treatment (Fig.1.b).

Fig.1.a **Fig.1.b**



(Fig. 1) The change in blood pressure (mmHg) during the study.

0: At the beginning of the experiment. 8: At the end of the experiment. GP1: Group 1, GP2: group 2 Sys. : Systolic blood pressure, dias: Diastolic blood pressure.

Following the 8-week study, a statistically significant reduction in mean blood pressure was observed from baseline in both groups. In the healthy control group (Group 1), systolic blood pressure decreased from 128.42±3.042 mmHg to 125.19±4.004 mmHg ($p \leq 0.05$), and diastolic blood pressure decreased from 83.58±3.518 mmHg to 81.41±1.531 mmHg ($p \leq 0.05$; $n = 20$). Similarly, in the hypertensive group (Group 2), systolic blood pressure decreased from 162.19±5.2 mmHg to 139.28±6.075 mmHg ($p \leq 0.05$), and diastolic blood pressure decreased from 101.07±3.3 mmHg to 85.81±4.428 mmHg ($p \leq 0.05$; $n = 20$).

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Effect of Lepidium Sativum seeds on Lipid Profile:

During the experiment, lipid profile levels decreased in value at the two groups (FIG 2)

Fig.2.a

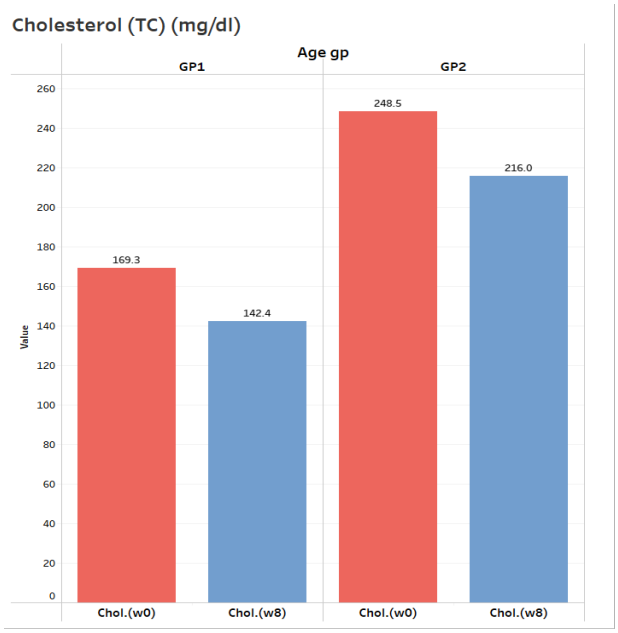


Fig.2.b

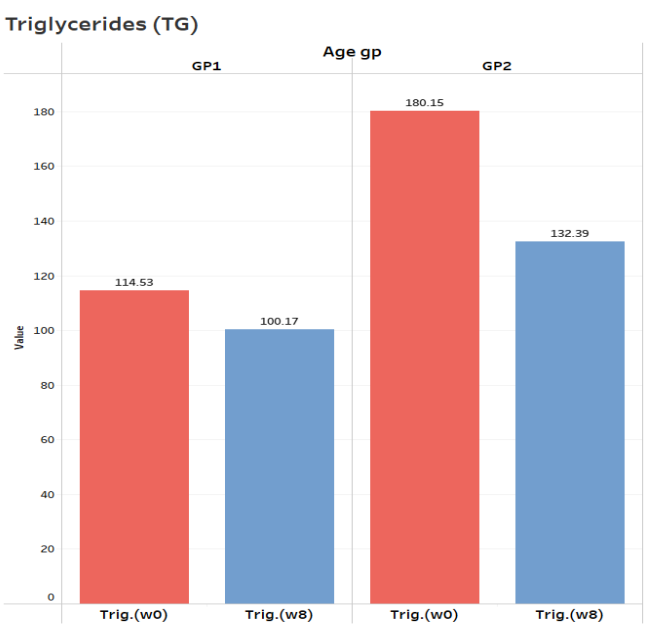


Fig.2.c

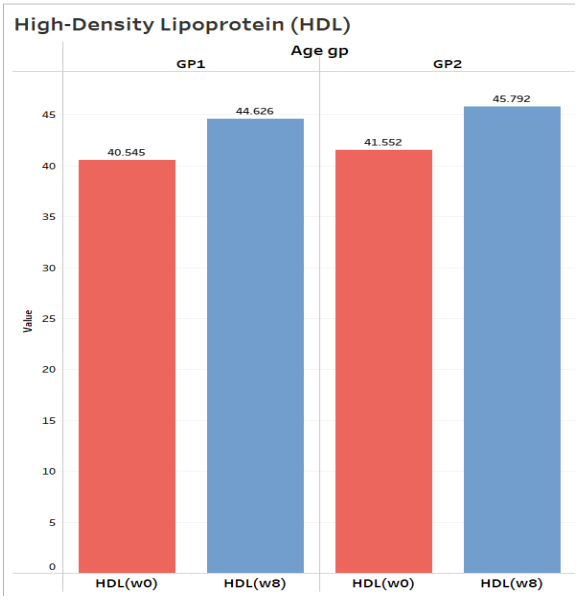
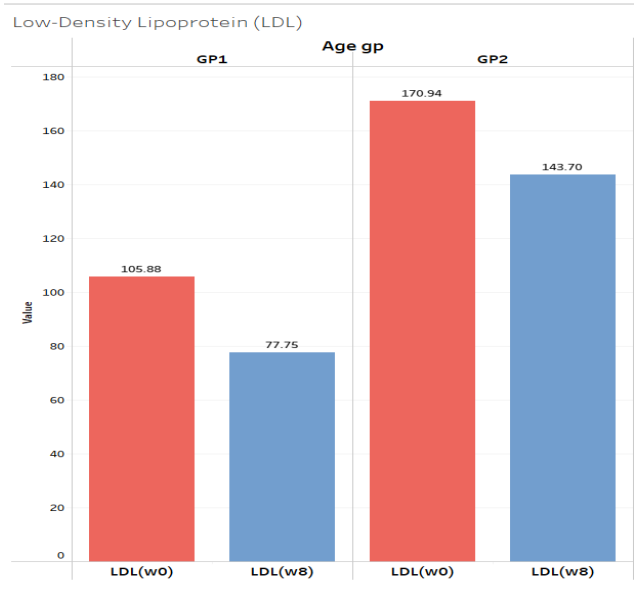


Fig.2.d



(Fig. 2) The change in Lipid profile (mg/dl) during the study

a: The Improvement in total cholesterol (TC) (mg/dl) during the study

b: The Improvement in triglycerides (TG) (mg/dl) during the study

c: The Improvement in high-density lipoprotein (HDL) (mg/dl) during the study

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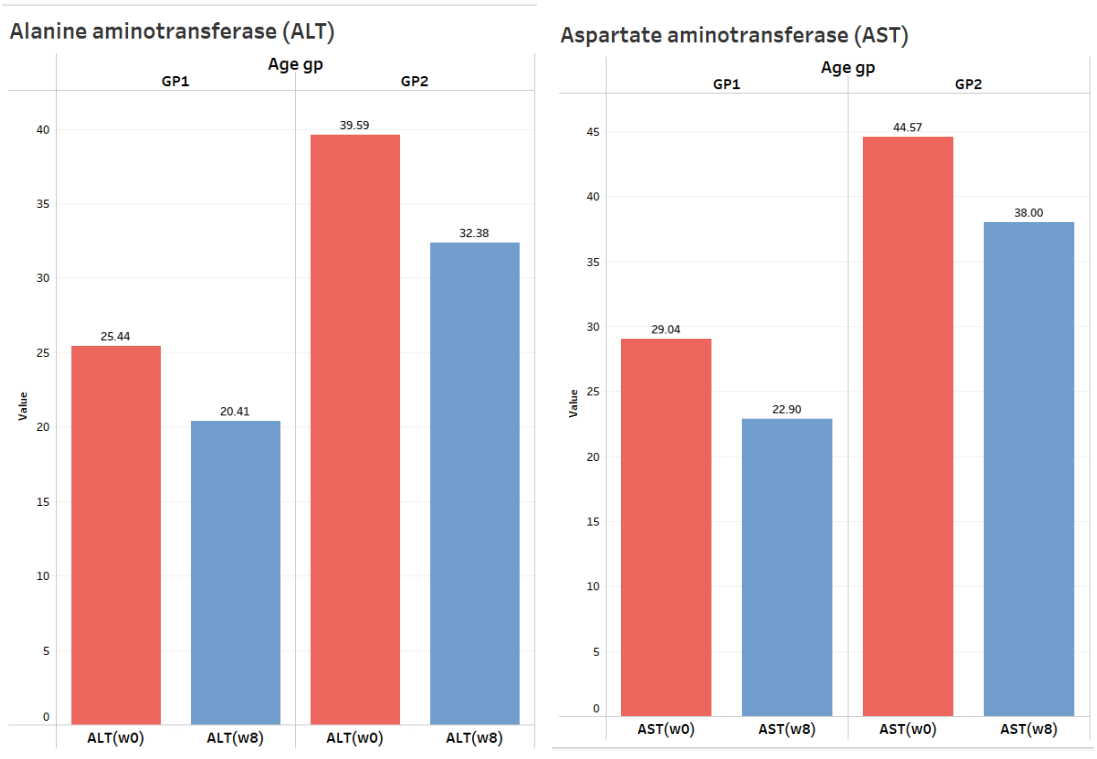
d: The Improvement in low-density lipoprotein (LDL) (mg/dl) during the study

Throughout the study, both groups exhibited decreases in lipid profile levels. Notably, Lepidium sativum (LS) seed consumption demonstrated a more pronounced effect on lipid profiles compared to blood pressure, resulting in statistically significant reductions in total cholesterol (TC), low-density lipoprotein cholesterol (LDL), and triglycerides (TG). In the healthy control group (Group 1), mean lipid profile measurements showed the following changes from baseline: TC decreased from 169.3±22.37 mg/dL to 142.4±25.51 mg/dL ($p < 0.05$), TG decreased from 114.5±8.85 mg/dL to 100.2±11.80 mg/dL ($p < 0.05$), and LDL decreased from 105.9±23.42 mg/dL to 77.8±26.43 mg/dL ($p < 0.05$; $n = 20$). Conversely, high-density lipoprotein (HDL) increased from 40.55±4.4 mg/dL to 44.63±4.4 mg/dL ($p < 0.05$). In the hypertensive group (Group 2), mean lipid profile measurements also decreased from baseline: TC decreased from 248.5±41.96 mg/dL to 216±30.37 mg/dL ($p < 0.05$), TG decreased from 180.1±42.24 mg/dL to 132.4±17.38 mg/dL ($p < 0.05$), and LDL decreased from 170.9±36.83 mg/dL to 143.7±28.77 mg/dL ($p < 0.05$; $n = 20$). HDL increased from 41.55±5.9 mg/dL to 45.79±4.02 mg/dL ($p < 0.05$).

Effect of Lepidium Sativum seeds on Liver Functions Tests:

Fig.3.a Fig.3.b



(Fig. 3): The change in liver function tests during the study

a: The change in ALT for gp 1& gp 2.

b: The change in AST for gp 1& gp 2.

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Figure (3) contains A: The change in ALT (Alanine aminotransferase): (The mean difference was 5.03, 7.21 U/L for gp1, gp2 respectively) and B: The change in AST (Aspartate aminotransferase): (The mean difference was 6.14, 6.57 U/L for gp1, gp2 respectively)

Effect of Lepidium Sativum seeds on Kidney functions tests:

Fig.4.a

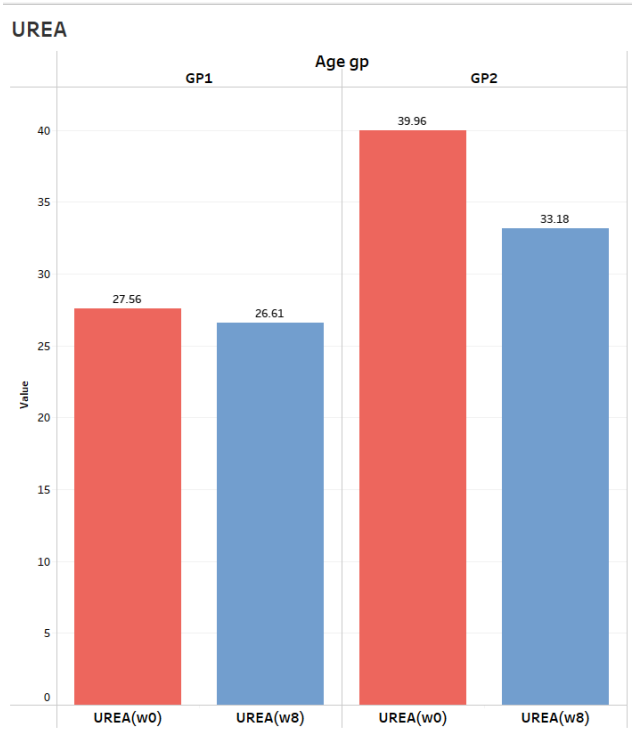
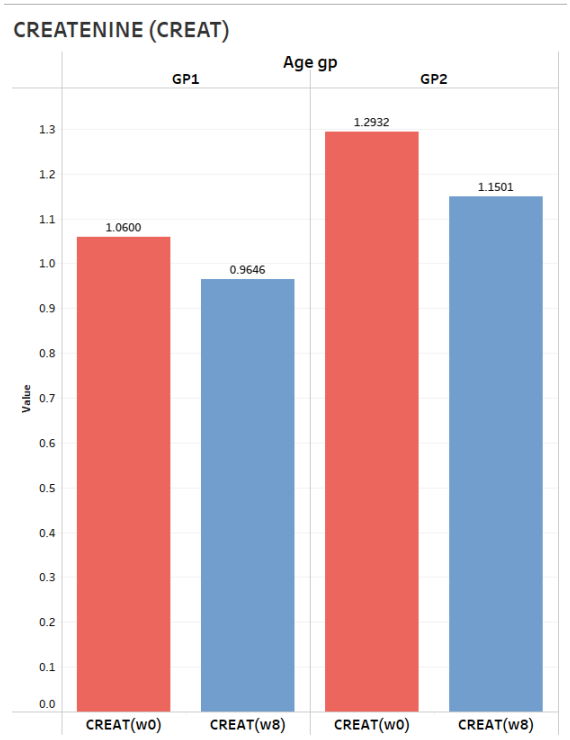


Fig.4.b



(Fig. 4) The change in kidney function tests during the study

a: The change in Urea for group 1& group 2.

b: The change in Creatinine for group 1& group 2.

Figure (4) consists of

A: The change in Urea: (the mean difference was 0.95, 6.78 mg/dL for gp1, gp2 respectively) and

B: The change in Creatinine: (the mean difference was 0.096, 0.143 mg/dL for gp1, gp2 respectively) during this study.

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Discussion

Effect of Lepidium Sativum seeds on hypertension:

Blood pressure measures changed significantly after treatment for the hypertensive group.

According to Maghrani et al. (2005), the aqueous extract of Lepidium sativum demonstrated significant antihypertensive effects in spontaneously hypertensive rats. Daily oral administration of 20 mg/kg for three weeks resulted in a notable reduction in blood pressure ($p<0.01$), while no significant changes were observed in normotensive rats.

Systolic blood pressure decreased significantly from the 7th day ($p<0.05$) to the end of treatment ($p<0.01$) in hypertensive rats.

No significant changes were recorded on heart rate after the aqueous treatment in hypertensive and normotensive rats. The diuretic effect of the aqueous extract of Lepidium sativum was studied in normotensive and spontaneously hypertensive rats.

The aqueous extract significantly enhanced the water excretion in normotensive rats ($p<0.001$) but not in hypertensive rats. Furthermore, oral administration of the aqueous extract at a dose of 20 mg/kg produced a significant increase of urinary excretion of sodium ($p<0.05$), potassium ($p<0.01$), and chlorides ($p<0.01$) in normotensive rats. In spontaneously hypertensive rats, the aqueous extract administration induced a significant increase in the urinary elimination of sodium ($p<0.01$), potassium ($p<0.001$), and chlorides ($p<0.001$)[10].

The intake of Lepidium sativum seeds produced a greater effect on lipid profiles than on blood pressure, leading to clinically significant decreases in total cholesterol (TC), low-density lipoprotein cholesterol (LDL), and triglycerides (TG).

Lepidium sativum contributes to a reduction in LDL cholesterol and an increase in vitamin E, an antioxidant, thereby potentially safeguarding liver health through the reduction of lipid oxidation.

Hypercholesterolemia, characterized by elevated cholesterol levels in the bloodstream, is a significant risk factor for cardiovascular diseases, including myocardial infarctions and cerebrovascular accidents.

Many studies proved that Lepidium Sativum helps to lower the level of cholesterol in blood. Another study performed in hypercholesterolemic albino male rats revealed that L. sativum seed extract improved lipid profile [decrease in cholesterol, TGs, LDL, and increase in high-density lipoprotein cholesterol (HDL)] and markedly diminished blood glucose in comparison to the control group[13].

In conclusion, the flavonoid and sapogenin extracts of L. sativum Linn. seed significantly reduced the Triton x-100 induced hyperlipidemia in rats and flavonoid extract showed protection against all parameters (TC, TG, LDLc, and VLDLc) of HCD diet induced hyperlipidemia indicating a promising anti-hyperlipidemic effect.

This effect needs further investigation into various models of hyperlipidemia to elucidate the mechanism of action of L. sativum as hypolipidemic. The flavonoid and sapogenin extracts

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of L. sativum should be further subjected to isolation and structural elucidation of the compounds.

Effect of Lepidium Sativum seeds on Liver functions:

A notable improvement in liver function, evidenced by reduced AST and ALT enzyme levels, was observed in both study groups. These findings suggest that Lepidium sativum seeds may have therapeutic potential for hepatic patients

Lepidium Sativum seeds protect the liver from damage by toxic agents like carbon tetra chloride (CCl4). The mechanism of the hepatoprotective action of the plant may be related to the ability of the plant to inhibit lipid peroxidation in the liver.

Flavonoids, triterpenes, and tannins are antioxidant agents and may interfere with free radical formation [13].

Effect of Lepidium Sativum Seeds on Kidney Functions:

Both study groups exhibited improvements in kidney function test results. The phytochemical constituents of Lepidium sativum may possess antioxidant properties, potentially mitigating drug-induced nephrotoxicity.[14].

In addition, L. sativum's stimulation of antioxidant markers in the kidneys of the control gp suggests that its antioxidant potential is an upstream mechanism that regulates its anti-inflammatory effect [15] [16].

Conclusion :

Lepidium sativum seeds are a source of bioactive compounds that demonstrate various health-promoting properties, including antihypertensive and hypocholesterolemic effects. This study reinforces existing evidence that Lepidium sativum seeds positively influence both blood pressure and lipid profiles. Recognizing the established benefits of dietary and lifestyle modifications in the primary prevention of hypertension and hypercholesterolemia, this study suggests that regular daily consumption of Lepidium sativum seeds may contribute to a reduction in both blood pressure and serum lipid levels.

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