



RESEARCH ARTICLE

Estimate the Role of *Lepidium Sativum* Extract against to Methimazole Induced Hypothyroidism in Male Albino Rats

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ABSTRACT

The current work objective to estimate the role of *Lepidium sativum* (LS) extract against to adverse effects of methimazole (ME) in male albino rats. In this work, 32 albino male rats were, used for estimate the potential effect of *Lepidium sativum* extract against (ME), distributed as follow: Group A: (control) rats were received distilled water at 1ml /100 g body weight .Group B: rats received (50mg/kg) (ME), orally every day for 10 weeks to induced hypothyroid. Group C: rats received 400mg/kg of *Lepidium sativum* extract orally every day for 10 weeks. Group C: rats received (50mg/kg) (ME), and treated with 400mg/kg of *Lepidium sativum* extract every day for 10 weeks. The results of the study showed that, in comparison to the control group, there were significant variations in oxidative stress and antioxidant enzymes between the groups (P 0.05). Hypothyroidism group's MDA, AST, ALT, and ALP levels were considerably higher (P 0.05), while Glutathione GSH and catalase (CAT) levels were lower. Results showed that MDA, GSH, and CAT levels in the treated group did not alter in a manner that was significant (P< 0.05). Regarding the histological aspect of Heart, the obtained cross sections from the control group revealed normal heart tissue with normal cardiocyte morphology, normal nuclei, and normal coronary arteries. The hypothyroidism group, however (administrated with ME). Along with significant congestion and a severe thickening of the coronary artery wall, there is also a severe lymphocyte infiltration and mild degeneration. cardiocyte hypertrophic modifications are another. According to the study's findings, therapy with *Lepidium sativum* extract improved both the state of oxidative stress and the condition of the heart tissue because of its antioxidant content, in contrast to the drug Methimazole, which caused changes in both oxidative stress and heart tissue.

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INTRODUCTION

The heart and thyroid gland have a complex relationship in both patients and healthy people (1). Thyroid hormones regulate the metabolic rate of the heart and body cells (2). Therefore, any defect in the thyroid gland affects the function of blood vessels and the heart (3). In recent years, interest in nutrients that have many health benefits has increased.(4) Nutritional supplements and herbs are major components of nutrients that work against many diseases (5). The (*Lepidium sativum*) garden cress has been widely used in various pathological conditions (6; 7). LS is one of the herbs that is used in African countries, West Asia, India and many countries (8).. The seeds are used enormously ophthalmic, aphrodisiac, diuretic, and/or contraceptive. The L. sativum seeds include a variety of phytochemicals, vital amino acids, fiber, lipids, omega-3 fatty acids, iron, calcium, and phosphorus (9). Many items made from L. sativum seeds are consumed either as a food ingredient

or as a health drink. Due to its extensive therapeutic uses, it has gained popularity all over the world. Prior research has shown that the plant contains anti-carcinogenic properties (10). Garden cress seeds have different biological effects and have a protective role for the liver against oxidative stress and inflammation. Some researchers have used anti-thyroid medications, such as methimazole, to create a hypothyroid model in order to study hypothyroidism (11). According to certain findings, due to its chemical makeup, its use results in cellular protection (12). Additionally, there is proof that antithyroid medications like thionamides have additional thyroidal effects in both humans and animals (13). Thionamides contribute to oxidative stress and cellular damage as one of its consequences (14). Generally speaking, cellular damage happens when the ratio of antioxidants to oxidants is upset and the antioxidant system fails to neutralize oxidants (15). Lipid peroxidation, a rise in reactive oxygen species, protein nitration, carbonylation, otherwise glutathionylation, as well as DNA fragmentation are all results of an intensified oxidant system(16).

Therefore, the current study's goal is to evaluate how well *L. sativum* extract protects male albino rats against the harmful effects of the ME induced hypothyroidism.

MATERIALS & METHODS

Animal model

The Public Company of Pharmaceutical Manufacture and Requirements Medicals in Samara, Iraq provided 32 adult male rats (wt. 220-265 gm), who were maintained on a regular pellet diet and water.

Drug

Methimazole (pharmaceutical company, Egypt) with dose (50 mg per kilogram per day in drinking water) (17).

Crude extract preparation

Lepidium sativum seeds, also referred to as garden cress, were purchased at a Ramadi, Iraq, local market. The ground seeds were briefly cleaned, dried, and ground into powder using an electric blender. For ten weeks, each rat received an oral stomach tube infusion of the newly made suspension of garden cress seeds powder at a amount of 400 mg/kg body weight once daily (18).

Experiment design group

In this study, eight male rats were divided into each group to study potential impact of *L. sativum* extract versus ME.

Group A: Control group, received distilled water at 1ml /100 g body weight for 10 weeks.

Group B: rats received 50mg/kg of ME orally every day for 10 weeks to induce hypothyroid.

Group C: rats received 400mg/kg of *L. sativum* extract orally every day for 10 weeks.

Group C: rats received 50mg/kg of ME and treated with 400mg/kg of *L. sativum* extract every day for 10 weeks.

Prepare of blood solution

Blood was drawn from anesthetized rats by a cardiac puncher and placed in test containers without EDTA. MDA, GSH, and catalase levels in the serum were estimated.

Histological study

Each rat's fresh heart was quickly chopped into pieces, fixed with 10% formalin, and dehydrated with ethanol in increasing concentrations. The dehydration of tissue samples was followed by cleaning in

two changes of xylene, impregnation in three changes of molten paraffin wax, embedding, and blocking. Hematoxylin-eosin was used to stain tissue slices that were 5µm thick (19).

Statistical analysis

Under the SPSS and Microsoft Excel XP systems, data were statistically analyzed using the Minitab statistical tool. The Range Duncan's Multiple tests was used to compare the means of the data. Values less than 0.05 were deemed statistically significant, but probability levels greater than 0.05 were regarded as non-significant: $P < 0.05$ highly significant (20).

RESULTS & DISCUSSION

Liver enzymes

According to the study's findings, there were significant differences among groups in liver enzymes ($P < 0.05$). Table 2 shows that the AST levels in the hypothyroidism group were considerably higher ($P < 0.05$) than those in the control group. Compared to control group, ALT and ALP levels in the hypothyroidism group were considerably higher ($P < 0.05$). When compared to the control group, the treated group's levels of AST, ALP, and ALT revealed non-significant changes ($P < 0.05$) after utilizing *L. sativum* extract.

Table 1: Levels of liver enzymes in the studied group

| | AST | ALT | ALP |
|--------------------------------|-------------|-------------|--------------|
| Control group | 17.57±3.06 | 14.16±1.61 | 49.23±4.17 |
| ME group | 51.27±0.36* | 60.35±6.13* | 98.12±12.43* |
| <i>L. sativum</i> group | 23.42±1.91 | 21.61±5.43 | 47.12±2.19 |
| <i>L. sativum</i> + ME | 24.51±5.58 | 22.37±4.57 | 61.42±7.37 |
| P value | 0.0001 | 0.022 | 0.038 |

This study also demonstrated that, when compared to control group, patients through hypothyroidism saw a substantial rise ($p < 0.001$) in the levels of the liver enzymes ALP, ALT, also AST. These results can be explained by the fact that thyroid hormones are essential for organ growth, development, and function and that any condition affecting the thyroid gland would affect the level of its hormones, causing an imbalance in the metabolism of many organs (21). The findings of this investigation were consistent with those of earlier studies, which demonstrated that patients with hypothyroidism had higher stages of the liver enzymes (ALP, ALT, also AST) (22). While Other studies discovered in another investigation that patients with hypothyroidism had significantly higher AST levels (23).

After being treated with *L. sativum* extract, liver enzymes and its tissues returned to normal status (24). Thus suggested that phenols may be used in the detoxification of the liver caused by drug toxicity due to their capacity to lower live enzyme activity (25). The antioxidant activity of saponins themselves has been linked to phenolic compounds' ability to protect and support against liver damage (26). The supplementation of LS in diet caused a reduction in activity of these enzymes as compared to ME group. Based on this result, our findings could argue that LS may have hepatoprotective effect (27).

Oxidative stress

According to the study's findings, there were significant differences among groups in oxidative stress and antioxidant enzymes ($P < 0.05$). Table 2 demonstrates that when compared to the control group, the MDA levels in the hypothyroidism group were significantly developed ($P < 0.05$). While GSH and CAT levels were considerably lower ($P < 0.05$) in hypothyroidism group compared to the control group. As soon as compared to the control group, the treated group's levels of MDA, GSH, and CAT revealed non-significant changes ($P < 0.05$) after utilizing *L. sativum* extract.

Table 2: Levels of MDA, GSH and catalase in the studied group

| | MDA | GSH | Catalase |
|--------------------------------|------------|--------------|------------|
| Control group | 1.28±0.26 | 0.457±0.048 | 1.36±0.27 |
| ME group | 2.23±0.36* | 0.315±0.021* | 0.82±0.05* |
| <i>L. sativum</i> group | 1.40±0.21 | 0.425±0.036 | 1.31±0.12 |
| <i>L. sativum</i> + ME | 1.59±0.37 | 0.41±0.031 | 1.18±0.07 |
| P value | 0.0001 | 0.0001 | 0.0001 |

Rat hypothyroidism was induced with the drug methimazole (ME) (28). a thioamide was given ME Drug Administration approval; it prevents the thyroid peroxidase-mediated iodination of tyrosine residues during the phases of iodine organification and iodotyrosine coupling in the thyroid gland, as well as conversion of T4 to T3 in extra thyroidal tissues(29). Because ME-induced hypothyroidism in rats is caused by oxidative stress, which is required to induce cell proliferation in the thyroid gland, resulting in tissue damage and apoptosis, resulting in goiter or thyroid enlargement, the current findings of increased MDA levels and decreased antioxidant enzyme levels when using ME drug were explained (30;31). Methimazole can induce cellular damage in a variability of ways due to its chemical structure or link between its chemical structure besides the physiological changes caused through a hypothyroid state. (32;33). By a heme group at active center, this medication permanently inactivates several peroxidases. It's likely that methimazole inhibits catalase and other heme group peroxidases that are involved in scavenging H_2O_2 . Because H_2O_2 participates in Haber-Weiss and Fenton reactions in cells that produce it as well as in nearby cubicles due to H_2O_2 diffusing through membranes, the antioxidant system's decline could result in an increase in an oxidation reaction in addition cellular damage (34).

In order to better understand the contribution of *L. sativum* to the current work (35), examined the total phenolic content and associated total antioxidant capacity of an aqueous extract of the herb (3 g of the herb/200 ml of hot water for infusion). By using the Folin-Ciocalteu assay, the total phenolics were quantified, and the ferric reducing/antioxidant power (FRAP) assay was used to assess the total antioxidant capacity (36). The phenol antioxidant coefficient (PAC) was computed in order to allow a practical assessment of the relative antioxidant capacity of phenolic isolated from the plant. Total phenolic content and FRAP showed a strong linear connection. By preventing the damage caused by harmful radicals, the presence of flavonoids, triterpenes, alkaloids, tannin, and coumarins in LS explains its function in hepatoprotection. Our findings support or are consistent with those of earlier studies or published results.

Histological study

The cross sections taken from the control group revealed normal heart tissue, including cardiocytes with normal shapes, normal nuclei, and normal coronary arteries (figure 1). The hypothyroidism group, however (administrated with ME). Along with significant congestion and a severe thickening

of the coronary artery walls, there is also a severe lymphocyte infiltration and mild degeneration. Additionally, cardiocyte hypertrophic modifications (figure 2). In our research, we looked into whether thyroidectomy otherwise methimazole-induced hypothyroidism results in cellular damage in several organs (37). Histologically, we demonstrated that only methimazole-induced hypothyroidism causes cellular damage in the heart (38). The portions of the group that received *L. sativum* extract displayed healthy cardiac tissue architecture (figure 3). Heart slices from the treated group after employing *L. sativum* extract revealed semi-normal heart tissue architecture and normal coronary arteries (figure 4).

Additionally, research on flavonoids and phenolic acids shows that they have higher antioxidant potential. These compounds' primary distinguishing trait is their capacity to function as metal chelators and free radical scavengers (39). These substances most likely generate coordination compounds by joining with metal ions. The compounds boost flavonoids' antioxidant action and are extremely stable (39). In the presence of copper ions, some of them may also experience the autoxidation process. *Lepidium* seed oil be made up of of fatty acid (oleic acid also linoleic acid), γ -tocopherol, δ -tocopherol besides flavonoid is stated to cause significant reduction in free oxidative species in blood (40).

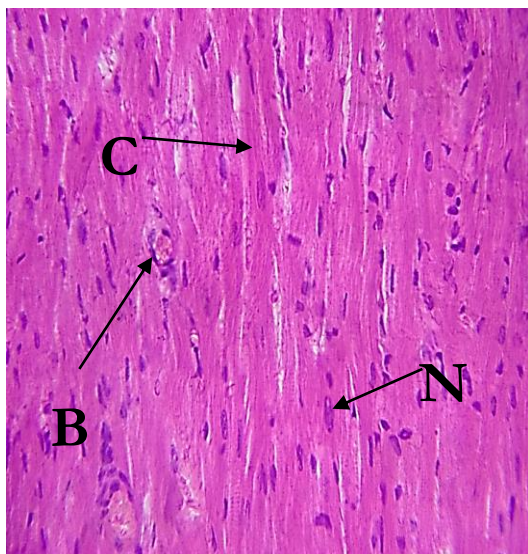


Figure (1): Heart cross section of group A showed normal structure of blood vessels (BV) and cardiocytes (CC) with its elongated nuclei (Ni) H&E X400.

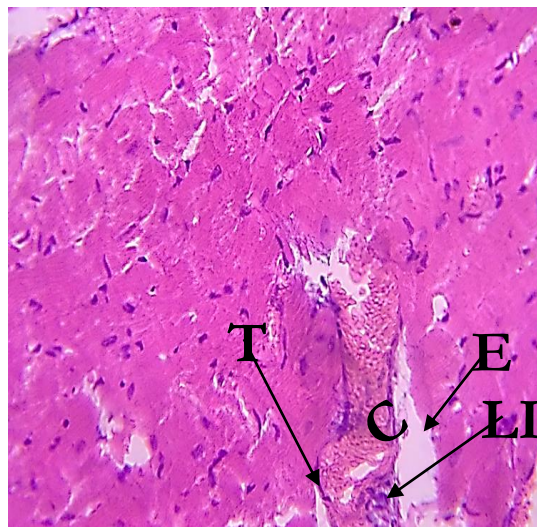


Figure (2): Heart cross section of group B showed thickening wall (TW) and congestion (CON) of coronary veins with lymphocytes infiltration (LI) and edema (ED) H&E X400.

The antioxidant impact of garden cress extracts, which derives from the presence of active chemicals such as polyphenols, phenolic acids, and flavonoids, is corroborated by the current study's findings in terms of the plant's potential to improve heart tissue (41). Phenolic chemicals interact with different free radicals while serving as antioxidants. Their antioxidant action is mediated by transition metal chelation, hydrogen atom transfer, single electron transfer, sequential electron transfer with proton loss, and single electron transfer.(47) Additionally, (42) assessed *L. sativum* antioxidant, anti-inflammatory, and anti-proliferative properties. In an open-chest cat heart preparation, an ethanolic extract of *L. sativum* (i.p.) has been demonstrated to considerably elevate blood pressure also increase the speed and force of auricular besides ventricular movements(43). It is also claimed that isolated rabbit auricles exhibit the cardio-stimulant activity. According to the study, the extract did not have any negative behavioral or toxic effects when administered intraperitoneally to mice at

doses up to 1000mg/kg (44). In the current investigation, it was found that LS dramatically improved the serum levels of the antioxidants GSH and CAT, repairing the oxidant/antioxidant balance (45,48). According to reports, LS and its metabolites are potent antioxidants that can directly detoxify different types of free radicals by donating electrons. Additionally, by repairing the antioxidant system and boosting the activities of numerous antioxidants, including GSH and CAT, it can provide indirect protection against oxidative damage (46,49).

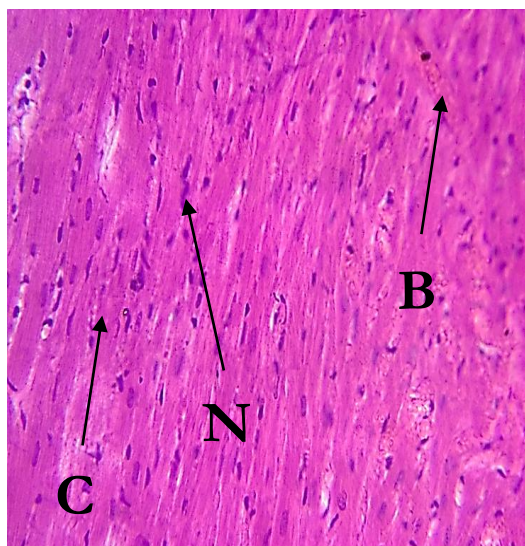


Figure (3): Heart cross section of group C showed blood vessels (BV) and cardiocytes (CC) with its elongated nuclei (Ni) H&E

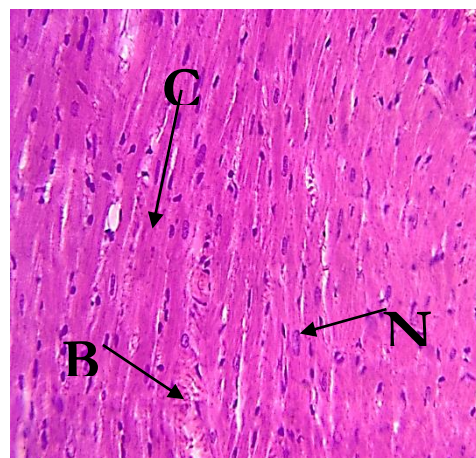


Figure (4): Heart cross section of group D showed blood vessels (BV) and cardiocytes (CC) with its elongated nuclei (Ni) H&E X400.

CONCLUSION

According to the findings of the current study, treatment with *L. sativum* extract improved both the state of oxidative stress and heart tissue due to its antioxidant content, whereas treatment with MI changed oxidative stress and caused a drop in antioxidant enzyme levels with some changes in heart tissue. The results of our current study indicated that the treatment with 400 mg/kg of (LS) extract could inhibit the side effects caused by Methimazole (50 mg/kg) throughout investigating biochemical and histological changes. The supplementation rats with (LS) extract has a therapeutic effect against biochemical and histological changes, perhaps because of its high content of active ingredients, including flavonoids and phenols, which make them powerful antioxidants ;

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