# Antioxidant Effects of Soursop Extract and Nigella Sativa Seeds Against Oxidative Stress Induced By Mono Sodium Glutamate in Male Rats

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مجلة البحوث في مجالات التربية النوعية

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# Antioxidant Effects of Soursop Extract and Nigella Sativa Seeds Against Oxidative Stress Induced By Mono Sodium Glutamate in Male Rats

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## Abstract

This study was conducted to determine the effect of Soursop extract and Nigella sativa seeds against oxidative stress induced by mono sodium glutamate in rats. Forty-eight adult albino rats weighing (180 ± 5 g) were divided randomly into six groups: the control group: fed on the basal diet, SE group: supplemented with Soursop extract (200 mg/kg b.w) daily by oral route, NSS group: fed a diet containing Nigella sativa seeds (30 g/kg feed), MSG group: fed a diet containing mono sodium glutamate (30 g/kg feed), MSG + SE group: administrated MSG (30 g/kg feed) together with Soursop extract (200 mg/kg b.w) daily by oral route, MSG + NSS group: administrated MSG (30 g/kg feed) together with Nigella sativa seeds (30 g/kg feed). The obtained results showed that the MSG group showed a significant increase in the serum levels of ALP, ALT, AST, and total bilirubin compared to the control group. While, the MSG + SE and MSG + NSS groups showed improvement in the levels of these biochemical parameters. MSG increased the appearance of signs of oxidative stress such as a significant increase in MDA levels with a mean value of (1195±15.05 nmol/g), while the MSG + SE and MSG + NSS groups showed a significant reduction in MDA levels with the mean value of (802.6±16.76 nmol/g and 810.7±17.43 nmol/g) respectively compared with the MSG group. The histopathological findings of the liver were in agreement with the results of serum parameters. In conclusion, the results of the study indicated that Soursop extract and Nigella sativa seeds had anti-inflammatory and antioxidant properties, which are potential mechanisms to enhance liver dysfunction.

**Keywords:** Soursop Extract, Nigella Sativa Seeds, Oxidative Stress

## 1. Introduction

Monosodium glutamate (MSG) is the natural sodium salt of glutamic acid that is used in many food industries as a flavor enhancer (**Helal et al., 2017)**. Although food safety organizations have considered that MSG consumption has no association with health risks, several studies have discussed its adverse effects and their relationship to differences in dosage, route of administration and duration of exposure (**Chakraborty, 2019)**.

Excessive consumption of MSG has been shown to cause liver and kidney damage (**Shi et al., 2014)**, it also causes oxidative stress in tissues, with degenerative changes in liver cells **(Abu Taweel et al., 2014)**. MSG improves the palatability of food and affects the center of appetite, thus causing an increase in body weight **(Gobatto et al., 2002)**. While MSG improves flavor and enhances appetite, it is considered a toxic substance to humans and experimental animals **(Belluardo et al., 1990)**. **Mondal et al., (2017)** showed that an oral gavage dose of MSG for a dose level of 0.8, 1.6, and 2.4 g/kg BW/day for 30 and 40 days respectively, causes suppression in the female's reproductive system in rats. Moreover, a daily dose (4 g/kg orally) of MSG was given for seven days induced kidney injury in rats (**Singh and Ahluwalia, 2012)**. The acceptable daily intake ADI of MSG for humans is 30 mg/kg/day, as the latest update of the Joint Food and agriculture organization FAO /WHO Expert Committee on Food Additives JECFA, the U.S. Food and Drug Administration FDA, and the European Food Safety Association EFSA **(Zanfirescu et al., 2019).**

The discrepancy between the generation of reactive oxygen species and antioxidants leads to the inactivation of free radical types of oxidants in cells, including proteins, lipids, or nucleic acids (**Halliwell, 1994)**. Supplements containing natural antioxidants have been shown to improve the body's efficiency in stressful conditions **(Samarghandian et al., 2013)**.

Soursop also called Graviola is fruit of the *(Annona muricata*) family. It is a perennial tree species used as herbal medicine, has various pharmacological functions, including cytotoxicity, antimicrobial, and wound care **(Sovia et al., 2017**). Soursop fruit has positive health effects, it has anti-diabetic and hypo-lipidemic,

hepato-protective and bilirubin-lowering. Also, it has powerful antioxidants activities, antihypertensive, anticancer, gastroprotective, and anti-inflammatory effects (**Ezirim et al., 2013 and Moghadamtousi et al., 2014).**

Nigella sativa, also known as black caraway or black cumin, is an annual flowering plant in the family *(Ranunculaceae).* Medicinal herbs possess a lot of phytochemical antioxidants that are very popular due to their largely safe, outstanding efficacy and low price. Among them, Nigella sativa (NS) which has successfully counteracted many health problems in Islamic countries and all over the world **(Hayatdavoudi et al., 2016).** Nigella sativa seeds (NSS) have important properties such as hypoglycemic, hypolipidemic, antioxidant, and anti-apoptotic (**Hosseinian et al., 2018).** The presence of a variety of bioactive components in NSS has prompted many researchers to ascertain the correctness of its use in the face of hepatic dysfunction **(Beheshti et al., 2018).** NSS has strong phytochemical profile that can combat feed additives that induced toxicities by suppressing free radical overproduction and enhancing redox circuitry **(Karimi et al., 2019)**.

NS has been traditionally used as an analgesic, antidiarrheal, stimulant of appetite, antimicrobial, antihypertensive, digestive, diuretic, liver tonic, and in dermatology. Numerous studies have proven that NS possesses medicinal properties such as anti-microbial, anti-oxidant, anti-diabetic, analgesic, anti-inflammatory, anti-cancer, anti-high blood pressure, anti-oxytocic, anti-convulsant, bronchodilator, diuretics, gastro-protective, hepato-protective, immunomodulator, pulmonary-protective, renal prophylactic, and anti-spasmodic properties **(Ahmad et al., 2013 and Ahmad et al., 2014).**

The current study was carried out to investigate the possible protective effect of Soursop extract and Nigella sativa seeds against oxidative stress induced by MSG using an experimental rat model.

## 2. Materials and Methods

### Materials:

Cellulose, Casein, vitamins, minerals, Monosodium glutamate and the kits which were used for biochemical analysis were purchased from El-Gomhoria Company for trading drugs, Egypt. Soursop dry extract was purchased from Sigma Aldrich Co. and Nigella sativa seeds were purchased from Imtenan Company, Egypt.

### Experimental Design:

Forty eight adult albino rats of Sprague-Dawley strain weighing (180 ± 5 gm) were purchased from Helwan Farm for Experimental Animals, Egypt. The rats were housed in healthy conditions (21-23°C) and were exposed to a natural 12 h light/dark cycle with free access to tap water ad libitum and fed on basal diet for one week before starting the experiment for acclimatization. After one week of acclimatization, the rats were randomly allocated into six groups (eight rats each):

**Control group:** received no treatment, fed on the basal diet.

**SE group:** supplemented with Soursop extract, (200 mg/kg b.w) daily by oral route.

**NSS group:** fed on a diet containing Nigella sativa seeds, after finely crushed by an electric mill mixer, and added to the diet as a powder at a dose of (30 g/kg feed).

**MSG group:** supplemented with mono sodium glutamate mixed with the basal diet at a concentration of 30 g/kg feed **(Zehra et al., 2017).**

**MSG + SE group:** administrated MSG at the dose of (30 g/kg feed) together with the administration of Soursop extract, the dry extract was dissolved in normal saline (0.9%) and administered (200 mg/kg b.w), daily by oral route.

**MSG + NSS group:** administrated MSG at the dose of (30 g/kg feed) together with Nigella sativa seeds, at a dose of (30 g/kg feed).

The experiment continued for all groups for a period of 30 days. The body weight and food intake were daily recorded. At the experimental ending (30 days), rats were fasted for 12-h then scarified. According to **(Drury and Wallington, 1980)**, blood samples were collected from the portal vein into dry clean

centrifuge tubes for serum separation, blood samples were centrifuged for 10 minutes at 3000 rpm to separate the serum. The liver was carefully dissected out and fixed in 10% formalin solution, to be used in the histological examination.

**Biochemical Analysis:**

Serum total cholesterol and triglyceride concentration were estimated according to the method of **(Allain et al., 1974) and (Fossati and Prencipe, 1982)** respectively. Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Alkaline phosphatase (ALP) activities in the serum were measured according to the method described by **(Reitman et al., 1957)** and **(Belfield et al., 1971)** respectively. The total bilirubin level, total protein (TP), and albumin (Alb) contents in the serum were estimated, as the method of **(Kaplan et al., 1984), (Gornall et al., 1949) and (Doumas et al., 1971)** respectively.

**Estimation of the Antioxidant Status in Liver Tissues:**

The liver homogenate malondialdehyde (MDA), glutathione (GSH), glutathione S transferase (GST), superoxide dismutase (SOD) and catalase (CAT) activity were determined according to **(Ohkawa et al., 1979)**, **(Beutler et al., 1963), (Habig et al., 1974), (Aebi et al., 1984) and (Nishikimi et al., 1972)** respectively.

**Histological examination:**

Scarified rat liver was washed in slain solution, dried by filter paper, weighed and placed 10 % in formalin solution for histopathological testing by the technique listed by **(Bancroft and Gamble, 2008).**

**Statistical analysis:**

Data were expressed as the mean ± SE using one-way ANOVA, followed by the Duncan post-test. All statistical analyses were carried out using SPSS for Windows software, version 16.0. (SPSS, Inc., Chicago, IL, USA). The differences were statistically significant at $p \leq 0.05$.

## 3. Results and Discussion

### Evaluation of the body weight gain of Experiment groups:

The results in figure (1) showed that the MSG-treated group recorded a significant increase in body weight compared to the control group ($p < 0.05$). The study data showed that MSG caused a significant increase in the body weight of rats. The reason for gaining weight may be due to that monosodium glutamate could improve the palatability of foods by exerting a positive influence on the appetite center, but it increases body weight (**Egbuonu et al., 2009).** Moreover, MSG improves chemical sensory perception **(Abd-Ella et al., (2016). (Moneim et al., 2018)** emphasized in their study that the main effects of MSG on body weight are an increase in interleukin IL-6 factors, resistin and tumor necrosis in adipose tissue. High levels of resistin and insulin in the blood can also lead to the deterioration of visceral adipose tissue.

There was a significant decrease in body weight in (MSG + SE) group compared to the MSG treated group, these results are in agreement with (**Chokshi, 2007), (Adewole et al., 2010) and (Arthur et al., 2011).** Also, there was a significant decrease in body weight in (MSG + NSS) group compared to the MSG-treated group and these results are in the same context with (**Hany et al., 2021)** and **(Atta, 2003).** (**Platel and Srinivasan, 2000), (Hannan et al., 2019)** confirmed that the Nigella sativa seed-fed groups showed significant improvements in the final body weight , Nigella sativa seeds greatly improved growth performance, and this growth performance promotion could be due to the nutritional value of key Nigella sativa components that contain high fatty acid percentages and essential amino acids. Moreover, Nigella sativa exerts an enhancing effect on digestive enzymes and gastrointestinal motility.

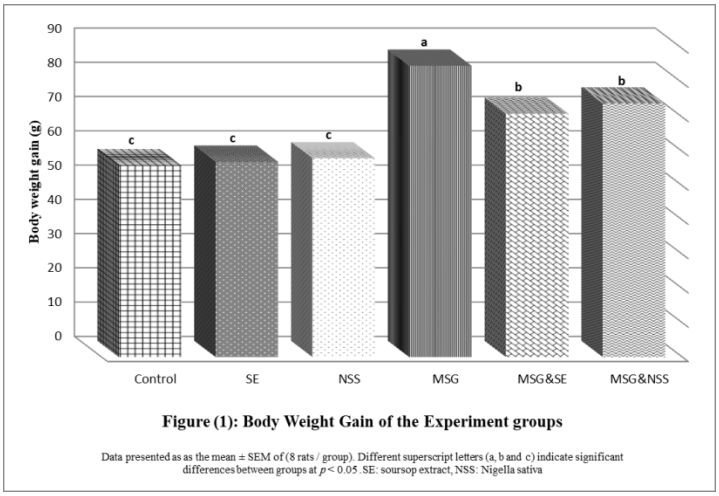



**Figure (1): Body Weight Gain of the Experiment groups**

Data presented as as the mean ± SEM of (8 rats / group). Different superscript letters (a, b and c) indicate significant differences between groups at $p < 0.05$. SE: soursop extract, NSS: Nigella sativa

**Evaluations the Biochemical Analysis of Experiment groups:**

As shown in table (1), the obtained result demonstrated that was a significant elevation in the levels of Total cholesterol and Triglyceride in MSG group with a mean value of (53.50±3.50 mg/dL and 67.56±5.61 mg/dL) compared to the control group (36.92± 2.61 mg/dL and 50.65± 2.10 mg/dL) respectively. While, (MSG + SE) and (MSG + NSS) groups showed significant reduction in levels of Total cholesterol with a mean value (42.12±2.01mg/dL and 41.45±2.71mg/dL) respectively, and level of Triglyceride with a mean value (53.43±2.30 mg/dL and 52.52±2.60 mg/dL) respectively, compared to MSG group.

Concerning the liver enzymes, there was a significantly high level of Alkaline phosphatase (ALP) in MSG group with a mean value of (252.63± 8.34 U/L) compared to the control group (189.34± 5.13 U/L). In addition, there were significantly high levels of Alanine aminotransferase (ALT) and Aspartate aminotransferase (AST) in MSG group with a mean value of (43.48± 4.52 U/L and 139.74± 4.08 U/L) compared to control group (22.54± 2.45 U/L and 123.67±9.32U/L) respectively. While, (MSG + SE) and (MSG + NSS) groups showed significant reduction in levels of (ALP) a mean value (179.92± 5.52 U/L and 177.65± 7.41 U/L), level of (ALT) a mean value (32.06± 2.26 U/L and 33.94± 3.26 U/L), level of (AST) with a mean value (135.75± 2.51 U/L and 133.85± 2.61 U/L) respectively compared to MSG group.

The results of Total bilirubin in the MSG group showed significantly elevation compared to control group (0.54± 0.034 mg/dL and 0.182±0.042 mg/dL) respectively and significant reduction in (MSG + SE) and (MSG + NSS) groups with the mean value (0.32± 0.023 mg/dL and 0.33±0.031 mg/dL) respectively compared to MSG group.

Conversely, the levels of total protein and albumin were significantly decreased in the MSG group with the mean value (2.09± 0. 35 g/dL and 1.05±0.25 g/dL) compared to control group (3.23± 0.42 g/dL and 2.014±0.32 g/dL) respectively. While the levels were well adjusted and significantly improved in (MSG + SE) and (MSG + NSS) groups, the mean value of Total protein (2.57± 0. 38 g/dL and 2.61±0.41 g/dL), the mean value of Albumin (1.68± 0. 25 g/dL and 1.57±0.27 g/dL) respectively compared with MSG group.

The results of increased levels of serum cholesterol and triglycerides in the group of MSG treated rats are in agreement with the previous findings of (**Shukry et al., 2020).** MSG can enhance the reductase activity of 3-hydroxy-3 methylglutaryl-CoA, a rate-limiting enzyme in cholesterol biosynthesis, causing the conversion of glucose metabolism to lipogenesis (**Ibegbulem et al., 2016).**

The results of the study showed that MSG can cause an increase in the levels of the liver enzymes ALT, AST, and ALP due to the cytotoxic effect of MSG, resulting in damage the cells of liver and release of these enzymes into the blood circulation **(Ortiz et al., 2006).** Furthermore, MSG toxicity produces ammonium ions that cause liver toxicity by forming ROS that interact with polyunsaturated fatty acids present in cell membranes causing degradation of plasma and mitochondrial membranes with the release of liver enzymes **(Tawfik and Al Badr, 2012).** The liver dysfunction caused by MSG manifested through a significant elevation in the levels of ALT, AST, ALP, activities and total bilirubin in comparison with the control group. These results corresponds to a previous report **(Eid et al., 2019)** and confirms the degenerative changes that occurred in hepatocytes.

Soursop extract and Nigella sativa seed were effective in returning these parameters to the control levels. The reduction in triglycerides and total cholesterol levels caused by soursop extract, that having a hypolipidemic effect and hypolipidemic factors such as tannins, which reduce cholesterol absorption and thus reduce body weight gain **(Kamal et al., 2017).** The hypolipidemic and antioxidant effects of soursop extract may be caused by the presence of some factors such as tannins and other polyphenols that cause absorption reduction of cholesterol by deactivating coenzyme A (HMG-CoA) hydroxymethylglutaryl reductase **(Usunobun et al., 2015).**

Soursop extract prevents intracellular enzyme leakage and liver injury caused by MSG **(Olakunle, 2014),** this supports the results of the study in the protective effect of soursop extract. Soursop extract significantly counteracted the harmful effect of MSG, the result obtained was in agreement with **(Syahida et al., 2012)**, which explained this result to the ability of soursop to restore body fluids and stimulate erythropoietin.

The hypolipidemic effect of Nigella sativa seeds in the study is consistent with the results of the study of hepatotoxicity-induced renal impairment **(Al Seeni et al., 2018).** The hypolipidemic effects of Nigella sativa seeds may be due to the inhibition of absorption of intestinal cholesterol and hepatic cholesterol biosynthesis, and regulation of low-density lipoprotein receptors (**Asgary et al., 2015).**

Also, the results agree with the findings of **(Beheshti et al., 2018)**, that Nigella seeds reverse the negative effects of MSG on the activity of liver enzymes, the reason for this may be due to the stabilization of the physical and chemical properties of the cell membrane by reducing the degree of oxidative stress, as well as to the enhancement of antioxidant stores. Certain bioactive components in Nigella sativa seeds capable of scavenging free radicals and regulating the expression of enzymatic antioxidants and cell-protective proteins reinforce this assumption **(Samarghandian et al., 2016)**.

**Table (1): Effect of MSG, Soursop extract and Nigella sativa seeds on the serum biochemical parameters**

| Parameters | Control | SE | NSS | MSG | MSG+ SE | MSG+ NSS |
|---|---|---|---|---|---|---|
| Total cholesterol (mg/dL) | 36.92±2.61$^{c}$ | 37.42±2.25$^{c}$ | 36.32±2.72$^{c}$ | 53.50±3.50$^{a}$ | 42.12±2.01$^{b}$ | 41.45±2.71$^{b}$ |
| Triglycerides (mg/dL) | 50.65±2.10$^{c}$ | 49.52±3.21$^{c}$ | 51.15±2.14$^{c}$ | 67.56±5.61$^{a}$ | 53.43±2.3$^{b}$ | 52.52±2.6$^{b}$ |
| ALP activity (U/L) | 189.34±5.13$^{c}$ | 190.456±6.01$^{c}$ | 191.58±6.21$^{c}$ | 252.63±8.34$^{a}$ | 179.92±5.52$^{b}$ | 177.65±7.41$^{b}$ |
| ALT activity (U/L) | 22.54±2.45$^{c}$ | 21.08±3.04$^{b}$ | 22.65±2.91$^{b}$ | 43.48±4.52$^{a}$ | 32.06±2.26$^{b}$ | 33.94±3.26$^{b}$ |
| AST activity (U/L) | 123.67±9.32$^{c}$ | 121.91±6.62$^{c}$ | 124.81±5.73$^{c}$ | 139.74±4.08$^{a}$ | 135.75±2.51$^{b}$ | 133.85±2.61$^{b}$ |
| Total bilirubin (mg/dL) | 0.182±0.042$^{c}$ | 0.193±0.043$^{c}$ | 0.189±0.051$^{c}$ | 0.54±0.034$^{a}$ | 0.32±0.023$^{b}$ | 0.33±0.031$^{b}$ |
| Total proteins (g/dL) | 3.23±0.42$^{a}$ | 3.12±0.43$^{a}$ | 3.20±0.37$^{a}$ | 2.09±0.35$^{c}$ | 2.57±0.38$^{ab}$ | 2.61±0.41$^{ab}$ |
| Albumin (g/dL) | 2.014±0.32$^{a}$ | 2.016±0.34$^{a}$ | 2.013±0.33$^{a}$ | 1.05±0.25$^{c}$ | 1.68±0.25$^{b}$ | 1.57±0.27$^{ab}$ |

Results are expressed as the mean ± SEM of (8 rats / group). Different superscript letters (a, b and c) indicate significant differences between groups at $p < 0.05$. SE: soursop extract, NSS: Nigella sativa seeds, MSG: monosodium glutamate, ALP: alkaline phosphatase, ALT: alanine aminotransferase, AST: aspartate aminotransferase.

## Evaluations the Liver Oxidative Status of Experiment groups:

As shown in table (2), there was a significant increase in MDA levels in the MSG group with a mean value of (1195±15.05 nmol/g) compared to the control group with a mean value of (683±35.41 nmol/g). While (MSG + SE) and (MSG + NSS) groups showed a significant reduction in MDA levels, the mean value (802.6±16.76 nmol/g and 810.7±17.43 nmol/g) respectively compared with MSG group.

The data in the same table clarified that there significant decrease in hepatic SOD, and CAT in the MSG group with the mean value (60.14±2.63 U/g and 127.65±3.94 U/g) compared to the control group (91.06±3.12 U/g and 188.41±3.92 U/g) respectively. On the contrary, the treated groups (MSG + SE) and (MSG + NSS) showed significant elevation as the mean value of SOD (80.86±3.01 U/g and 77.84±3.31 U/g) and the mean value of

CAT(171.54±3.89 U/g and 173.13±3.87 U/g) respectively compared with MSG group.

Concerning to GST and GSH levels in the MSG group, results showed that there significantly reduction with a mean value of (1.33±0.31 U/g and 2.63±0.16 nmol/g) compared to the control group (5.45±0.34 U/g and 5.64±0.32 nmol/g) respectively. While the treated groups (MSG + SE) and (MSG + NSS) showed significant elevation in these parameters, the mean value of GST(3.35±0.35 U/g and 3.16±0.18 U/g) and the mean value of GSH (4.32±0.15 U/g and 4.05±0.16 nmol/g) respectively compared with MSG group.

Intake of MSG caused an increased appearance of evidence of oxidative stress, such as MDA, and reduced levels of SOD, CAT, GST and GSH, as a result of the depletion of SOD and accumulation of H2O2 as a result of ROS composition, these results agreed with **(Sharma, 2014) and (Calis, 2016). (Asl et al., 2013)** proved that the conversion of most GSH in the liver to glutathione disulfide (GSSG) by the enzyme glutathione reductase to protect living cells from damage caused by toxic substances led to a reduction in the level of GSH. The reason for high levels of MDA is the difficulty of transporting glutamate through the cell membrane, which causes the initiation of lipid oxidation (LPO) and alters the redox state of the cell and results in membrane damage.

Soursop extract improved the oxidative state of liver cells and returned them to their normal state, due to the antioxidant activity of soursop, which has a protective role against free radicals (OH) and $H_2O_2$ **(Baskar et al., 2007).** Soursop can stop the rise of LPO **(Spitz et al., 2004),** also it can turn ROS into nontoxic or dangerous compounds **(Ekaluo et al., 2016)**. Soursop has powerful antioxidant properties due to the presence of acetogenin, which can play an essential and important role in scavenging free radicals **(Baskar et al., 2007).**

The results of the study demonstrated the ability of Nigella sativa seeds to modify the oxidative state of liver cells and returned them to their normal state, which corresponds with (**Hany et al., 2021)** that analyses the phytochemical constituents of Nigella sativa seeds have revealed strong antioxidant free

radical DPPH scavenging activity, which may be attributed to the high levels of phenolic and flavonoid constituents, as the results of his study showed that the total phenol and flavonoid compounds and the 2, 2- diphenyl- 1- picrylhydrazyl (DPPH) scavenging activities of Nigella sativa seeds equaled 2.077 mg gallic acid equivalents,0.565 mg catechin equivalents and 1.367 g Trolox equivalents, respectively. Also, **(Adetuyi and Ibrahim, 2014)** found that DPPH functions associated with phenolic and flavonoid components.

**Table (2): Effect of MSG, Soursop extract and Nigella sativa seeds on the liver oxidative status**

| Parameters | Control | SE | NSS | MSG | MSG+ SE | MSG+ NSS |
|---|---|---|---|---|---|---|
| MDA (nmol/g) | 683.7±35.41$^{c}$ | 677.5±34.42$^{c}$ | 679.89±36.21$^{c}$ | 1195±15.05$^{a}$ | 802.6±16.76$^{b}$ | 810.7±17.43$^{b}$ |
| SOD (U/g) | 91.06±3.12$^{a}$ | 94.42±3.10$^{a}$ | 95.13±2.60$^{a}$ | 60.14±2.63$^{c}$ | 80.86±3.01$^{b}$ | 77.84±3.31$^{b}$ |
| CAT (U/g) | 188.41±3.92$^{a}$ | 193.11±2.91$^{a}$ | 191.56±2.54$^{a}$ | 127.65±3.94$^{c}$ | 171.54±3.89$^{b}$ | 173.13±3.87$^{b}$ |
| GST (U/g) | 5.45±0.34$^{a}$ | 5.78±0.54$^{a}$ | 5.62±0.42$^{a}$ | 1.33±0.31$^{c}$ | 3.35±0.35$^{b}$ | 3.16±0.18$^{b}$ |
| GSH (mmol/g) | 5.64±0.32$^{a}$ | 5.46±0.30$^{a}$ | 5.36±0.42$^{a}$ | 2.63±0.16$^{c}$ | 4.32±0.15$^{b}$ | 4.05±0.16$^{b}$ |

Results are expressed as the mean ± SEM of (8 rats / group). Different superscript letters (a, b and c) indicate significant differences between groups at $p < 0.05$. SE: soursop extract, NSS: Nigella sativa seeds, MSG: monosodium glutamate. Malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT), glutathione S transferase (GST) and glutathione (GSH).

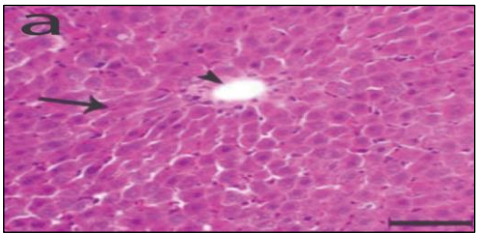
## Histological examination:

As shown in figure(2), it was observed that the control group had normal hepatocytes arranged in cords around the central vein. The group of Soursop extract and group of Nigella sativa seed showed normal liver cells arranged in cords separated by blood sinusoid. It was observed that MSG group, showed periportal hepatic necrosis associated with mononuclear cells infiltration and hepatic vacuolation, single-cell necrosis and a loss of cellular details and nuclei of some hepatocytes. While, the group rat of (MSG+SE) showed a few pyknotic nuclei of hepatocytes and a mild degree of hepatocyte degeneration. In the (MSG + NSS) there limited centrilobular hepatic vacuolation and mononuclear cell infiltration were observed.

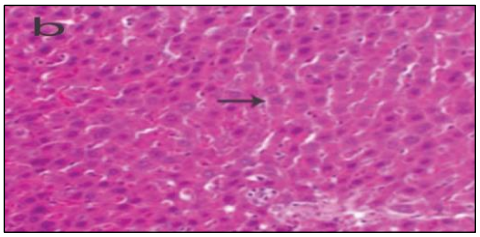
Regarding the histopathological results, it was observed in the control group, Soursop extract group, and Nigella seed group normal hepatocytes arranged in regulated cords around the central

vein, while periportal hepatic necrosis associated with mononuclear cell infiltration, hepatic vacuolation was observed in MSG group, these results are similar to (**Bhattacharya, 2011) and (Mustafa, 2016).** Because of MSG, the cell becomes unable to completely repair the damage and the cause is excess glutamine. Thus, vesicular degeneration and necrosis of the hepatic tissues are expected to occur **(Gill and Pulido , 2005).** In addition, MSG has been shown to cause oxidative stress and hepatotoxicity **(Cheville, 2009).** The vacuolization of hepatocytes was clarified as a ballooning degeneration. The explanation was the cellular defense mechanism for harmful substances, that aggregates and attempts to prevent interference with biologically influencing components. Furthermore, The elevated level of MDA caused by the LPO effect of MSG may lead to liver necrosis **(Ortiz et al., 2006).** The changes in liver cells observed in the (MSG) group agreed with **(Eid et al., 2019) and (El bassuoni et al., 2018).** Moreover, administration of Soursop extract had a good therapeutic effect on the liver structure of rats in the (MSG+SE) group, these results are in agreement with **(Faleye and Dada, 2016)**.

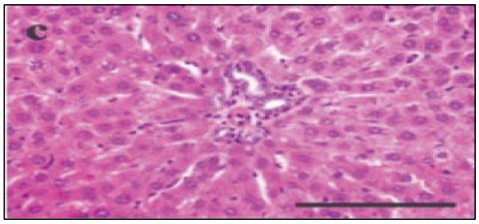
The results of the noticeable improvement in hepatocytes in group (MSG+ NSS) agreed with **(Eshami et al., 2015).** The active phytochemical component of Nigella sativa seed such as TQ, thymol, and α-hederin play an essential role in protecting the liver from harmful factors by inhibiting iron mediated lipid peroxidation, nuclear factor kappa B, cyclooxygenase, and lipoxygenase. TQ stimulates the process of cell division and proliferation resulting in enhanced regeneration after tissue damage **(Kanter, 2011).** Eating Nigella sativa seeds had benefits in preventing the development of MSG-induced apoptosis which can be understood based on the antioxidant and anti-inflammatory properties **(Hosseinian et al., 2018).**



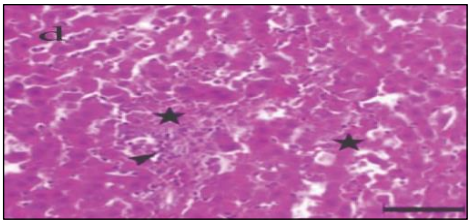

**(a)** Liver of control rat showing normal hepatocytes (arrow) arranged in cords around the central vein (arrowhead).



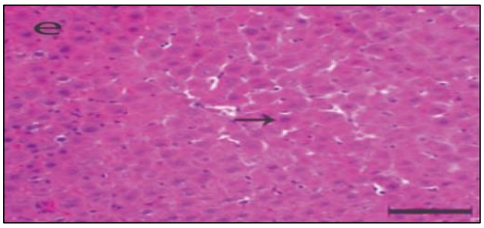

(b) Liver of (SE) rat showing normal hepatocytes arranged in cords separated by blood sinusoids (arrow).



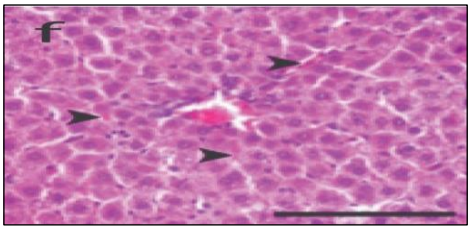

(c) Liver of (NSS) rat showing normal arrangement of the hepatic cells and the portal area containing branches of the hepatic artery and portal vein.




(d) Liver of (MSG) rat showing periportal hepatic necrosis (stars) associated with mononuclear cell infiltration (arrowhead).




(e) Liver of (MSG+SE) rat showing a few pyknotic nuclei (arrow) and a mild degree of hepatocyte degeneration.




(f) Liver of (MSG+NSS) rat showing normal arrangement of the hepatic cords in the parenchyma with minimally congested hepatic sinusoids (arrowheads).

**Figure(2): Histological examination of Experiment groups**

## 4. Conclusion

The present study scientifically proved that Soursop extract and Nigella sativa seeds produced great therapeutic effects against monosodium glutamate MSG and improved liver enzymes. The results of both groups of soursop extract and Nigella sativa seeds are very similar in the protective effect against the changes induced by MSG. The study recommends the necessity of raising nutritional awareness of the importance of these plants for its qualities and biological effects.

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# التأثيرات المضادة للأكسدة لمستخلص القشطة الشائكة وبذور حبة البركة ضد الإجهاد التأكسدي الناجم عن الجلوتامات أحادية الصوديوم في ذكور الفئران

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## الملخص العربي

أجريت هذه الدراسة لتحديد تأثيرمستخلص القشطة الشائكة وبذور حبة البركة ضد الإجهاد التأكسدي الناتج عن الجلوتامات أحادية الصوديوم في الفئران. تم تقسيم (48) من ذكور الفئران الألبينو البالغة وزن (180 ± 5 جم) بشكل عشوائي إلى ست مجموعات، المجموعة الأولى الضابطة تغذت على الغذاء الأساسي، المجموعة الثانية تناولت مستخلص القشطة الشائكة (200 مجم / كجم من وزن الجسم) يوميًا عن طريق الفم ، المجموعة الثالثة تغذت على نظام غذائي يحتوي على بذور حبة البركة (30 جم / كجم من الغذاء الأساسي) ، المجموعة الرابعة تغذت على نظام غذائي يحتوي على جلوتامات أحادية الصوديوم (30 جم / كجم من الغذاء الأساسي)، المجموعة الخامسة تغذت على نظام غذائي يحتوي على جلوتامات أحادية الصوديوم (30 جم / كجم من الغذاء الأساسي) مع مستخلص القشطة الشائكة (200 مجم / كجم من وزن الجسم) يوميًا عن طريق الفم ، المجموعة السادسة تغذت على نظام غذائي يحتوي على جلوتامات أحادية الصوديوم (30 جم / كجم من الغذاء الأساسي) مع بذور حبة البركة (30 جم / كجم من الغذاء الأساسي). أظهرت النتائج أن مجموعة الفئران التي تناولت جلوتامات احادية الصوديم أظهرت ارتفاعا معنويا في مستويات AST،ALT،ALP، البيليروبين الكلي مقارنة بالمجموعة الضابطة. بينما أظهرت المجموعات التي تناولت مستخلص القشطة الشائكة أو بذور حبة البركة تحسناً ملحوظا في مستويات هذه القياسات البيوكيميائية. جلوتامات أحادية الصوديوم تسببت في زيادة ظهور علامات الإجهاد التأكسدي في الفئران مثل الارتفاع في مستويات MDA بمتوسط (1195 ± 15.05 نانومول/جم)، بينما أظهرت المجموعات التي تناولت مستخلص القشطة الشائكة أو بذور حبة البركة انخفاضًا كبيرًا في مستويات MDA بمتوسط (802.6 ± 16.76 نانومول/جم و 810.7 ± 17.43 نانومول/ جم) على التوالي مقارنة بمجموعة الفئران التي تناولت جلوتامات احادية الصوديم. أكدت نتائج الفحص الهستوباثولوجي لأنسجة الكبد النتائج السابقة. في الختام ، أشارت نتائج الدراسة إلى أن مستخلص القشطة الشائكة وبذور حبة البركة كان لهما خصائص مضادة للالتهابات ومضادة للأكسدة ، وهي آليات محتملة لتعزيز حالة ضعف الكبد وكذلك حماية خلايا الكبد من مادة جلوتامات احادية الصوديم. لذلك ، يمكن اعتبار مستخلص القشطة الشائكة وبذور حبة البركة من بين النباتات التي لها دور كبير في حماية ووقاية خلايا الكبد.

**الكلمات المفتاحية:** مستخلص القشطة الشائكة ، بذور حبة البركة ، الإجهاد التأكسدي