Official Journal Issued by Faculty of Veterinary Medicine

**Benha Veterinary Medical Journal**

Journal homepage: https://bvmj.journals.ekb.eg/

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*Original Paper*

# *Salvia officinalis* L. oil extract attenuates cisplatin-induced hepatorenal damage via modulating oxidative stress and apoptosis

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**ARTICLE INFO**

**Keywords**

*Gas-chromatography, TNF alpha, Sage plant, Immunohistochemistry, Histopathology*

*Received* 12/02/2024
*Accepted* 24/03/2024
*Available On-Line* 01/04/2024

**ABSTRACT**

Cisplatin is one of the most powerful drugs used in cancer treatment, and it has several side effects, including hepatotoxicity and nephrotoxicity. This study aimed to see if Salvia officinalis essential oil extract (SOE) might protect rats' liver and kidneys against cisplatin damage. Twenty-four male albino rats were divided into 4 groups (6 rats each). G1 (control), G2 (SOE), G3 (cisplatin), and G4 (cisplatin+ SOE). Cisplatin-treated rats showed increased serum ALT, AST, ALP, cholesterol, triglyceride, LDL-cholesterol, creatinine, and urea concentrations and decreased total protein and albumin concentrations. Moreover, cisplatin-treated rats significantly increased levels of MDA and decreased SOD and CAT levels in hepatic and renal tissue compared to the control group. SOE administration at a dose of 100mg SOE L./kg.b.wt. with once intraperitoneal (7.5 mg cisplatin/kg.b.wt.) on the 10th day of the experiment renormalized and reversed the hepatorenal damage induced by the cisplatin group due to its antioxidant and anti-inflammatory effects. Histopathological alteration and immunohistochemistry (TNF-alpha) examination showed improvement in the microscopic pictures of both the liver and kidneys after using SOE.

## 1. INTRODUCTION

Cisplatin is a very efficient anticancer medication that is used to treat a variety of malignancies. However, as an anticancer medicine, it has several negative effects (Razak et al., 2021). After infusion, cisplatin rapidly diffuses into multiple organs, reaching greater amounts in the liver. Cisplatin is biotransformed by the cytochrome P450 (CYP450) enzyme complex. One of the enzymes known as cytochrome P450 2E1 (CYP2E1) is a prominent enzyme that has been implicated in hepatotoxicity. As the primary excretory pathway for cisplatin, renal parenchyma accumulates more than other tissues. Cisplatin enters the renal proximal tubular cells via an organic transporter like copper, causing damage to the nuclear DNA and the generation of ROS, ultimately leading to cell death (Abd Rashid et al., 2021).

*Salvia officinalis L.* (SO) has potent antioxidant and anti-inflammatory effects. It has a protective role as a nanoparticle against the harmful effects of some toxic agents (Raheem et al., 2020). The bioactive phytochemicals found in SO oil and the polyphenols found in the aqueous extract (SOE) showed that they protect rats from oxidative damage caused by dangerous products. *Salvia officinalis L.* has potentially beneficial medicinal properties against environmental toxins (Rashwan et al., 2021). *Salvia officinalis l.* total extract has high flavonoids, so Salvia has antioxidant and anti-inflammatory properties (Othman et al., 2022). The point of this study was to find out how SO can help the hepatorenal system fight oxidative stress and apoptosis caused by cisplatin in rats.

## 2. MATERIALS AND METHODS

### *2.1. Chemicals*

Cisplatin commercial product (MYLAN®) (1 mg/ml) was purchased from El Ezaby Pharmaceuticals in Egypt. Imtenan Company (Cairo, Egypt) provided the oil extract of SO (Bio-diagnostic Company), Cairo, Egypt, and provided all used analytical kits.

### *2.2. Gas chromatography-mass spectrometry (GC-MS) analysis of SO oil extract*

The chemical composition of SO oil extract samples was determined using a GC-TSQ mass spectrometer from Thermo Scientific (Austin, TX, USA) and a direct capillary column TG-5MS (30 m x 0.25 mm x 0.25 m film thickness). The components were identified by comparison of their 1 (mass spectra with those of WILEY 09) and 2 (NIST14 mass spectral database). International Journal of 1. (analytical mass spectrometry) and 2. (chromatography), 2016, 4, 14–25. (Al-Ibrahemi et al., 2023)

### *2.3. Animals*

The rats used in this study were obtained from the Veterinary Serum and Vaccine Research Institute in Abbasia, Cairo, Egypt. They began with a starting weight of 200–240 g and received a powder meal that included 0.85% phosphorus, 0.35% magnesium, 1.12% calcium, 25.3% crude protein, and 2.5 IU g1 vitamin D3.

The Ethical Committee of the Faculty of Veterinary Medicine at Benha University in Egypt (Ethical No.

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BUFVTM 21-02-23) approved all procedures used in this experiment.

*2.4. Experimental design*

Twenty-four rats were divided randomly into four equal groups. Group 1: Rats served as the control and were administered food oil orally by stomach tube daily. Group 2: rats were administered a 100-mg extract of *SO l./kg b.wt* orally (Yousry et al., 2021). Group 3: rats were administered (7.5 mg Cisplatin/kg b.wt.) once I/P injection on the 10$^{th}$ day of the experiment (Alshahrani et al., 2022). Group 4: rats in this group were administered a 100-mg extract of SO*/kg b.wt*. orally daily and 7.5 mg of cisplatin/kg b.wt. once intraperitoneally on the 10$^{th}$ day. The experiment continued for fourteen consecutive days; during this time, there was daily observation of rats in all groups.

*2.5. Serum collection and tissue sampling*

Rats, after being anesthetized with isoflurane for one day, received the final treatment at the end of the experiment. Blood was drawn directly from the hearts of rats. Blood was put in plain tubes, allowed to coagulate, and then centrifuged at 3000 rpm for at least 15 minutes. After blood collection, the rats were slaughtered, and their liver and kidneys were promptly removed. The isolated (liver and kidney) tissues were split into two slides. The first component was kept at -2 °C to prepare tissue homogenates for determining the activities of MDA, CAT, and SOD. The second half was fixed in 10% neutral-buffered formalin for histopathological and immuno-histochemical analyses.

*2.6. Serum biochemical analysis*

Serum ALT, AST, and ALP levels were estimated according to the methods described by Babson et al. (1966); total protein and albumin levels were estimated according to Doumas et al. (1971; Koller and Kaplan, 1984). Serum urea values were determined using kits (Bio Diagnostics Company, Egypt) according to Coulombe and Favreau (1963); in addition, serum creatinine was determined according to Bartels et al. (1972). While serum cholesterol, triglycerides, and HDL cholesterol concentrations with also estimated, according to Friedewald (1972). Serum LDL-cholesterol, total cholesterol, HDL cholesterol, and triglycerides are used in ready-to-use kits from the BIOMED company, EGYPT.

*2.7. Determination of antioxidant markers*

One gram of liver and kidney tissue was homogenized with an electrical homogenizer and 5 cc of phosphate buffer (pH 7.4). Tissue homogenates were centrifuged for 60 minutes at 105,000 g and 4 °C. The resulting supernatants were separated into aliquots and kept at 80 °C to assess oxidative stress and antioxidant status. MDA levels were estimated (Ohkawa et al., 1979). Tissue SOD activity was determined (Nishikimi et al., 1972), and catalase (CAT) was measured (Aebi, 1984).

*2.8. Histopathological analysis*

Small tissue specimens were collected from the kidney and liver and fixed in 10% neutral buffered formalin. Then, 4-6µm tissue paraffin sections were routinely prepared and stained with H&E stain (Bancroft and Stevens et al., 2016). The stained sections were examined using a Leica microscope (CH9435 Hee56rbrugg) from Leica Microsystems, Switzerland.

*2.9. Immunohistochemistry Staining Protocol*

Immunohistochemistry was performed on paraffin tissue slices that were fixed on positively charged slides using the complicated ABC technique (avidin, biotin, and peroxidase). Immunostained sections were examined and photographed using a Leica microscope at various magnifications (CH9435 Hee56rbrugg) (Leica Microsystems, Switzerland).

*2.10. Statistical analysis*

Using the SPSS software, version 20.0 (SPSS Inc., Chicago, IL), all data were statistically analyzed using one-way ANOVA with Duncan's multiple comparison test. $P \leq 0.05$ is considered statistically significant.

## 3. RESULTS

3.1. Gas chromatography–mass spectrometry (GC-MS) analysis of *Salvia Officinalis* l (oil extract)

GC-MS was performed to identify volatile substances and detection for molecules found inside *salvia officinalis l.* oil extract.

*Salvia officinalis l.* oil extract GC-MS analysis {table 1, fig 1} revealed about 29 relative molecules. Volatile oils which are (essential oils) are a mixture of (Triglyceride-cholesterol- phospholipids- (saturated fatty acids) such as stearic acid, palmitic acid and unsaturated like oleic acid and linoleic acid (Al-Ibrahemi et al., 2023, April).

Table 1: Chemical composition of *Salvia officinalis essential* oil extract as identified by GC.MS:

| NO | Compound Name | Area % | RT | Molecular Formula |
|---|---|---|---|---|
| 1 | Palmitic Acid methyl ester | 6.70 | 25.93 | C17H34O2 |
| 2 | Hexadecanoic acid, methyl ester | 6.70 | 25.93 | C17H34O2 |
| 3 | Dotriacontane | 2.59 | 28.45 | C32H66 |
| 4 | Isochiapin B | 2.59 | 28.45 | C19H22O6 |
| 5 | Isochiapin B %2< | 2.59 | 28.45 | C19H26O6 |
| 6 | Tert-Hexadecanethiol | 2.59 | 28.45 | C16H34S |
| 7 | 7-HEPTADECENE, 1-CHLORO- | 2.59 | 28.45 | C17H33Cl |
| 8 | 9,12-Octadecadienoic acid (Z,Z)-, methyl ester | 18.21 | 28.97 | C19H34O2 |
| 9 | Linoleic Acid methyl ester | 18.21 | 28.97 | C19H34O2 |
| 10 | Methyl 9-cis,11-trans-octadecadienoate | 18.21 | 28.97 | C19H34O2 |
| 11 | 9-Octadecenoic acid, methyl ester, (E)- | 26.30 | 29.16 | C19H36O2 |
| 12 | 11-Octadecenoic acid, methyl ester | 26.30 | 29.16 | C19H36O2 |
| 13 | cis-13-Octadecenoic acid, methyl ester | 26.30 | 29.16 | C19H36O2 |
| 14 | 9-Octadecenoic acid (Z)-, methyl ester | 26.30 | 29.16 | C19H36O2 |
| 15 | trans-13-Octadecenoic acid | 26.30 | 29.16 | C19H36O2 |
| 16 | Heptadecanoic Acid,16-Methyl-, Methyl Ester | 3.37 | 29.71 | C19H38O2 |
| 17 | Heptadecanoic acid, 9-methyl-,methyl ester | 3.37 | 29.71 | C19H38O2 |
| 18 | Heptadecanoic acid, 10-methyl-,methyl ester | 3.37 | 29.71 | C19H38O2 |
| 19 | 14-á-H-PREGNA | 1.72 | 31.47 | C21H36 |
| 20 | 17-Pentatriacontene | 1.72 | 31.47 | C35H70 |
| 21 | Tetrapentacontane, 1,54-dibromo- | 1.72 | 31.47 | C54H108Br2 |
| 22 | 1,54-Dibromotetrapentacontane | 1.72 | 31.47 | C54H108Br2 |
| 23 | Octatriacontyl pentafluoropropionate | 1.74 | 33.61 | C41H77F5O2 |
| 24 | Dotriacontane | 1.66 | 34.63 | C32H66 |
| 25 | Hahnfett | 1.92 | 36.74 | N/A |
| 26 | cis-13-Eicosenoic acid | 6.90 | 37.47 | C20H38O2 |
| 27 | cis-11-Eicosenoic acid | 6.90 | 37.47 | C20H38O2 |
| 28 | Erucic acid | 5.71 | 39.62 | C22H42O2 |
| 29 | 9-Hexadecenoic acid, 9-octadecenyl ester | 4.50 | 39.87 | C34H64O2 |

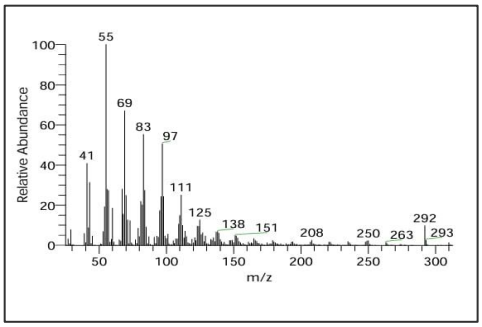


Figure 1: GC-MS analysis of (*Salvia officinalis L*) oil extract:

3.2. Effect of *Salvia Officinalis* l. oil extract and/or Cisplatin on serum biomarkers

Cisplatin (7.5 mg/kg.b.wt.) injection on the 10th day of the experiment resulted in a significant increase in serum levels {ALT, ALP, AST, urea, and creatine} and a decrease in albumin and serum total protein (TP) activities compared to the control. Supplementation of (100mg extract of SO/kg.b.wt.) together with cisplatin (7.5 mg cisplatine/ kg.b.wt.) for 14 consecutive days showed corrected results on serum hepatic (Fig. 2) and renal bio markers (Fig.3).

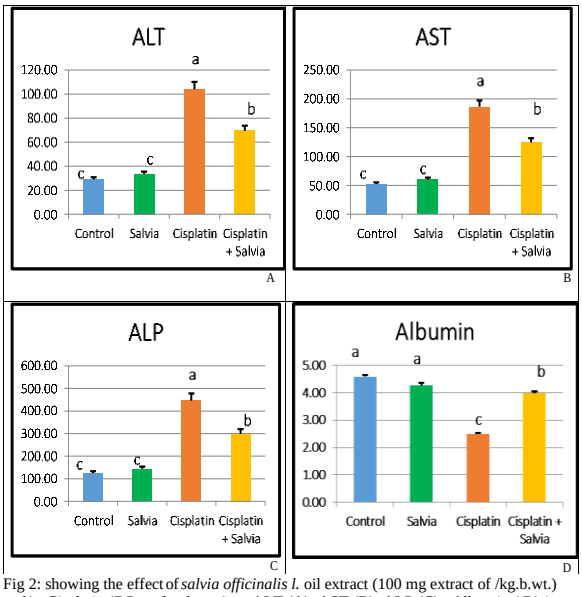


Fig 2: showing the effect of *salvia officinalis l.* oil extract (100 mg extract of /kg.b.wt.) and/or Cisplatin (7.5 mg/kg. b. wt.) on ALT (A), AST (B), ALP (C), Albumin ( D) in serum of male albino rats.

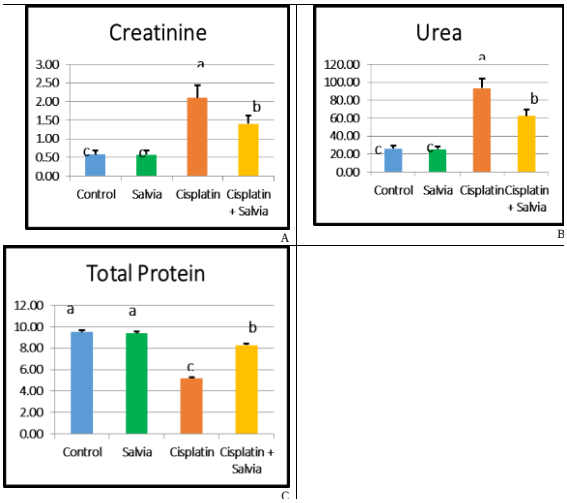


Fig 3: showing the effect of *Salvia officinalis l.* oil extract (100 mg extract of /kg.b.wt.) and/or Cisplatin (7.5 mg/kg. b. wt.) on creatinine (A), urea (B), total protein (C) in serum of male albino rats.

3.3. Effect of *Salvia Officinalis* l. oil extract and/or Cisplatin on lipid profile

Cisplatin (7.5 mg/kg.b.wt.) injection on 10th day of the experiment significantly elevated lipid profile of (LDL, Cholesterol, Triglyceride) level and decreased (HDL) levels compared to those in the control group (100mg extract of SO./kg.b.wt.) for 14 consecutive days showed a significant decline in (LDL, Cholesterol, Triglyceride) levels and increased (HDL level) compared with cisplatin group in (Fig.4).

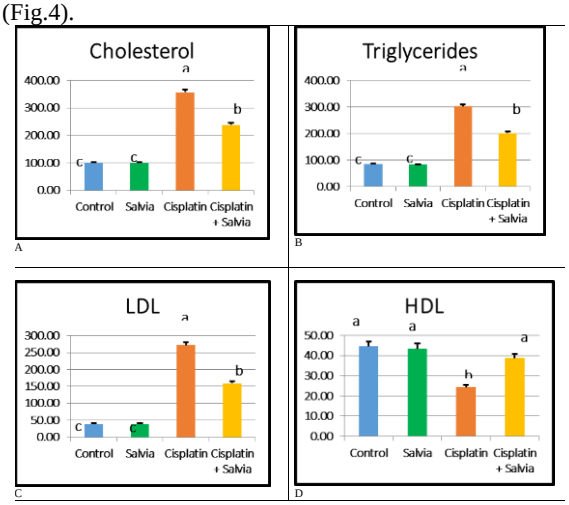


Fig 4: showing the effect of *Salvia officinals l.* oil extract (100 mg extract of /kg.b.wt.) and/or Cisplatin (7.5 mg/kg. b.wt.) on cholesterol (A), Triglyceride (B), LDL-c (C) and HDL-C (D)) in serum of male albino rats.

3.4. Effect of *Salvia Officinalis l.* oil extract and/or Cisplatin on oxidative stress markers

Cisplatin at 7.5 mg/kg.b.wt. injection on 10th day of the experiment dramatically increased in hepatic and renal MDA and decreased in HCAT, HSOD, RSOD and RCAT compared with the control. On the other hand, (100mg extract of SO/kg.b.wt.) co-treatment in rats injected with cisplatin significantly attenuated the hepatorenal oxidative stress and lipid peroxidation when compared with cisplatin group (Fig. 5).

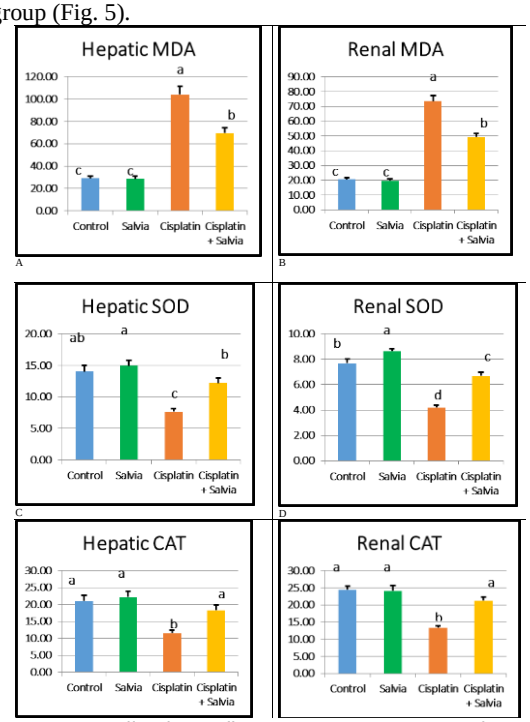


Fig 5: showing the effect of *salvia officinals l.* oil extract (100 mg extract of /kg.b.wt.) and/or Cisplatin (7.5 mg/kg.b.wt.) on antioxidant parameters: hepatic MDA (A), renal MDA (B), hepatic SOD (C), renal SOD (D), hepatic CAT (E) and renal CAT (F) in male albino rats

3.6. Histopathological findings

The microscopic examination of the line sections from the control and SO oil extract groups revealed a typical structure of hepatic tissue with intact lining of central veins and regular hepatic cords with normal light vesicular hepatocytes, along with hepatic sinusoids assembled in an unusual structure (Figs. 6A and B). Contrary to this, the majority of the hepatic sections from rats in the cisplatin group showed severe hydropic degeneration and necrosis of the hepatic cells with dilatation of the central veins. Additionally, microvascular steatosis along with interstitial edema was observed (Fig. 6C). SO oil extract pretreatment attenuated this hepatic damage-induced cisplatin, where there was an obvious improvement in the hepatic tissue as central veins were dilated. The majority of the hepatocytes appeared normal, with light and vesicular nuclei. However, some hepatic cells showed hydropic degeneration, and others appeared with pyknotic nuclei. Also, mild microvascular steatosis and sinusoidal dilatation were infrequently seen (Fig. 6D).

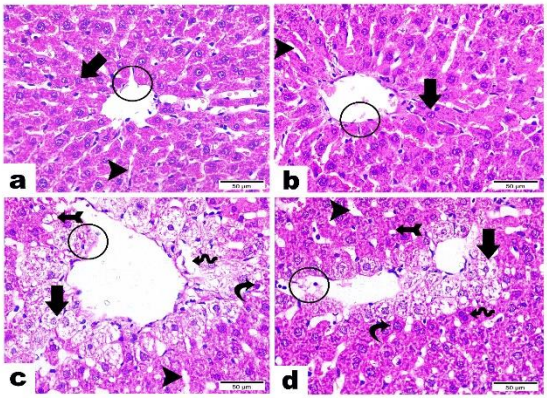


Figure (6): Photomicrographs displaying the effect of salvia officinalis l. oil extract on the histopathological changes of the hepatic tissue (central vein area) in the groups (H&E stain, x400 & scale bar= 50$\mu\mu$m) as follow: control group (a) & salvia group (b) demonstrating the typical structure of hepatic tissue with an intact central vein (circle), regular hepatic cords with normal light vesicular hepatocytes (arrows), along with hepatic sinusoids (arrowheads). cisplatin group (c) dilatation of the central vein, hydropic degeneration of hepatocytes (arrow), and some hepatocytes appear with a pyknotic nucleus (curvy arrow). microvascular steatosis (arrow with tail) with interstitial edema (wave arrow). Hepatic sinusoids had a normal look (arrowhead). cisplatin and SO oil extract group (d) displays the central vein appears with moderate dilatation. Most hepatocytes appeared normal curvy arrow), some appeared with hydropic degeneration (arrow), and others appeared with pyknotic nuclei (wave arrow). mild microvascular steatosis (arrow with tail). Dilatation of the sinusoid (arrowhead)

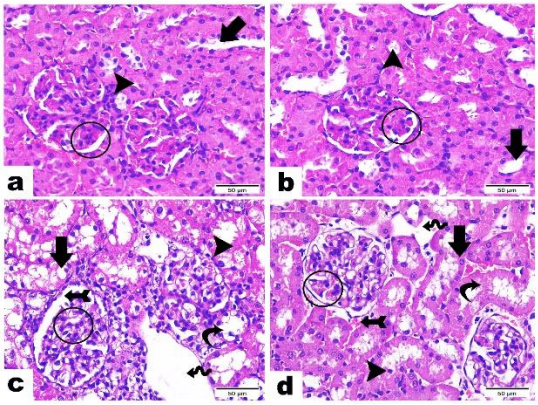


Figure (7): Photomicrographs displaying the effect of SO oil extract on the kidney tissue (renal cortex area) among studied groups (H&E stain, x400 and scale bar= 50$\mu\mu$m) as follow: control group (a) and salvia group (b) demonstrating the standard structure of renal cortex area with regular glomerulus and renal corpuscle (circles), well organized proximal (arrowheads), and distal convoluted tubules (arrows). cisplatin group (c) showing severe degenerative changes with renal corpuscle vacuolation (circle), increasing glomerular space (arrow with tail). Some renal tubules showing vacuolation (arrow), and others dilated with squamous cells (curvy arrow), interstitial edema (wave arrow), with necrotic area (arrowhead). Cisplatin and SO group (d) displaying restored renal corpuscle with regular organization with some vacuolation, most renal tubules appeared normal with light and vesicular lining cells (arrow), some seemed with epithelial desquamation (curvy arrow), and others appear with pyknotic nuclei of lining cells (arrowhead), small focal interstitial edema (wave arrow).

3.8. Immunohistochemical Findings

The immunoexpression of tumor necrosis factor α (TNFα) as a potent mediator of inflammation we used to assess the anti-inflammatory effect of SO extract in the liver and kidney tissues. The examined liver section from control and SO oil extract treated groups displayed scarce positive cytoplasmic reactivity with TNF$\boldsymbol{\alpha}$ along hepatocytes (Fig. 8 A and B) of (liver). On the other hand, the liver sections from cisplatin group showed intense positive cytoplasmic reactivity with TNF$\boldsymbol{\alpha}$ along hepatocytes (Fig. 8 C) of (liver). While, the sections in the cisplatin and SO oil extract group exhibited moderate positive cytoplasmic reactivity with TNF$\boldsymbol{\alpha}$ along hepatocytes (Fig. 8 D) of (liver) . Similarly, the kidney sections from control group and SO. oil extract group displayed very few positive cytoplasmic reactivity along renal corpuscle and renal tubules (Fig. 8 A and B) from (kidney). While the renal sections from cisplatin group showed the intense positive cytoplasmic reaction along renal corpuscle and renal tubules (Fig. 8 C) of (kidney) while the section cisplatin and SO oil extract group revealed moderate positive cytoplasmic reactivity along renal corpuscles and renal tubules (Fig. 8 D) from (kidney).

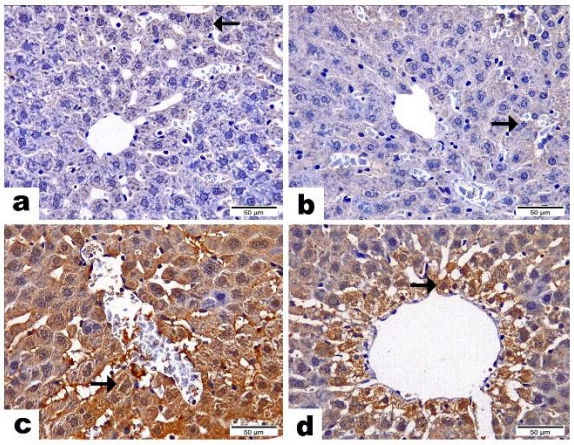


Figure (8): Photomicrographs showing the expression of TNF$\boldsymbol{\alpha}$ along hepatic tissue (central vein area) between inspected groups (TNF$\boldsymbol{\alpha}$, x400, scale bar= 50µm) as follow: Sections from control group (a) and *salvia officinalis l.* oil extract treated group (b) displaying scarce positive cytoplasmic reactivity with TNF$\boldsymbol{\alpha}$ along hepatocytes (arrows). Section from cisplatin group (c) showing the intense positive cytoplasmic reactivity with TNF$\boldsymbol{\alpha}$ along hepatocytes (arrow). Section cisplatin and SO extract group (d) highlighting moderate positive cytoplasmic reactivity with TNF$\boldsymbol{\alpha}$ along hepatocytes (arrow).

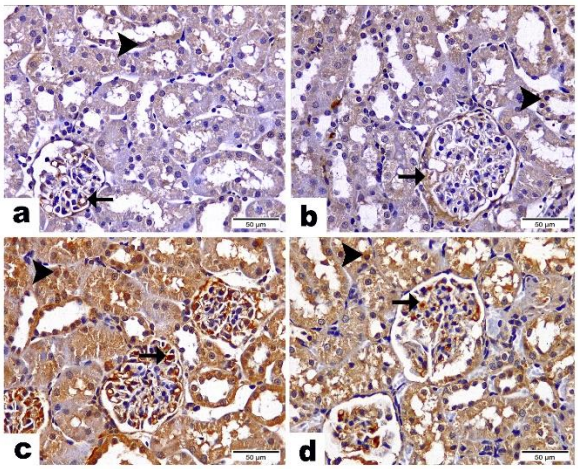


Figure (8): Photomicrographs showing the expression of tumor necrosis factor alpha (TNF$\boldsymbol{\alpha}$) along kidney tissue (renal cortex area) between inspected groups (s x400, scale bar= 50µm) as follows: Sections from control group (a) and SO oil extract group (b) displaying very few positive cytoplasmic reactivity along renal corpuscle (arrows), and renal tubules (arrowheads). Section from cisplatin group (c) highlighting the intense positive cytoplasmic reaction along renal corpuscle (arrow), likewise renal tubules (arrowhead). Section cisplatin and SO group (d) revealing moderate positive cytoplasmic reactivity along renal corpuscle (arrow), and renal tubules (arrowhead).

## 4. DISCUSSION

Cisplatin is one of the most frequently used chemotherapeutic agents in the world. It causes hepatic and renal injuries. In the cisplatin group, serum AST, ALT, ALP, urea, and creatinine were increased, as were serum cholesterol, triglycerides, and LDL. On the other hand, it decreased levels of total protein, albumin, and HDL. Meanwhile, MDA increased with a decrease in CAT and SOD in the liver and kidney tissues. Our result displayed some pathological changes in the liver and kidney tissues, followed by apoptosis. Our results came in agreement with (Elsayed et al., 2021), (Okafor et al., 2020), (Mobasher et al., 2023), (Oyetayo et al., 2020), (Elkomy et al., 2020), and (Elgendey et al., 2021).

Because the kidney is the primary excretory pathway for cisplatin, renal parenchyma tends to accumulate more than other tissues. Cisplatin enters the renal proximal tubular cells via an organic transporter like copper, causing damage to the nuclear DNA and the generation of ROS, finally leading to cell death. After infusion, cisplatin diffuses quickly into multiple organs, attaining larger amounts in the liver. Cisplatin is bio-transformed by the cytochrome P450 (CYP450) enzyme complex (Abd Rashid et al., 2021). In the present investigation, it was shown that administration of a single dose of cisplatin induced dramatic hepatocyte injury, evidenced by hepatocyte degeneration with nuclear condensation, sinusoidal dilatation in the liver, and infiltration of cells, in addition to renal congestion and glomerular damage in the kidney, and this result was agreed upon (Un et al., 2020; Prasad et al., 2021).

The results of histopathological and immunohistochemical tests, as well as serum analysis of biomarkers in the kidneys and liver, showed that the liver and kidney tissues got better after being treated with SO oil extract. This finding was consistent with the results of previous studies (Raheem et al., 2020; Jedidi et al., 2022). The study displays that SO has a major effect on controlling liver and kidney injuries, and our result came in agreement with Jedidi et al. (2023).

*Salvia* has antioxidant and anti-inflammatory properties (Othman et al., 2022). The pretreatment with SO oil extract brought back the normal levels of all antioxidant enzymes, including MDA, SOD, and CAT. This was similar to what other studies have found (Bahri et al., 2020; Alharbi et al., 2022). *Salvia officinalis l.* contains these bioactive components, which are saturated and unsaturated fatty acids. It has chemicals in it like hexadecanoic acid, methyl ester, which kills microbes (Shaaban et al., 2021), and palmitic acid, methyl ester, which is cytotoxic and antitumor (Andonova et al., 2023); it also has (7-Heptadecene, 1-Chloro-) and isochiapin B, which fights cancer and free radicals (Qanash et al., 2022). In addition, SO contains (9,12-octadecadienoic acid), which is considered an antioxidant, anti-cancer, and antimicrobial (Momodu et al., 2020). Unsaturated fatty acids have anti-cancer properties (Farag et al., 2022), as does linoleic acid methyl ester, which is an unsaturated fatty acid (Lamani et al., 2022).

(Tert-Hexadecanethiol) and (Dotriacontane) are affordable anticancers (Parimalachelvam et al., *2023*) and have different biological activities like antioxidant activity, anticancer activity, and potential bacterial inhibition roles (Qanash et al., 2022). (Methyl 9-cis, 11-trans-octadecadienoate) has a phytochemical character (Singh et al., 2020). (9-Octadecenoic acid, methyl ester, (E)-), (11-Octadecenoic acid, methyl ester), and (cis-13-Octadecenoic acid, methyl ester), which are considered antimicrobial (Zahara et al., 2022). Also, octadecenoic acid is considered a potent antioxidant and anti-inflammatory (Ho et al., 2022). (14-á-H-PREGNA) is a bioactive compound (Bensaad et al., 2022). Both 14-á-H-PREGNA and 17-Pentatriacontene are herbal alternatives for different diseases and have biological activities like anti-oxidant, anti-microbial, sedative, anxiolytic, anti-cancer, anti-inflammatory, and anti-microbial activities (Fathi et al., 2022). (Tetrapentacontane, 1,54-dibromo-) is a bioactive compound considered a new source of therapy (Benasaad et al., 2022). (Octatriacontyl pentafluoropropionate) is anticancer (Fathi et al., 2022). (HAHNFETT) is a potential biomarker (Mayoli et al., 2022). (Cis-13-Eicosenoic acid) considers the chemical composition of *Salvia officinalis* L., which has physico-chemical characters working as antitumor and DNA protective expression (Andonova et al., 2023). (Erucic acid) as a drug carrier and neuroprotective (Galanty et al., 2023).

## 4. CONCLUSIONS

Administration of cisplatin induced hepatic and renal toxicities associated with oxidative damage. Pretreatment with *salvia officinalis* L. essential oil extract ameliorate this cisplatin induced hepatorenal oxidative injuries by exertion antioxidant and anti-inflammatory effects.

## 5. REFERENCES


1. Abd Rashid, N., Abd Halim, S. A. S., Teoh, S. L., Budin, S. B., Hussan, F., Ridzuan, N. R. A., and Jalil, N. A. A. 2021. The role of natural antioxidants in cisplatin-induced hepatotoxicity. Biomedicine and Pharmacotherapy, 144, 112328. https://doi.org/10.1016/j.biopha.2021.112328
2. Alharbi, Y. M., Sakr, S. S., Albarrak, S. M., Almundarij, T. I., Barakat, H., and Hassan, M. F. 2022. Antioxidative, Antidiabetic, and Hypolipidemic Properties of Probiotic-Enriched Fermented Camel Milk Combined with Salvia officinalis Leaves Hydroalcoholic Extract in Streptozotocin-Induced Diabetes in Rats. Antioxidants, 11, 4 , 668. https://doi.org/10.3390/antiox11040668
3. Al-Ibrahemi, N., Al-Yasssiry, A. S., Al-Laith, Z. N., and Al-Musawi, B. H. 2023. Phytochemical Study of Volatile Oils for the Ocimum basilicum L. and Mentha spicata By Gas Chromatography Technique. In IOP Conference Series: Earth and Environmental Science , Vol. 1158, No. 6, p. 062004 . IOP Publishing. Ameilorative effect of lycopine against cisplatin toxicity in rats. https://doi.org/10.1080/15569543.2020 .1857772
4. Alshahrani, S., Tripathi, P., Ashafaq, M., Sultan, M. H., Moni, S. S., Tripathi, R., and Malhan, A. M. 2022. Role of renin blocker , (Aliskiren) on Cisplatin induced-nephrotoxicity in rats. Toxin Reviews, 41, 1 , 175-185. https://doi.org/10.1080/ 15569543.2020.1857772
5. Andonova, T., Muhovski, Y., Apostolova, E., Naimov, S., Petkova, Z., Teneva, O., and Dimitrova-Dyulgerova, I. , 2023 . Koelreuteria paniculata Seed Oil—A Rich Natural Source of Unsaturated Fatty Acids and Phytocompounds with DNA Protective Potential. Foods, 12, 11, 2230. https://doi.org/10.3390/foods12112230
6. Bahri, S., Ben Ali, R., Abdennabi, R., Ben Said, D., Mlika, M., Ben Fradj, M. K. and Jameleddine, S. B. K. 2020. Comparison of the protective effect of Salvia officinalis and Rosmarinus officinalis infusions against hepatic damage induced by hypotermic-ischemia in Wistar rats. Nutrition and Cancer, 72, 2, 283-292. https://doi.org/10.1080/01635581.2019. 1631359
7. Bancroft JD, Stevens A 2016. Theory and Practice of histological techniques. Churchill Livingstone, London. Edition: 7th P: 120:131.
8. Bensaad, M. S., Dassamiour, S., Hambaba, L., Kahoul, M. A., Sami, R., Al Masoudi, L. M., and Benajiba, N. 2022. Chemical profile by gas chromatography/mass spectrometry of ethyl acetate and N-butanol extracts of Centaurea tougourensis Boiss. and Reut. Journal of Biobased Materials and Bioenergy, 16, 1 , 140-149.
9. Elgendey, F., Waheed, R. M., Ibrahim, S. S., Said, A. M., and Elsayed, F. I. Elkomy, A., Abdelhiee, E. Y., Fadl, S. E., Emam, M. A., Gad, F. A. M., Sallam, A., ... and Aboubakr, M. 2020.

L-carnitine mitigates oxidative stress and disorganization of cytoskeleton intermediate filaments in cisplatin-induced hepato-renal toxicity in rats. Frontiers in Pharmacology, 11, 574441. https://doi.org/10.3389/fphar.2020.574441

10. Elsayed, A., Elkomy, A., Elkammar, R., Youssef, G., Abdelhiee, E. Y., Abdo, W., and Aboubakr, M. 2021. Synergistic protective effects of lycopene and N-acetylcysteine against cisplatin-induced hepatorenal toxicity in rats. Scientific Reports, 11, 1, 13979. https://doi.org/10.1038/s41598-021-93196-7
11. Farag, M. A., and Gad, M. Z. 2022. Omega-9 fatty acids: Potential roles in inflammation and cancer management. Journal of Genetic Engineering and Biotechnology, 20, 1 , 1-11. https://doi.org/10.1186/s43141-022-00329-0
12. Fathi, M., Ghane, M., and Pishkar, L. 2022. Phytochemical composition, antibacterial, and antibiofilm activity of Malva sylvestris against human pathogenic bacteria. Jundishapur Journal of Natural Pharmaceutical Products, 17, 1 . https://doi.org/10.5812/jjnpp.114164
13. Galanty, A., Grudzińska, M., Paździora, W., and Paśko, P. 2023. Erucic acid—both sides of the story: a concise review on its beneficial and toxic properties. Molecules, 28, 4 , 1924. https://doi.org/10.3390/molecules28041924
14. Ho, K. L., Tan, C. G., Yong, P. H., Wang, C. W., Lim, S. H., Kuppusamy, U. R., and Ng, Z. X. 2022. Extraction of phytochemicals with health benefit from Peperomia pellucida , L. Kunth through liquid-liquid partitioning. Journal of Applied Research on Medicinal and Aromatic Plants, 30, 100392. https://doi.org/10.1016/j.jarmap.2022.100392
15. Jedidi, S., Aloui, F., Selmi, S., Selmi, H., Sammari, H., Ayari, A.,and Sebai, H. 2022. Antioxidant Properties of Salvia officinalis Decoction Extract and Mechanism of Its Protective Effects on Ethanol-Induced Liver and Kidney Injuries. Journal of Medicinal Food, 25, 5 , 546-556. https://doi.org/10.1089/jmf.2021.0134
16. Jedidi, S., Rtibi, K., Selmi, H., Aloui, F., Dhawefi, N., and Sebai, H. 2023. HepatoNephroprotective Actions of Salvia officinalis Decoction Extract Against Extraintestinal Alterations Induced with Acetic Acid-Colitis Model in Rats. Journal of Medicinal Food. 26, 6 , 390-400 https://doi.org/10.1089/jmf.2023.0006
17. Lamani, S., Anu-Appaiah, K. A., Murthy, H. N., Dewir, Y. H., and Rikisahedew, J. J. 2022. Analysis of free sugars, organic acids, and fatty acids of wood apple , Limonia acidissima L. fruit pulp. Horticulturae, 8, 1 , 67. https://doi.org/10.3390/horticulturae8010067
18. 21. Mayoli, R. N., Isutsa, D. K., Nyende, A. B., and Mweu, C. M. 2022. Evaluation of Endogenous Phytocomponents and Amino Acids Associated with Direct Somatic Embryogenesis of Coffee , Coffea arabicaL. . 8 , 01 https://doi.org/10.24297/jaa.v8i1.7377
19. Mittal, D., Singh, A., Kohli, K., and Verma, A. K. 2022. Engineering biosafe cisplatin loaded nanostructured lipid carrier: optimisation, synthesis, pharmacokinetics and biodistribution. Journal of Microencapsulation, 39, 6 , 522-538.https://doi.org/10.1080/02652048.2022.2131919
20. Mobasher, M. A., Ahmed, E. I., Hakami, N. Y., Germoush, M. O., Awad, N. S., and Khodeer, D. M. 2023. The Combined Effect of Licorice Extract and Bone Marrow Mesenchymal Stem Cells on Cisplatin-Induced Hepatocellular Damage in Rats. Metabolites, 13, 1 , 94.https://doi.org/10.3390/metabo13010094
21. 24. Momodu, I. B., Okungbowa, E. S., Agoreyo, B. O., and Maliki, M. M. 2022. Gas Chromatography–Mass Spectrometry Identification of Bioactive Compounds in Methanol and Aqueous Seed Extracts of Azanza garckeana Fruits. Nigerian Journal of Biotechnology, 38, 1 , 25-38. https://doi.org/10.4314/njb.v38i1.3S
22. Natarajan, A., Prabakarakrishnan, R., Govindaraju, K., Sugumar, V., Sathiskumar, K., Narenkumar, J., and Kumar, B. S. 2023. Hepato and renoprotective activity of Kappaphycus alvarezii ethanolic extract in cisplatin causes hepatic and kidney harm in Albino Wistar rats. Aquaculture International, 1-16. https://doi.org/10.1007/s10499-023-01064-0
23. Okafor, I. A., Nnamah, U. S., and Nnaka, J. 2020. Liver Function Analyses and Spleen Histology Assessment Following the Co –administration of Cisplatin and Methanolic Extract of Portulaca Oleracea in Wistar Rats: An Experimental Study. Natural Product Sciences, 26, 3 , 252-258. https://doi.org/10.20307/nps.2020.26.3.252
24. Othman, M. S., Khaled, A. M., Aleid, G. M., Fareid, M. A., Hameed, R. A., Abdelfattah, M. S., and Moneim, A. E. A. 2022. Evaluation of antiobesity and hepatorenal protective activities of Salvia officinalis extracts pre-treatment in high-fat diet-induced obese rats. Environmental Science and Pollution Research, 29, 49 , 75043-75056. https://doi.org/10.1007/s11356-022-21092-2
25. Oyetayo, F. L., Akomolafe, S. F., and Osesanmi, T. J. 2020. Effect of dietary inclusion of pumpkin , Cucurbita pepo L seed on nephrotoxicity occasioned by cisplatin in experimental rats. Journal of Food Biochemistry, 44, 10 , e13439. https://doi.org/10.1111/jfbc.13439
26. Parimalachelvam, G., Nagendran, N., and Balakrishnan, S. 2023. Assessment of anti-cancer properties of Chlorella sorokiniana against A375, A549 and HeLa cell lines using GC-MS analysis and MTT assay. Sci Academique, 4, 1 , 55-71.
27. Prasad, R., and Prasad, S. B. 2021. Histoprotective effect of rutin against cisplatin-induced toxicities in tumor-bearing mice: rutin lessens cisplatin-induced toxicities. Human and Experimental Toxicology, 40, 2 , 245-258. https://doi.org/10.1177/0960327120947793
28. Qanash, H., Yahya, R., Bakri, M. M., Bazaid, A. S., Qanash, S., Shater, A. F., and TM, A. 2022. Anticancer, antioxidant, antiviral and antimicrobial activities of Kei Apple , Dovyalis caffra fruit. Scientific Reports, 12, 1 , 5914. https://doi.org/10.1038/s41598-022-09993-1
29. Raheem, H. A., Mousa, R. F., and Hassan, A. H. 2020. Evaluation Protective Role of Salvia officinalis Silver Nanoparticles Against Toxic Effect of Bisphenol a in Female Rats. Indian Journal of Forensic Medicine and Toxicology, 14, 2 , 852-857.
30. Rashwan, H. M., Mohammed, H. E., El-Nekeety, A. A., Hamza, Z. K., Abdel- Aziem, S. H., Hassan, N. S., and Abdel-Wahhab, M. A. 2021. Bioactive phytochemicals from Salvia officinalis attenuate cadmium-induced oxidative damage and genotoxicity in rats. Environmental Science and Pollution Research, 28, 68498-68512.
31. Razak, S., Afsar, T., Bibi, N., Abulmeaty, M., Bhat, M. A., Inam, A., and Algarni, A. 2022. Sulindac acetohydrazide derivative attenuates against cisplatin induced organ damage by modulation of antioxidant and inflammatory signaling pathways. Scientific Reports, 12, 1 , 11749. https://doi.org/10.1038/s41598-022-15950-9
32. Shaaban, M. T., Ghaly, M. F., and Fahmi, S. M. 2021. Antibacterial activities of hexadecanoic acid methyl ester and green-synthesized silver nanoparticles against multidrug-resistant bacteria. Journal of Basic Microbiology, 61, 6 , 557-568.
33. Singh, P., Kumawat, H. L., and Agrawal, T. 2020. GC-MS Analysis of Bio-Active Compounds of Carica papaya L. Male Flower. International Journal of Chemical Separation Technology, 6, 1 , 23-34.
34. Tran, Q. H., Nguyen, T. T., and Pham, K. P. 2020. Development of the high sensitivity and selectivity method for the determination of histamine in fish and fish sauce from Vietnam by UPLC-MS/MS. International Journal of Analytical Chemistry, 2020.
35. Un, H., Ugan, R. A., Kose, D., Bayir, Y., Cadirci, E., Selli, J., and Halici, Z. 2020. A novel effect of Aprepitant: Protection for cisplatin-induced nephrotoxicity and hepatotoxicity. European Journal of Pharmacology, 880, 173168.
36. 39.Yousry, S. M., Taha, R. A. M., El-Banna, H. A., and Emam, S. R. 2021. Curative and protective effect of salvia officinalis oil on isoprenaline- induced congestive heart failure in rats. Adv. Anim. Vet. Sci, 9, 11 , 1895- 1907.
37. Zahara, K., Bibi, Y., Arshad, M., Kaukab, G., Al Ayoubi, S., and Qayyum, A. 2022. In-vitro examination and isolation of antidiarrheal compounds using five bacterial strains from invasive species Bidens bipinnata L. Saudi Journal of Biological Sciences, 29, 1 , 472-479.
38. Zhang, Q. Y., Yan, Z. B., Meng, Y. M., Hong, X. Y., Shao, G., Ma, J. J., and Fu, C. Y. 2021. Antimicrobial peptides: mechanism of action, activity and clinical potential. Military Medical Research, 8, 1-25.