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Effect of *Salvia Officinalis* (Sage) Oil on Paracetamol Induced Hepatotoxicity in Broilers

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Abstract

THE purpose of this study was to assess the hepatoprotective effect of *Salvia officinalis* (Sage) oil against paracetamol-induced hepatotoxicity in broilers. Forty eight healthy, one-day-old Cobb chicks were divided into 4 groups, (12 chicks each): The first group (G1) was given a basal diet for 21 days, the second group (G2) started receiving paracetamol on the 15th day until the experiment ended, the third group (G3) received S. officinalis oil at 20 ml /Kg of diet for two weeks, then paracetamol for one week, and the fourth group (G4) received paracetamol for one week then S. officinalis oil for two weeks. Blood, serum, and liver samples were collected from each group at the end of the trial for hematological, biochemical, and histopathological assessment. After feeding *S. officinalis* oil to broilers that had overdosed on paracetamol, the level of hematological parameters (lymphocyte percentage, monocyte percentage, HCT percentage, WBC percentage, RBC count, and Hb content), total protein, and albumin was significantly increased, and the activities of ALT, AST, and ALP were decreased in comparison to the paracetamol group. Moreover, the *S. officinalis* oil increased the activities of antioxidant enzymes, lowered the amount of reduced glutathione, and decreased the concentration of malondialdehyde. Furthermore, after treatment, a notable decrease in the mRNA expression of TLR4 and lL-1β was seen in hepatic tissues of G3 and G4. In conclusion, *S. officinalis* oil reduces oxidative stress and inflammation, which lessens the hepatic damage produced by paracetamol in broilers. Future studies are advised to evaluate the effects of *S. officinalis* components independently.

Keywords: broilers, paracetamol, *Salvia officinalis*, hepatotoxicity, oxidative stress.

Introduction

The liver is a vital organ that controls the body's processes of excretion, metabolism, detoxification, and storage, among others. Broilers may develop liver damage as a result of metabolic disorders or chemical poisoning [1]. One of the main theories for liver injury is oxidative insult, which occurs when the liver tissues are exposed to reactive oxygen species (ROS) generated from particular xenobiotics and pharmaceuticals [2].

Numerous plant extracts have been shown to have a liver damage prevention effect. The plant *Salvia officinalis* L., commonly known as Sage, is indigenous to the Middle East and Mediterranean regions. It belongs to the Labiatae/Lamiacea family. There are four primary chemical components in the genus Salvia: phenolic acids, monoterpenes, diterpenes, and flavonoids. Numerous biological activities are exhibited by these substances, such as anticancer, hypolipidemic, hypoglycemic, antibacterial, antiviral, antioxidant, and anti-inflammatory properties [3].

As far as we are aware, no research has been done on how S. officinalis essential oil affects paracetamol-induced hepatotoxicity in broiler chicks. Taking all of this into account, the purpose of this study was to determine whether the essential oil of S. officinalis could protect broilers from paracetamol-induced hepatotoxicity by monitoring liver function parameters, oxidative stress biomarkers, histopathological changes, and the

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expression patterns of genes related to glutathione peroxidase 4 (GPx4), superoxide dismutase (SOD), and interleukin-1β (IL-1β), toll-like receptor 4 (TLR-4), and superoxide dismutase (SOD) in liver tissues.

Material and Method

Ethical statement

The Animal Ethics Committee of the Faculty of Veterinary Medicine, Mansoura University, Mansoura, Egypt, approved the research protocol (Approval No. Ph.D./72).

Oil extract and drugs

The essential oil of Salvia officinalis (Sage) was acquired from Sigma Co. located in EL Dokki square, Cairo, Egypt**.** Dose: 20 ml/kg diet [4].

Paracetamol (Cetal®): 500 mg/tablet provided by EIPICO Pharmaceutical Company, (10^{th}) of Ramadan, Egypt. Dose: 2 g/kg body weight [5]. Since paracetamol has a strong damaging effect on liver cells, it is utilized as a reference to cause hepatotoxicity in broilers.

Animals and ethical statement

A week was spent housing 48 clinically healthy Cobb chicks, one day old, and weighing 45 ± 3.0 g on average. They were acquired from the Faculty of Agriculture, Mansoura University, Egypt, and housed in an environmentally controlled environment with wood shavings as litter at a depth of 10 cm. All chicks had unlimited access to food and water.

Experimental design

A total of 48 one-day-old Cobb chicks, a mixed six, were divided into 4 groups at random (12 chicks / group). For 21 days, the first group which acted as the control received a baseline diet. Oral paracetamol (APAP) at a dose of 2 g/kg body weight was given to the second group from the fifteenth day forward till the conclusion of the trial. The third group received *S. officinalis* (Sage) oil at 20 ml / kg diet for two weeks, followed by paracetamol (APAP) at 2 g / kg body weight for one week until the end of the experiment from the fifteenth to the twenty-first day. The fourth group received paracetamol at 2 g / kg for one week from the first to the seventh day, followed by *S. officinalis* (sage) oil (20 ml / kg diet) for two weeks from the eighth to the twenty-first day.

Sample collection

Six broilers were randomly selected for each group at the experiment's conclusion, which occurred on the 22^{nd} day. Blood samples were taken from the wing vein of each chosen broilers and placed in two test tubes. The first tube was filled with EDTA salt, which was utilized in a hematological test using the Wintrobe method. [6] In the meantime, a transparent serum sample was obtained by centrifuging the second blood sample which was taken in the blank tube for fifteen minutes at 3,000 rpm. After that, the serum was removed and kept in storage at -20°C to estimate liver function indicators further. Following that, xylazine and ketamine injections intraperitoneally at 0.6 and 0.7 ml.kg-1 of body weight were used to euthanize all of the chosen broilers. Three pieces of liver were obtained, and the first was homogenized and centrifuged to get the supernatant for evaluation of the oxidative stress indicators. The remaining component was kept at -80 °C to determine the expression pattern of certain genes, while the second portion was preserved at 10% formalin for histological analysis.

Evaluation of S. officinalis essential oil's impact on ALT, AST, ALP, total protein, and albumin in serum of treated broilers

The quantities of the enzymes alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in serum were measured calorimetrically using the Young et al. [7] technique. The serum ALP levels were measured in compliance with [8]. A spectrophotometer was utilized to perform a colorimetric measurement of the blood total protein level in accordance with Henry et al.'s guidelines [9]. The colorimetric measurement of the blood albumin level was carried out in compliance with Doumas et al. [10] using a spectrophotometer.

Evaluation of the impact of S. officinalis essential oil on markers of renal function (serum creatinine and uric acid levels)

The serum creatinine level was determined by colorimetric analysis [11]. Serum uric acid is measured using a colorimetric method. [12].

Evaluation of lipid peroxidation and oxidative stress in hepatic tissues

The concentration of malondialdehyde (MDA) in liver tissue that had been homogenized was assessed using the Satoh method [13] Additionally, the amounts of reduced glutathione (GSH), a non-enzymatic antioxidant biomarker, were determined using the method of Beutler et al. [14]. Furthermore, as previously reported by Lledıas and Sun et al. [15&16], the antioxidant enzymes catalase (CAT) and superoxide dismutase (SOD) were also measured.

Reverse transcription and RNA extraction

The manufacturer's instructions for the Direct-ZOlTM RNA Mini Prep (catalog No. R2050) Trizol reagent has been followed in order to extract total RNA from hepatic tissues (17). The amount of isolated RNA was measured and verified using a Nano Drop® ND-1000 Spectrophotometer. Each

sample's cDNA was produced using the Sensi Fast TM cDNA synthesis kit from Bioline (product number Bio 65,053), in accordance with the manufacturer's instructions. In a total amount of 20 µl, the reaction mixture contained 1 µl of reverse transcriptase, 4 µl of 5x Trans Amp buffer, 1 µl of total RNA up to 1 ug, and 17 µl of DNase-free water removed. The completed reaction solution was put in a heat cycler, and the following steps were then carried out: 10 minutes of primer annealing at 25°C, 5 minutes of deactivation at 85°C, and 15 minutes of reverse transcription at 42°C. Samples were kept in storage at 4°C.

Real-time quantitative PCR analysis

Superoxide dismutase (SOD), glutathione peroxidase 4 (GPX4), Toll-like receptor 4 (TLR-4) and inflammatory interleukin-1β (IL-1β) relative concentrations were determined by real-time PCR and the SYBR Green PCR Master Combine (2x Sensi Rapid TM SYBR, Bioline, track number Bio-98,002) enzyme assays. The target genes' primer sequences are displayed in Table 1.(25-28) As the cornerstone directive for standardization Glyceraldehyde-3-phosphate dehydrogenase (GAPDH), a housekeeping gene, was used. Using the $2^{-\Delta\Delta Ct}$ (Ct: cycle threshold) method, the relative expression of each gene in proportion to the GAPDH gene was determined for each sample [18].

Screening for histopathology

Formalin 10% was used to preserve the liver tissues. The liver samples were then treated until they were submerged in hard paraffin, following the procedure outlined by El Nisr et al. [19]. Following that, they were sliced into 5 µm-thick pieces and put to hematoxylin and eosin (H and E) staining.

Analytical statistics

The gathered data was statistically calculated using computerized SPSS version 20 (SPSS Inc., Chicago, IL, USA) for Windows. The data were expressed as mean ± SE. After completing a one-way analysis of variance, Tukey's test was used to compare the results of the various experimental groups. When $P < 0.05$, it was deemed statistically significant.

Results

Impact of S. officinalis essential oil on hematological markers

Comparing the paracetamol-exposed broilers to the control group, Fig 1 and 2 demonstrated a substantial decrease ($P < 0.0001$) in the total red blood cell count (RBCs), hemoglobin (Hb) content, hematocrit (HCT%), count of white blood cells (WBCs), lymphocyte percentage, and monocyte percentage. Conversely, the heterophiles percentage was significantly higher ($P < 0.0001$) in broilers given paracetamol compared to the control group. In the meantime, compared to the group that received paracetamol alone, the administration of sage oil either before or after paracetamol treatment significantly increased ($P < 0.0001$) the RBCs count, Hb count, HCT %, count of WBCs, lymphocyte %, and monocyte % or lowered the heterophiles %.

Serum hepatic injury biomarkers

When comparing the ALT, AST, and ALP levels in the paracetamol treated group to those in the control group, there was a significant rise ($P < 0.0001$). On the other hand, the paracetamol group's serum concentrations of total protein and albumin were significantly lowers ($P < 0.0001$) than those of the control group. In contrast to the broilers given paracetamol alone, the groups that received *S. officinalis* essential oil before or after paracetamol exposure showed a significant decrease ($P < 0.0001$) in ALT, AST, and ALP activity as well as an increase in total protein and albumin levels (Fig 3).

Serum renal injury biomarkers

Fig 4 shows that the serum levels of creatinine and uric acid in paracetamol-intoxicated broilers were significantly higher ($P < 0.0001$) than those in the control group. Conversely, broilers given S. officinalis either before or after paracetamol administration showed a significant decrease ($P < 0.0001$) in the levels of creatinine and uric acid.

Oxidative status and antioxidant biomarkers in hepatic tissues

When compared to the control group, the administration of paracetamol only resulted in a substantial ($p < 0.05$) rise in MDA content and a decrease in SOD, GSH, and CAT activity content. Compared to broilers given paracetamol alone, the broilers given S. officinalis either before or after showed a noteworthy decrease in MDA content and a considerable rise in GSH content, as well as SOD and CAT activity (Fig 5).

Expression of IL-1β, TLR4, SOD and GPx4 genes in hepatic tissues

Comparing the paracetamol group to the control one, Fig 6 showed a significant increase ($P < 0.0001$) in the expression of the TLR4 and IL-1β genes. Conversely, broilers treated with S. officinalis and paracetamol (either prior to or following paracetamol) showed a significant down regulation ($P < 0.0001$) in the expression of these two genes. In comparison to the control group, the paracetamol group exhibited a notable down regulation ($P < 0.0001$) in the expression of the SOD and GPx4 genes. In contrast, the SOD and GPX4 genes were found to be significantly more expressed in the *S. officinalis* then paracetamol group and broilers given paracetamol then *S. officinalis* groups than that in paracetamol treated group.

Histopathology of the liver

The hepatic parenchyma's normal histological appearance, surrounded by normal polyhedral and angular hepatocytes around a central vein, was revealed by the histopathological screening (Fig 7A). In contrast, the paracetamol group displayed biliary hyperplasia, which was characterized by a profusion of periductular fibroblast aggregations (fibrosis), piled-up epithelial cells with significant anisokaryosis, and a large number of lymphocytes and plasma cells mixed in with a small number of newly formed bile ductules (Fig 7B). The *S. officinalis* oil + paracetamol group showed focal inflammatory aggregations, rare, dispersed liver necrosis, and limited microvesiculation (Fig 7C). It's interesting to note that the paracetamol + *S. officinalis* group showed restoration of normal hepatic parenchyma with sporadic, localized necrotic hepatocytes encircled by a sparse lymphocyte population (Fig 7D).

Discussion

For a long time, poultry have been treated with paracetamol (acetaminophen) as a growth promoter and antipyretic. On the other hand, excessive paracetamol dosages result in undesirable side effects such hepatotoxicity, which is shown in the depletion of glutathione reserves, increased lipid peroxidation, elevated liver enzymes, or even abrupt death with fatal toxicity [20-22]. Therefore, the current study investigated the hepatoprotective qualities of *Salvia officinalis* (Sage) essential oil against paracetamol-induced liver damage in broilers. Broilers given paracetamol had significantly lower RBC counts, Hb contents, HCT%, WBC counts, lymphocyte and monocyte percentages, and higher heterophile percentages when compared to the control group. These findings concur with those of Marmat and Rathore [23], who found that the paracetamol group had a significant drop in MCH content, RBCs, and Hb. Ranganathan [5] also reported that birds receiving paracetamol had notably decreased Hb and WBC levels in comparison to birds in the control group. By contrast, when S. officinalis was given either before or after paracetamol exposure, the paracetamol group saw a decrease in heterophile % and an increase in RBCs, HCT%, lymphocytes, and monocytes. The majority of sage oil's therapeutic benefits and antioxidant qualities, which shield cells and tissues from oxidative damage and lipid peroxidation and enhance hemostasis and productivity under pressure, have been linked to the presence of flavonoids, glycosides, and fumaric acid. The increase in Hb content, HCT%, and RBC count may be explained by this. Numerous further researches support these findings. For instance, sage oil has antioxidant and free radical scavenger qualities that support tissue and cellular integrity while reducing hemoglobin levels, according to Petrová et al. [24]. In a similar vein, Salvia officinalis's antioxidant activity, which protects RBCs from oxidative damage, may be the cause of the rise in RBC count after its usage in broiler feed, according to Al-Sherify and A-Alwany [25]. Additionally, when sage oil (1% and 2%) was applied, Al Saadi et al. [4] reported that the treatment group's hematological parameters increased dramatically. Finally, Atea and Hassan [26] found that sage crude oil increased the frequency of RCs and PCV in rats receiving indomethacin.

Additionally, the study showed that broilers fed paracetamol alone had significantly higher levels of ALT, AST, and ALP as well as lower levels of total protein and albumin when compared to the control group. The findings are supported by Joulideh's [27] results, which indicated that 650 mg/kg of acetaminophen in broilers resulted in liver damage as well as an increase in AST, ALT, and ALP. Additionally, when paracetamol was given to birds, Ranganathan et al. [5] saw a considerable increase in the blood concentrations of AST and ALT. In contrast, compared to the broilers given paracetamol alone, the groups given S. officinalis oil either before or after demonstrated a significant drop in ALT and AST levels as well as an improvement in total protein and albumin levels. These findings are consistent with Shahrzad et al.'s [28] observation that rats administered Salvia officinalis extract had markedly lower levels of ALT, AST, and ALP activity when compared to animals exposed to hepatotoxicity. Additionally, S. officinalis medication was shown to lower the elevated liver enzymes (ALT, AST, and ALP) in mice exposed to carbon tetra chloride (CCl4), according to Essawy et al. [29]. Moreover, Kudiar et al. [30] discovered that the treatment of rats with Salvia officinalis alcohol extract led to a considerable increase in the levels of albumin and globulin. The antioxidant qualities of the sage components probably assisted them in offsetting the decrease in total protein level by decreasing oxidative stress and raising protein synthesis [31]. The main component of sage oil, 1, 8-cineole, has anti-inflammatory and antioxidant properties, which may explain for part of its liver-protective benefits, according to Kozi et al. [32]. Additionally, it was demonstrated that 1, 8-cineole decreased bleeding and necrosis while also lowering elevated serum transaminase activity. Santos and others [33].

Furthermore, the outcomes showed that the paracetamol-intoxicated broilers had significantly higher blood levels of creatinine and uric acid than the broilers in the control group. In contrast, uric acid and creatinine levels were significantly lower in the groups that took *S. officinalis* either before or after paracetamol. These results are in line with those of Eidi et al. [34], who discovered that giving sage alcoholic extract to rats treated with streptozotocin-induced diabetes dramatically reduced the rats' levels

of urea, uric acid, and creatinine. Furthermore, blood urea, uric acid, and creatinine were decreased in rats treated with ethanolic extracts from S. officinalis following their administration of chlorpyrifos[35] Additionally, the results demonstrated that exposure to paracetamol resulted in a significant rise in the MDA content, a decrease in the GSH content, and an increase in the activities of SOD and CAT when compared to the control group. The broilers fed S. officinalis exhibited lower levels and fewer actions in the aforementioned indices when compared to the paracetamol group. The findings of Aziz et al.'s study [36], which discovered that the group using paracetamol had significantly greater MDA concentrations than the control group, are in line with the results of paracetamol. Moreover, paracetamol lowers GSH levels while increasing lipid peroxidation, according to Marmat et al. [37]. Welch et al. [38] have suggested that S. officinalis may provide hepatoprotective effects due to its ability to scavenge free radicals or inhibit the formation of free radicals and lipid peroxidation in cell membranes. According to the findings, sage may be employed as a strong exogenous cytoprotective agent to shield cells from oxidative damage. Our findings concur with those of Fahmy et al. [39], who found that administering sage oil reduced the damage that CCl4 caused to the kidneys and liver. The ability of S. officinalis oil to raise GSH levels and GPX activity in the tissues of the liver and kidneys, as well as to lessen oxidative stress and lipid peroxidation brought on by CCl4, was credited by the scientists for this improvement. In addition, the research revealed a significant rise in TLR4 and IL-1β gene expression in the paracetamol-administered group relative to the control group. In contrast, the expression patterns of these two genes were significantly downregulated in the hens treated with S. officinalis, either prior to or following the administration of paracetamol. Similarly, total flavonoids decreased the relative mRNA expression levels of IL-6, IL-1β, and TNF-α in the liver, according to Tao et al. [40]. This discovery unveiled the possible pathways by which total flavonoids mitigate hepatic injury by averting oxidative stress and inflammation. Moreover, Farahpour et al. [41] reported that S. officinalis essential oil exhibited anti-inflammatory qualities by reducing IL-1β gene expression. Furthermore, compared to the control group, the paracetamol group's SOD and GPx4 gene expression was considerably downregulated. By contrast, compared to the APAP group, the SOD and GPX4 gene expressions were significantly higher in the S. officinalis + APAP and APAP + S. officinalis groups. These findings are in line with the findings of Rashwan et al. [42], who noted a notable increase in the relative mRNA expression of the GPx1 and SOD genes in rats treated with S. officinalis after they were intoxicated with cadmium. A large number of periductular fibroblast aggregations (fibrosis), piled-up epithelial cells with moderate anisokaryosis, and a large number of lymphocytes and plasma cells mixed in with a small number of newly formed bile ductules were the characteristics of biliary hyperplasia seen in the hepatic tissues of the paracetamol-intoxicated group, according to the histopathological analysis. Nonetheless, the histological appearance of the hepatic parenchyma was normal in the Salvia officinalis and control groups. In contrast, Raganathan et al. [5] observed that APAP-treated chicken liver showed notable congestion, periportal fibrosis, and infiltration of mononuclear cells. But according to Essawy et al. [29], the hepatic architecture of the control and S. officinalis-treated mice was normal, showing a central vein, conspicuous nuclei, nucleoli, and a compact arrangement that showed the typical shape of hepatocytes Additionally, according to Mouradetal.[43], sage oil reduced the histological abnormalities in the liver and kidney caused by tamoxifen. Sage oil's anti-inflammatory and antioxidant properties might have contributed to the reversal of the histological alterations caused by paracetamol in the liver.

Conclusion

By reducing oxidative stress and inflammation, *Salvia officinalis* essential oil protected the hepatic tissue of broilers against hepatotoxicity caused by paracetamol. Future studies are advised to determine the characteristics of the S. officinalis oil's ingredients and evaluate the impact of each one separately**.**

Authors' contributions

Conceptualization: Data curation: Ghada A. Abou Zead. Formal analysis: Ghada A. Abou Zead, Ahmed I. Ateya. Funding acquisition: Ghada A. Abou Zead. Investigation: Magdy Amer, Ghada A. Abou Zead, Azza E. Hassan.

Conflicts of interest

The authors declare no conflict of interests.

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This study didn't receive any funding support.

TABLE 1. Primer sequences of target genes

Genes	Forward Primer (5'-3')	Reverse primer (5'-3')	Gen Bank accession number	Annealing temperature (ºC)	References
IL-1β	ATGTCGTGTGTGATGAGCGGC	AGGCGGTAGAAGATGAAGCGG	FJ537852.1	58	[18]
TLR-4	GTTCCTGCTGAAATCCCAAA	TATGGATGTGGCACCTTGAA	NM_001030693	58	[19]
SOD	AGG GGGTCATCCACTTCC	CCCATTTGTGTTGTCTCC AA	NM_205064.1	58	[20]
GPx4	GCCACCTCCATCTACGACTTC	TTGGTGATGATGCAGACGAAG	NM_204220	56	[21]
GAPDH	ATGACCACTGTCCATGCCATCCA	AGGGATGACTTTCCCTACAGCGTT	NM_204305.1	56	[19]

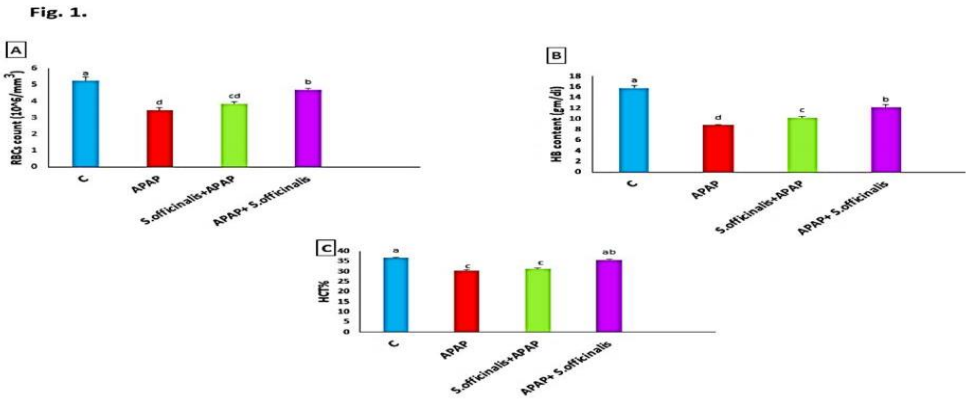

Fig. 1. The effect of *Salvia officinalis* oil (20 ml/kg basal diet) on total erythrocytes count, Hb, and HCT% in paracetamol-intoxicated chickens: (A) RBCs count, (B) Hb content, (C) HCT%. Data are expressed as Mean ± SE (N = 6). Bars carrying different letters are significantly different from one another (p<0.05). C: control, *S. officinalis*: *Salvia officinalis*, (APAP): paracetamol, RBCs: red blood cell count, Hb: hemoglobin, HCT: hematocri

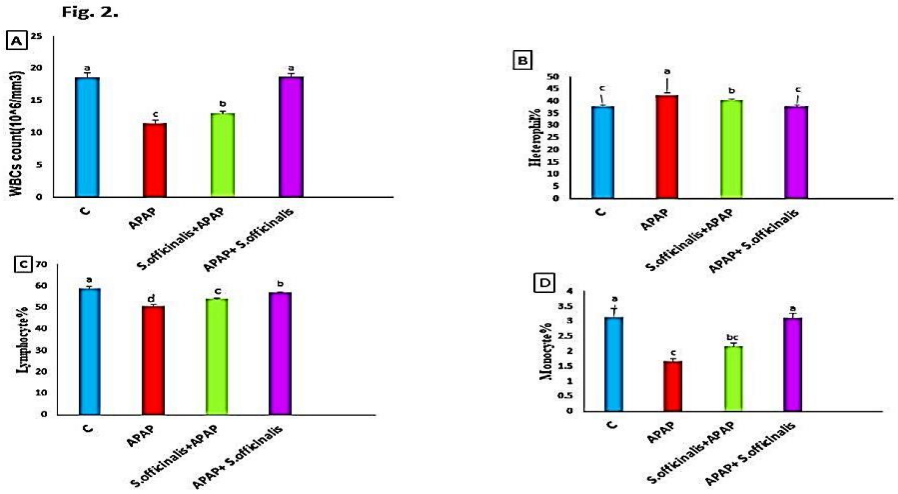

Fig. 2. The effect of S. officinalis oil (20 ml/kg basal diet) on WBCs, heterophiles %, lymphocyte % and monocyte % in paracetamol-intoxicated chickens: (A) WBCS, (B) Heterophiles, (C) Lymphocyte and(D) monocyte. Data are expressed as Mean ± SE (N=6). Bars carrying different letters are significantly different from one another (p<0.05). C: control, *S. officinalis*: *Salvia officinalis*, APAP: paracetamol and WBCs: white blood cells count.

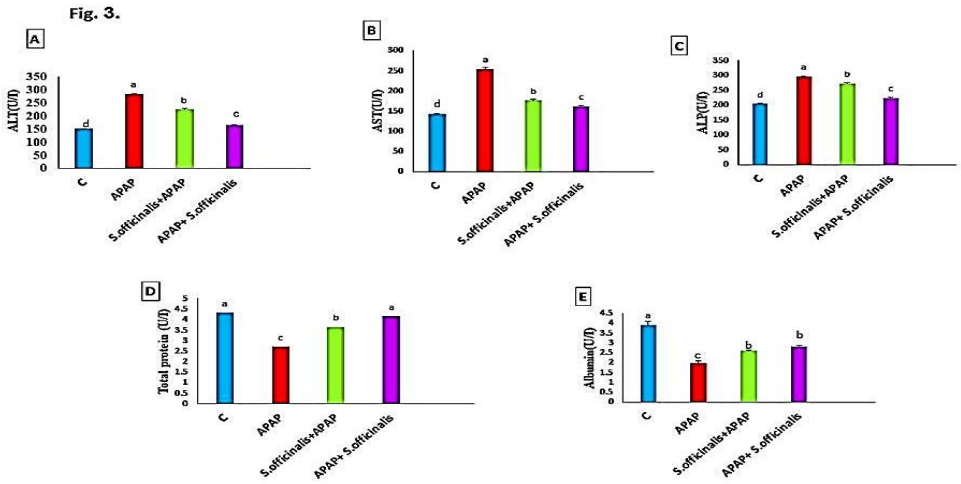

Fig. 3. The effect of sage oil (20 ml/kg basal diet) on liver function parameters in paracetamol intoxicated chickens. (A) ALT, (B) AST, (C) ALP, (D) Total protein, (E) Albumin. (Mean ± SE) (n=6). Bars carrying different letters are significantly different from one another (p<0.05).C: control, *S. officinalis*: *salvia officinalis*, APAP: paracetamol, ALT: alanine aminotransferase, AST: aspartate aminotransferase, ALP: alkaline phosphatase.

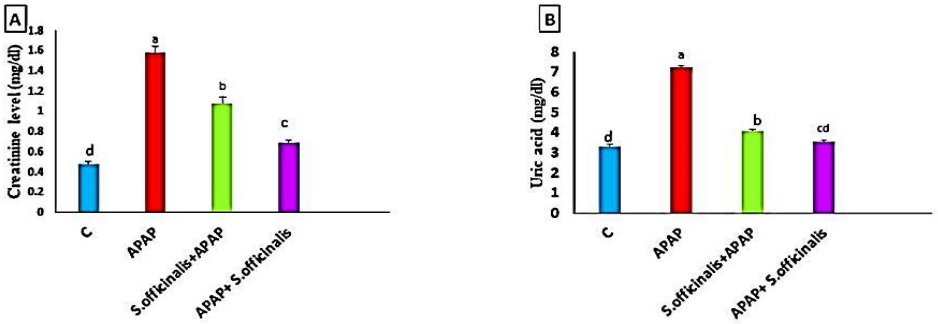

Fig. 4. The effect of sage oil (20 ml/kg basal diet) on kidney function parameters in paracetamol intoxicated chickens. (A) Creatinine level, (B) uric acid level. (Mean ± SE) (N=6). Bars carrying different letters are significantly different from one another (p<0.05). C: control, *S. officinalis*: *Salvia officinalis*, APAP: paracetamol.

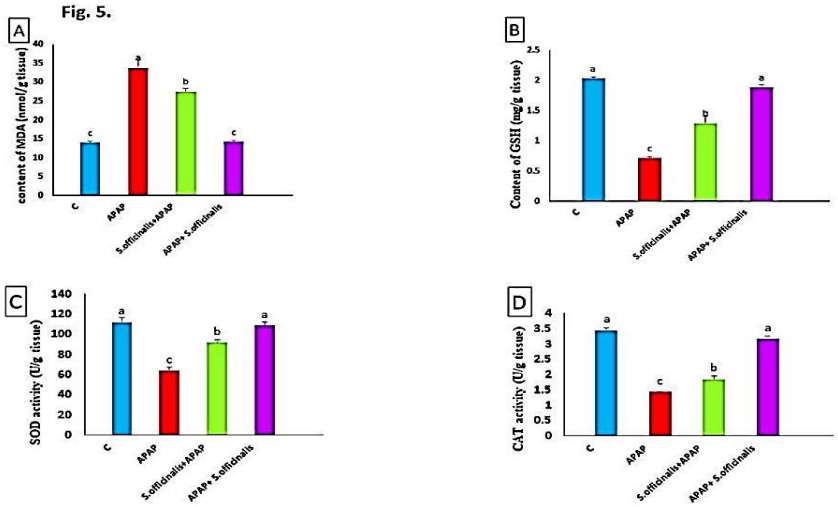

Fig. 5. The effect of sage oil (20 ml/kg basal diet) on oxidative stress biomarkers (MDA, GSH, SOD, and CAT) in paracetamol intoxicated chickens: (A) MDA level, (B) GSH activity, (C) SOD activity, (D) CAT activity. (Mean ± SE) (N=6). Bars carrying different letters are significantly different (p < 0.05). C: control, S. officinalis: Salvia officinalis, APAP: paracetamol.

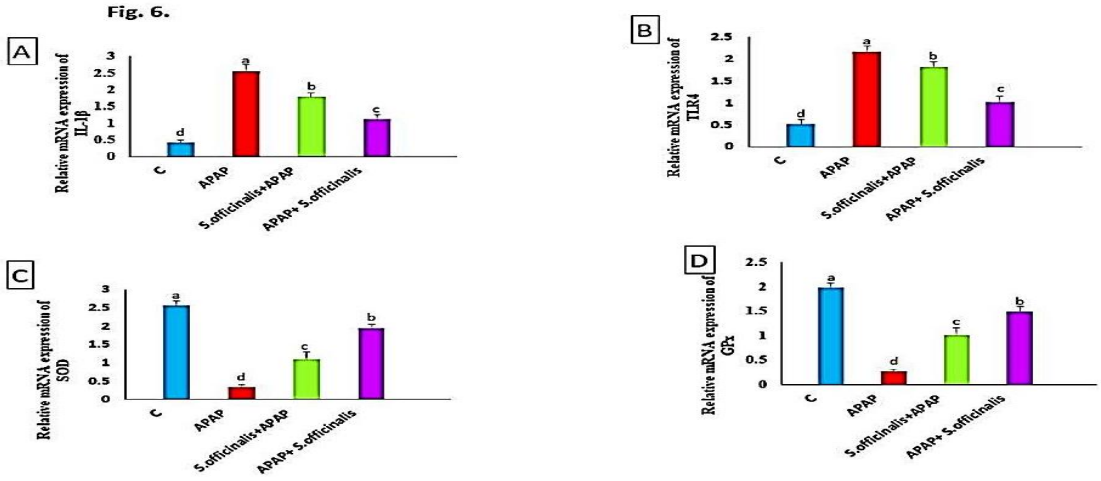

Fig. 6. The effect of sage oil (20 ml/kg basal diet) on target gens (IL-1B, TLR4, SOD, and GPX) in paracetamol-intoxicated chickens. (A) IL-1β, (B) TLR4, (C) SOD, (D) GPX genes. (Mean ± SE) (N=6).Bars carrying different letters are significantly different from one another (p<0.05). C: control, *S. officinalis*: *Salvia officinalis*, APAP: paracetamol, IL-Iβ, interleukin- 1β, TLR4: Toll like receptor-4, SOD: superoxide dismutase, GPX: glutathione peroxidase.

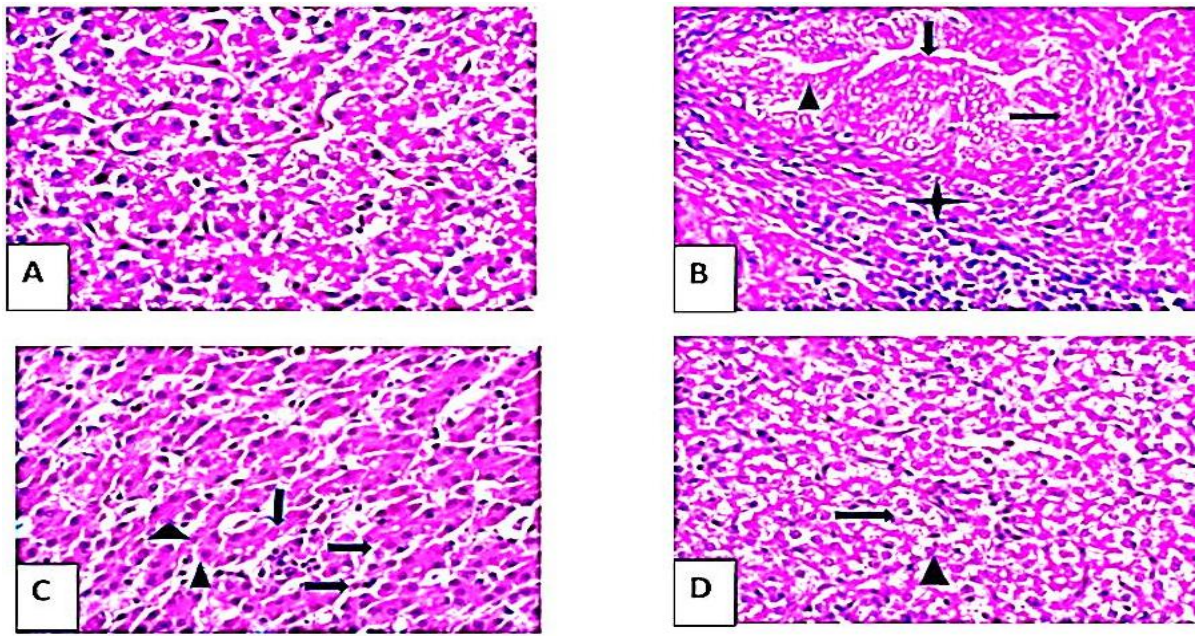

Fig 7. Representative photomicrograph of broiler liver from different experimental groups. A) Control group: liver displayed normal histological appearance of hepatic parenchyma. B) Paracetamol group shows biliary hyperplasia characterized by piling up epithelial cells with moderate anisokaryosis (thick arrow) and abundant periductular aggregations of fibroblasts (fibrosis) (arrowhead), numerous lymphocytes and plasma cells (star) admixed with few numbers of newly formed bile ductules (thin arrow). C) *S. officinalis* + Paracetamol group reveal restoration of normal hepatic parenchyma with focal, occasional, individual necrotic hepatocytes (thin arrow) surrounded with few lymphocytes (arrowhead). D) Paracetamol + *S. officinalis* group exhibit minimal microvesiculation (thin arrows), few, scattered hepatic necrosis (arrowhead) and focal inflammatory aggregations (thick arrow). Scale bar = 50 µm. The sections were stained with H&E, X400.

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تأثير زيت المرمرية الطبية علي السمية الكبدية الناتجة عن الباراسيتامول في دجاج اللحم

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الملخص

أستهدفت هذه الدراسة تقييم التأثير الوقائي للكبد لزيت المرمرية ضد السمية الكبدية الناجمة عن الباراسيتامول في دجاج اللحم. تم تقسيم 48 فرخًا سليمًا بعمر يوم واحد إلى 4 مجموعات (12 فرخًا لكل منها): أعطيت المجموعة الأولى نظامًا غذائيًا أساسيًا لمدة 21 يومًا ؛ بدأت المجموعة الثانية في تلقي الباراسيتامول في اليوم الخامس عشر حتى نهاية التجربة ؛ تلقت المجموعة الثالثة 20 مل من زيت المرمرية / كجم من الغذاء لمدة أسبوعين ، ثم أعطي الباراسيتامول لمدة أسبوع واحد ؛ وتلقت المجموعة الرابعة الباراسيتامول لمدة أسبوع واحد ثم زيت المرمرية لمدة أسبوعين. تم جمع عينات الدم والمصل والكبد من كل مجموعة في نهاية التجربة للتقييم الدموي والكيميائي الحيوي والنسيجي. بعد تغذية دجاج التسمين الذي تناول جرعة زائدة من الباراسيتامول بزيت المرمرية ، ارتفع مستوى المعايير الدموية (نسبة الخلايا الليمفاوية، ونسبة الخلايا الوحيدة، ونسبة خلايا الدم البيضاء، وعدد خلايا الدم الحمراء، ومحتوى الهيموجلوبين)، والبروتين الكلي، والألبومين بشكل ملحوظ، وانخفضت أنشطة ALT و ASTو ALP مقارنة بمجموعة الباراسيتامول. علاوة على ذلك، زاد زيت المرمرية من أنشطة إنزيمات مضادات الأكسدة، وخفض كمية الجلوتاثيون المختزل، وخفض تركيز مالونديالدهيد. علاوة على ذلك، بعد العلاج، لوحظ انخفاض ملحوظ في التعبير عن mRNA لـ TLR4 و lL-1β في أنسجة الكبد في المجموعة الثالثة المجموعة لرابعة. وفي الختام، يقلل زيت المرمرية من الإجهاد التأكسدي والالتهاب، مما يقلل من الضرر الكبدي الناتج عن الباراسيتامول في دجاج التسمين. ينصح بإجراء دراسات مستقبلية لتقييم تأثيرات مكونات نبات المرمرية بشكل مستقل.

الكلمات الدالة: دجاج التسمين، الباراسيتامول، المرمرية الطبية، السمية الكبدية، الإجهاد التأكسدي.