doi: 10.22201/fmvz.24486760e.2025.1285
Vol. 12 | 2025

Veterinaria México OA
Publicación Digital de la Facultad de Medicina Veterinaria y Zootecnia
https://veterinariamexico.fmvz.unam.mx/

Ameliorating effect of *Cynara scolymus* (artichoke) against thiamethoxam-induced hepatotoxicity in poultry

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Abstract

This study investigated the effects of thiamethoxam (TMX), a neonicotinoid insecticide, on liver health in chickens and examined whether artichoke extract (ART) could offer protection. Forty-eight healthy chicks were divided into four groups: a control group given saline, a TMX group given TMX, a TMX + ART group given both TMX and ART and a protective ART + TMX group given ART first, then TMX. The results showed that artichoke extract significantly improved blood parameters and reduced liver damage markers compared to the TMX group. It also decreased oxidative stress and boosted antioxidant defenses. Gene expression analysis revealed that ART downregulated inflammatory markers in the liver. Histological examination confirmed that artichoke extract helped restore normal liver structure. Overall, artichoke extract effectively mitigated TMX-induced liver damage by reducing oxidative stress and improving biochemical and antioxidant markers.

Keywords: *Cynara scolymus*; Poultry; Thiamethoxam; Liver; Oxidative stress.

Submitted: 2023-10-26
Accepted: 2024-12-06
Published: 2025-02-21

Additional information and declarations can be found on page 14

Cite this as:

Moktar A, Amer MS, Hassan AE, Ateya A, El-Ashry ES. Ameliorating effect of *Cynara scolymus* (artichoke) against thiamethoxam-induced hepatotoxicity in poultry. Veterinaria Mexico OA. 2025;12. doi: 10.22201/fmvz.24486760e.2025.1285.

doi: 10.22201/fmvz.24486760e.2025.1285
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Study contribution

Pesticides are among the most dangerous agricultural compounds for many mammalian systems. They can cause a variety of illnesses, such as cancer, leukemia, asthma, hypersensitivity, and hepatotoxicity. Therefore, this study was designed to evaluate the toxic effects of thiamethoxam on the liver in poultry. The results revealed the significant antioxidant and anti-inflammatory properties of *Cynara scolymus* against the liver toxicity caused by thiamethoxam in poultry. These findings suggest that *Cynara scolymus* may be a promising therapeutic agent to reduce thiamethoxam-induced hepatic damage in poultry.

Introduction

Neonicotinoids, a significant class of insecticides, have replaced earlier pesticide classes such as organochlorines, organophosphates, and carbamates in both veterinary medicine and the safeguarding of a wide range of agricultural crops.(1) Due to the widespread use of neonicotinoids, their persistence in crops, and their lengthy half-lives in soils (greater than 350 days for thiamethoxam (TMX)), humans and non-target creatures are regularly exposed to them.(2) Neonicotinoids work to kill insects by interfering with postsynaptic nicotinic acetylcholine receptors, which are essential for excitatory cholinergic neurotransmission in insects' central nervous systems.(3) A second-generation neonicotinoid with major selectivity for insect nicotinic acetylcholine receptors, TMX has high efficacy and a broad-spectrum insecticidal effect.(4)

The liver is essential for survival. Its strategic location, blood supply, and crucial role in metabolism and detoxification of endogenous and external substances make this organ a primary target for various toxicants. In poultry, hepatic injury may arise due to exposure to chemical poisoning or internal metabolic disorders. Recently, supplementation with natural compounds rich in biologically active molecules has gained considerable attention in preventing and treating many diseases.(5)

Artichoke is one of the most valuable bioenergetic crops for general-purpose application. Since it is a source of inulin, fructose, and pectin, Its green mass contains a high concentration of carbohydrates such as fructose, glucose, and sucrose. The plant's dry mass contains up to 17 % protein with a balanced amino acid composition. Incorporating inulin and bioethanol process waste from artichoke into feed composition may improve the economic efficiency of animal husbandry while ensuring the ecological safety of animal products.(6) Previous research on various farm animals has identified artichoke as a potential feed ingredient substitute, including its fresh or ensiled stems and leaves for dairy cows and pigs, as well as its fresh or powdered tubers for pigs and poultry. Its unique composition offers potential health advantages for pigs, laying hens, broilers, Japanese quail, sheep, fish, rabbits, cattle, horses, goats, bees, and wasps.(7)

Numerous plant extracts have been shown to exert a protective effect against hepatic injury. The Chicory family includes the medicinal plant *Cynara scolymus*, the artichoke. Vitamin C, carotenoids, hydrocinnamic acid, luteolin, glycosides, cynaroside, and β-rutinoside are among the many natural antioxidants found in this plant, as well as prebiotics including fructan, inulin, and oligofructose. Polyphenols, like cynarine and its derivatives, which have a major protective effect on the

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liver, are abundant in it. *Cynara scolymus* (CS) also contains potent components with antibacterial and antioxidant qualities, including organic acids, tannins, and vitamins.[8–10] These researchers found that CS and its derivatives might be a beneficial addition to broiler diets as dietary supplements. Many studies have demonstrated that CS beneficially influences the broiler immune system, performance, feed conversion ratio, weight gain, fertility, blood lipid and cholesterol levels, and liver protection, among other benefits.[11–13] Abdo et al.[14] found that the only change in carcass parameters brought about by CS consumption was a decrease in abdominal fat. During the growth, however, the extra CS powder in the diet resulted in lower blood cholesterol and fat levels and higher blood protein concentrations.

This study was conducted to assess the possible protective effect of artichoke extract against hepatotoxicity caused by TMX in chickens by monitoring the liver function parameters, oxidative stress biomarkers, histopathological alterations, and the expression pattern of interleukin-6 (IL-6), (NFκB), catalase (CAT), and glutathione peroxidase (GPX) genes in liver tissues.

Materials and methods

Ethical statement

The procedures for managing animals in experiments and the design for this work were approved by the Egyptian Faculty of Veterinary Medicine's Research Ethics Committee (Approval number: PhD/74).

Method

One-day-old Sasso chicks weighing an average of 40–45 g, 48 clinically healthy non-vaccinated chicks were obtained from a local poultry farm in Gamasa City, Dakahlia government. Two weeks before the experiment, the chickens were housed at the poultry lab at the Animal Health Research Institute in Mansoura, it was maintained at typical conditions of 22 to 25 °C and 45 to 55 % relative humidity. The chickens were cared for in a clean environment and they were provided with a diet consisting of yellow maize, choline chloride, soybeans, powdered limestone, table salt, mixed vitamins, calcium phosphate type 2, soy vegetable oil, and (60 %) corn gluten.

Chemicals

Thiamethoxam 25 % (Actara®) was purchased from local pesticides market at the Egyptian Ministry of Agriculture outlets and administered as an oral dosage of 500 mg/kg BW.[15] Artichoke extract (*C. scolymus*) was purchased from ABChem Company for pharmaceutical raw materials (Egypt). Other reagents were all of the highest analytical quality.

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Experimental design

Chicks were split into four equally sized groups (n = 12 chicks in each group) following a one-month of acclimatization as follows: (G1) Control: Chicks were given regular saline orally from day one until the end of the experiment (60^{th} day); (G2) TMX: TMX was administered to chicks from 30^{th} day of age until 60th day of age; (G3) chicks received TMX (500 mg/kg) and 500 mg/L[16] of artichoke extract in drinking water from the 30^{th} day of age until the 60^{th} day of age; (G4) chickens received 500 mg/L of artichoke extract in the water from day one until the 30^{th} day of age then were given TMX (500 mg/kg) until the 60^{th} day. Each therapy was administered daily in water.

Sample collection

Chickens from each group were randomly selected at the end of the experiment. Blood samples were taken from the wing vein of each chosen chicken and placed in two test tubes. The first tube was filled with EDTA for a hematological test. The second sample was placed in a blank tube and centrifuged for 15 minutes at 3 000 rpm to obtain a translucent serum sample. The serum was removed and kept at -20 °C to estimate liver and kidney function biomarkers. Following the euthanasia of all the chosen chickens, the liver was removed and split into three sections. The first section was homogenized and centrifuged to extract the supernatant, which was then used to evaluate the oxidative stress biomarkers. For histopathological analysis, the second component was maintained at 10 % formalin, while the remaining fraction was kept at -80 °C to determine the expression pattern of certain genes.

Hematological and biochemical measurement

Various hematological parameters were estimated for the Coles method.[17] Using the method of Young et al., the concentrations of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) in serum were determined using a colorimetric method.[18] In compliance with Sapan et al.,[19] a spectrophotometer was used to perform a colorimetric assessment of the serum total protein level. According to Doumas et al.,[20] a spectrophotometer was used to determine the serum albumin level colorimetrically. The serum creatinine level was determined by colorimetric analysis.[21] Serum urea was measured using a colorimetric method.[18]

Evaluation of the oxidative/antioxidative capability of hepatic tissue

Malondialdehyde (MDA) content in hepatic tissues was found to be a marker of lipid peroxidation.[22] As a nonenzymatic antioxidant biomarker, reduced glutathione (GSH) levels were also assessed using the method of Beutler.[23] Two antioxidant enzymes, CAT and superoxide dismutase (SOD), were also evaluated using the methods of Aebi and Weydert et al.,[24, 25] respectively.

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Reverse transcription and RNA extraction

According to the manufacturer's guidelines, using TRIzol reagent a 50 mg liver sample was used to extract the total RNA. (Direct-zol RNA MiniPrep, catalogue No. R2050). NanoDrop (UV-Vis spectrophotometer Q5000) was used to assess RNA quality and quantity, while gel electrophoresis was performed to evaluate sample integrity. Each sample's cDNA was created using a cDNA synthesis kit from SensiFAST following the manufacturer's instructions (Bioline, catalog No. Bio-65 053). Total RNA up to 1 g, 5× Trans Amp buffer in 4 L, and 1 L of reverse transcriptase were included in the reaction mixture, along with DNase-free water to make up a total volume of 20 L. A heat cycler was used to deposit the finished reaction mixture, and the following program was run: 10 min of primer annealing at (25 °C).

Quantitative real-time PCR

Proportional measurement of the antioxidant mRNA levels (CAT and GPX) and inflammatory (IL-6 and NFκB) markers was done using real-time PCR (2× SensiFastTM SYBR, Bioline, catalog No. Bio-98 002). The primer sequences are displayed (Table 1). The housekeeping gene glyceraldehyde-3-phosphate dehydrogenase (GAPDH) was used as a constitutive control for normalization. The reaction mixture, prepared in a total volume of 20 µL, was composed of 0.8 µL of each primer, 10 µL of 2× SensiFast SYBR, 3 µL of cDNA, and 5.4 µL of deionized distilled water. Following 45 cycles of 94 °C for 15 s, annealing temperatures as given in Table 1 for 20 s, and 72 °C for 20 s, the PCR cycling conditions were as follows.

Table 1. Primer's sequence and melting temperature used in real-time quantitative PCR

Gene	Oligonucleotide sequence	GenBank accession number	Annealing temperature	Reference
CAT	f5,-GGGGAGCTGTTTACTGCAAG-3, r5,-CTTCCATTGGCTATGGCATT-3,	AJ719360.1	62	(26)
GPX1	f5,-AACCAATTCGGGCACCAG-3, r5,-CCGTTCACCTCGCACTTCTC-3,	HM590226	56	(27)
IL6	f 5,- CCCTCACGGTCTTCTCCATA-3, r 5,- CTCCTCGCCAATCTGAAGTC-3,	NM_204628.1	58	(28)
NFkB	f5,-TCAACGCAGGACCTAAAGACAT-3, r5,-GCAGATAGCCAAGTTCAGGATG-3,	NM205134	58	(29)

A melting curve analysis was carried out following the amplification stage to verify the specificity of the PCR product. The 2-Ct technique utilized to determine the relative expression of each sample's gene in relation to a control and the GAPDH gene.(30)

Histopathological examination

Liver samples were fixed in neutral-buffered formalin at a 10 % concentration for 24 hours at room temperature. Following alcohol dehydration, xylene clearing, embedding in paraffin wax, and sectioning to a thickness of 5 µm, the samples were

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processed. Following hematoxylin and eosin staining (H&E), the paraffin sections were viewed under a light microscope. Images were acquired using a starting magnification of 400×. (Nikon Eclipse E200-LED, Tokyo, Japan).[31]

Statistical analysis

Data are presented as means with SEM. One-way analysis of variance was used to analyze the data. (ANOVA) and post hoc Duncan's multiple comparison test. The statistical significance between various groups was shown by P values less than 0.05.

Results

Variations in hematological levels

Figure 1 revealed a significant reduction ($P < 0.0001$) in hemoglobin (Hb), white blood cell (WBC) count ($P < 0.0001$), lymphocyte (%) ($P = 0.0390$), and monocyte (%) ($P = 0.0047$) in TMX group compared with the control group. Meanwhile, the administration of artichoke either before or after TMX treatment significantly elevated the Hb, WBC count, lymphocyte (%), and monocyte (%) relative to the group received TMX only. (Figure 1).

Variations in biochemical parameters

As shown in Figure 2, poultry given TMX alone had significantly higher ($P < 0.0001$) ALT and AST levels than those in the control group. On the other hand, the TMX group's serum concentrations of total protein and albumin were significantly lower ($P = 0.0011$ and $P < 0.0001$ respectively) than those of the control group. In contrast to the chickens that received only TMX, the groups that received artichokes either before or after being exposed to thiamethoxam showed a significant decrease ($P < 0.0001$) in ALT and AST activity as well as an increase in total protein and albumin levels.

Compared to the chickens in the control group, creatinine serum levels and urea were significantly greater ($P < 0.0001$) in the TMX-intoxicated chicks. Conversely, chickens given artichokes either before or after TMX administration showed a significant decrease ($P < 0.0001$) in both urea and creatinine levels (Figure 3).

Antioxidant biomarkers and hepatic oxidative status

Compared to the control group, the administration of TMX only resulted in a substantial rise ($P < 0.0001$) in MDA content and a decrease in SOD ($P = 0.0002$), GSH ($P = 0.0009$), and CAT ($P = 0.0056$) activity content. Compared to chickens given TMX alone, those given artichokes either before or after showed a notable decrease in MDA content and a significant increase in GSH content, SOD, and CAT activities (Figure 4).

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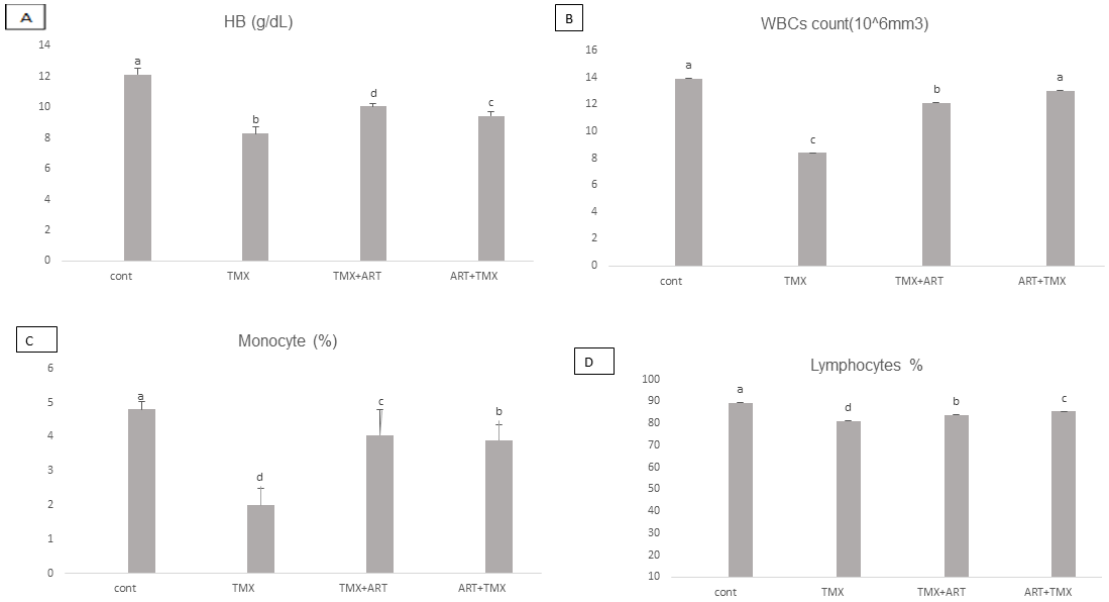

Figure 1. The effect of artichoke extract (500 mg/L) on Hb, WBCs count, monocyte (%) and lymphocyte (%) in thiamethoxam-intoxicated chickens. (A) Hb, (B) WBCs count, (C) monocyte (%), (D) lymphocyte (%). Data are expressed as Mean ± SE (n = 5 chickens). Bars carrying different letters are significantly different from one another ($P < 0.05$). G1: Control (Cont), G2: TMX; Thiamethoxam, G3: TMX + ART; Thiamethoxam + Artichoke extract, G4: ART + TMX; Artichoke extract + Thiamethoxam.
Hemoglobin (Hb)
White blood cells count (WBC)

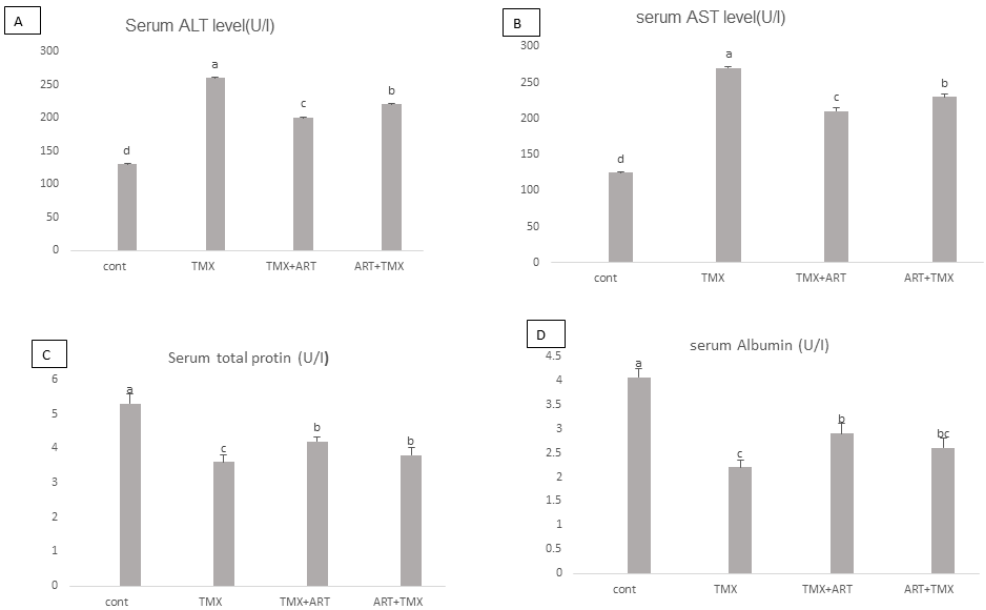

Figure 2. Effect of artichoke extract (500 mg/L) on serum (ALT, AST, total protein and albumin) in thiamethoxam intoxicated chickens. (A) Serum ALT, (B) Serum AST, (C) Serum total protein, (D) Serum albumin. Data are expressed as Mean ± SE (n = 5 chickens). Bars carrying different letters are significantly different from one another ($P < 0.05$). G1: Control (Cont), G2: TMX; Thiamethoxam, G3: TMX + ART; Thiamethoxam + Artichoke extract, G4: ART + TMX; Artichoke extract + Thiamethoxam.
Alanine aminotransferase (ALT)
Aspartate aminotransferase (AST)

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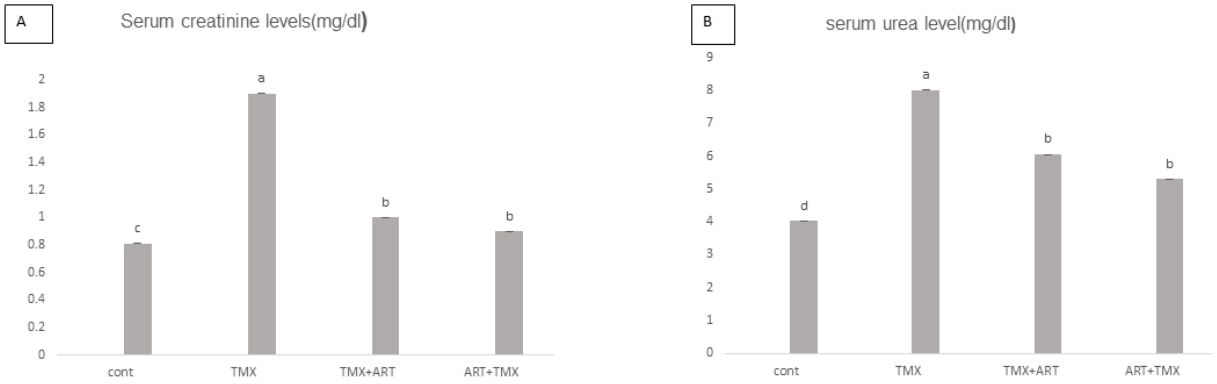

Figure 3. Effect of artichoke extract (500 mg/L) on creatinine serum level (A), and urea serum levels in thiamethoxam intoxicated chickens. (B) Data are expressed as Mean ± SE (n = 5 chickens). Bars carrying different letters are significantly different from one another ($P < 0.05$). G1: Control (Cont), G2: TMX; Thiamethoxam, G3: TMX + ART; Thiamethoxam + Artichoke extract, G4: ART + TMX; Artichoke extract + Thiamethoxam.
SOD: superoxide dismutase, GSH: glutathione reductase, MDA: malondialdehyde, CAT: catalase

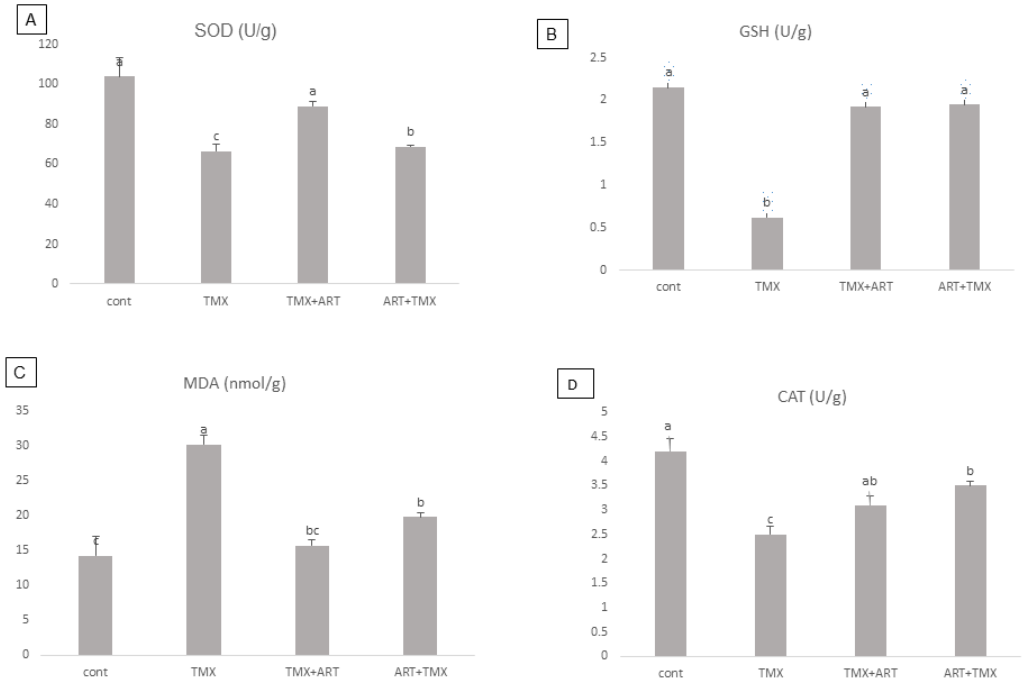

Figure 4. Effect of artichoke extract (500 mg/L) on oxidative stress biomarkers (SOD, GSH, MDA, and CAT) in thiamethoxam intoxicated chickens. (A) SOD level, (B) GSH activity, (C) MDA activity, (D) CAT activity. Data are expressed as Mean ± SE (n = 5 chickens). Each bar carrying different letters is significantly different ($P < 0.05$). G1: Control (Cont), G2: TMX; Thiamethoxam, G3: TMX + ART; Thiamethoxam + Artichoke extract, G4: ART + TMX; Artichoke extract + Thiamethoxam.

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Gene expression in the liver

Figure 5 showed that the TMX group's expression of the NFκB and IL-6 genes was significantly upregulated ($P < 0.0001$) compared to the control group. Conversely, the chickens treated with artichokes with TMX (either before or after TMX) showed a substantial downregulation ($P < 0.0001$) in the expression of these two genes. In comparison to the control group, the TMX group exhibited a notable downregulation ($P < 0.0001$) in the expression of the SOD and CAT genes. In contrast, TMX + ART and ART + TMX groups showed a considerable increase in the expression of the SOD and CAT genes compared to the TMX group.

Histopathology of the liver

Histopathological analyses of the liver were conducted in each treatment group compared to the control group to assess potential pathology alterations. The control group showed a normal histological appearance of hepatic parenchyma (Figure 6A), whereas the liver tissue in the TMX-treated group (Figure 6B) exhibited alterations in the normal hepatic cord architecture, which was replaced by an abundance of perivascular fibrous connective tissue (fibrosis), as well as an increase in the number of small bile ducts lined by epithelial cells with a high nuclear to cytoplasmic ratio (ductular reaction), in addition to a lack of inflammatory cells and necrotic hepatocytes, biliary adenomatous hyperplasia, regenerative nodules walled by fibrous connective tissue and infiltrated and surrounded by inflammatory cells, diffuse hepatic necrosis with shrunken, hypereosinophilic cytoplasm and pyknotic or karyorrhectic nucleus infiltrated with few leukocytic infiltrations.

Furthermore, TMX + ART (Figure 6C) showed focal replacement of hepatic parenchyma with mild perivascular heterophilic aggregations admixed with few fibroblasts and macrophages and multifocal hepatic necrosis invaded with few inflammatory cells. However, ART + TMX group (Figure 6D) showed showing mild to moderate inflammatory cells infiltrated necrotic hepatocytes and mild fibrosis represented by plumb fibroblast focally replaced hepatic parenchyma.

Discussion

Thiamethoxam is a neonicotinoid insecticide commonly used in agriculture and known for its growing environmental impact. This study aimed to investigate whether variations in hematological parameters, oxidative stress, and hepatic and renal function induced by TMX could be alleviated by *Cynara scolymus*. The results revealed a significant decrease in Hb content, WBC count, lymphocytes (%), and monocytes (%) in TMX-given chickens compared with the control group. Several studies have confirmed these results. For example, Gul et al.[15] found that treatment with TMX for 15–30 days reduced the Hb concentration of adult cockerels. Similarly, recent studies have shown that the blood profile of TMX-treated fish was significantly altered compared with that of unexposed fish.[32]

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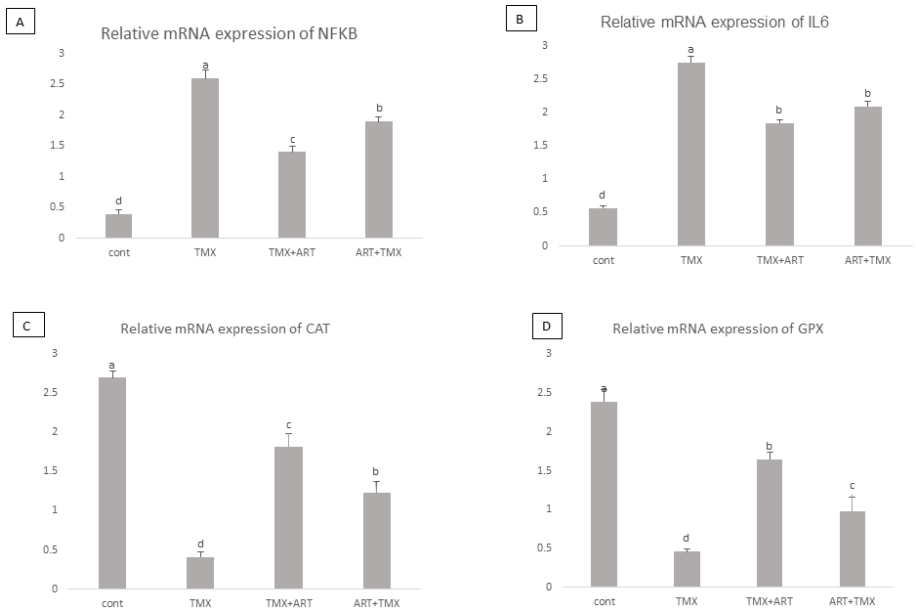

Figure 5. Effect of artichoke extract (500 mg/L) on target gens (NFκB, IL-6, CAT, and GPX) in thiamethoxam-intoxicated chickens. (A) NFκB, (B) IL-6, (C) CAT, (D) GPX genes. Data are expressed as Mean ± SE (n = 5 chickens). Bars carrying different letters are significantly different from one another ($P < 0.05$). G1: Control (Cont), G2: TMX; Thiamethoxam, G3: TMX + ART; Thiamethoxam + Artichoke extract, G4: ART + TMX; Artichoke extract + Thiamethoxam.
NFκB: nuclear factor kappa B, IL-6: interleukin 6, CAT: catalase, GPX: glutathione peroxidase.

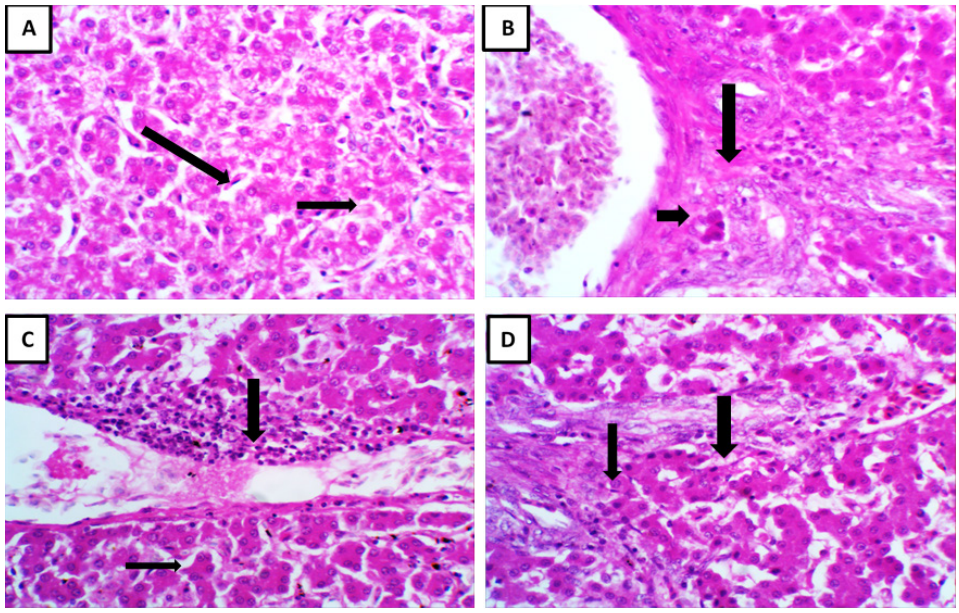

Figure 6. Representative photomicrograph of poultry liver from different treatments.
A) The control group shows the normal histological appearance of hepatic parenchyma, H&E, 400×.
B) Thiamethoxam exposed liver, showing loss of normal hepatic cord architecture and replacement by abundant perivascular fibrous connective tissue.
C) Thiamethoxam + Artichoke therapeutic liver, showing focal replacement of hepatic parenchyma with mild perivascular heterophilic aggregations admixed with few fibroblasts and macrophages.
D) Artichoke + Thiamethoxam protective liver, showing mild fibrosis represented by plumb fibroblast focally replaced hepatic parenchyma

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Meanwhile, the administration of artichoke before or after TMX exposure elevated the Hb level, lymphocyte, and monocyte (%) relative to the TMX group. The improvement of these parameters may be attributed to reducing reactive oxygen species (ROS) thereby reducing red blood cell fragility and restoring the total Hb concentration in the blood.[33–35] On the other hand, it was reported that *Cynara scolymus* is rich in phenolic compounds belonging to different classes such as benzoic and cinnamic derivatives, flavonoids, and tannins.[14, 36] Flavonoids have been shown to stimulate the secretion of erythropoietin, which in turn activates stem cells in the bone marrow to produce red blood cells.

Finally, Ben Salem et al., and El-Boshy et al.[37, 38] stated that the use of *Cynara scolymus* significantly increases hematological parameters in the treated group. Furthermore, the study highlighted a significant increase in ALT, AST; and reduction in total protein and albumin in chickens administered TMX only compared with the control group. The findings are consistent with those reported by Elhamalawy et al.,[39] who noted that administering TMX at a dose of 1/10 LD50 to mice caused significant changes in biomarkers associated with liver (AST, ALT, ALP (alkaline phosphatase), and albumin). Similarly, Gul et al.[15] observed a significant increase in ALT and AST levels following the administration of thiamethoxam in the treated group.

Additionally, Hataba et al.[40] observed that when rats were administered TMX, AST, and ALT concentration in the blood considerably elevated. Conversely, compared to chickens that received TMX alone, the groups offered artichokes after or before TMX had a significant drop in ALT and AST levels and an improved total protein and albumin. These findings are consistent with those of Colak et al.,[41] who found that elevated levels of serum liver enzymes were significantly decreased by treatment with *Cynara scolymus* extract in carbon tetrachloride-induced hepatic injury. Also, Heidarian[42] suggested that artichoke extract decreased the elevated liver enzyme levels in rats intoxicated with lead and in those with diabetes-induced hepatotoxicity.

Furthermore, El-Boshy et al.[38] stated that therapy with artichoke decreased the elevated liver enzymes (ALT, AST, and ALP) induced by cadmium toxicity in rats. Additionally, Zaker-Esteghamati et al.[43] reported that *Cynara scolymus* lowers liver enzymes in broiler chickens (AST, ALT, ALP). However, the readings remained higher than the range for the control group.

In addition, the findings showed that the TMX-intoxicated birds had considerably higher urea blood levels and creatinine than the hens in the control group. On the other hand, hens treated with ART before or after TMX showed a significant reduction in creatinine and urea levels. These results are according to those of Hataba et al.[40] who observed significantly higher urea and creatinine concentrations. In addition, Gul et al.[44] discovered that broiler chicks treated with TMX had higher urea and creatinine blood levels. The artichoke extract groups demonstrated enhanced kidney function when administered before or after thiamethoxam compared to the pesticide-treated group, as evidenced by a significant decrease in serum urea and creatinine levels. This is consistent with findings by Hataba et al. and Benalia.[40, 45]

Oxidative stress, considered a critical mediator in causing damage to cell membranes, lipids, proteins, and DNA, was triggered by an accumulation of ROS.[46] The oxidative stress caused by xenobiotics has been measured using lipid perox-

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idation. It has been suggested as one of the molecular mechanisms responsible for the toxicity of pesticides. Although it is impossible to completely avoid pesticide exposure, the use of certain exogenous antioxidants may help mitigate their toxicity. Sometimes the endogenous antioxidant system fails to repair the oxidative damage that has already occurred.[47] The obtained results revealed that the exposure to TMX led to significant elevation in the MDA content and reduction in the content of GSH, and the activities of SOD, and CAT compared with the control group.

Chickens administered artichoke elicited a reduction in the levels and activities in the previously mentioned indices compared to the TMX group. The effect of TMX is consistent with findings by Jameel et al.[48] who said that MDA concentration was significantly increased in the group administered TMX than in the control group. Also, Ezeji and Onwurah[49] reported that TMX decreases GSH levels and enhances lipid peroxidation. The obtained findings are consistent with those of Mirderikvandi et al.,[16] who reported the effects of artichoke extract on the level of antioxidants in chicken thigh meat (*Cynara scolymus*). Additionally, Küçükgergin et al. and Refaie et al.,[50, 51] detected induction of glutathione peroxidase (GPX) by artichoke leaf extract might contribute to its antioxidant effects in both the liver and heart of rats.

Reactive oxygen species are removed with the aid of catalase. Therefore, a rise in its concentration may facilitate the scavenging of hazardous chemicals.[52] The recorded data are consistent with Duzguner and Erdogan,[53] who explained that one mechanism of neonicotinoid neurotoxicity in vertebrates involves altering the activity of antioxidant enzymes during oxidative stress. Our data are in agreement with Ismail, who stated that compared with the positive control group, the rats given cyclophosphamide to generate oxidative stress displayed significantly reduced levels of CAT, SOD, and glutathione peroxidase (GPX) in their liver tissues. Similar results on CAT and SOD to those mentioned earlier by Küçükgergin et al.[50]

NF-κB, also known as an inducible transcription factor called the nuclear factor of the -chain, regulates several genes involved in triggering and sustaining inflammatory and immune-modulated processes. Laurindo et al.[54] recorded that IL-6 and NFκB gene expression are prominently and considerably increased in the chicken liver tissue of the thiamethoxam-treated group. These findings could be collectively explained as reported by El Euony et al. and El Okle et al.[55, 56] Neuronal inflammatory biomarkers' gene expression was altered by thiamethoxam poisoning. Compared with the control group, there were statistically significant increases in the expression of the IL-6, and NF-κB genes in chickens treated with TMX.

Furthermore, Yang et al.[57] suggested that these findings, rather than the P38-MAPK pathway, the NF-κB pathway may be the primary cause of inflammation brought on by high concentrations of thiamethoxam exposure. The NF-κB signaling pathway was reported as being stimulated by thiamethoxam. Rats exposed to acetamiprid had similar results. According to this study, the expression of the CAT and GPX genes is significantly downregulated in chickens given thiamethoxam treatment. Our result aligns with Coulon et al.[58] who stated that in the transcription of genes associated with detoxication after 5 days of exposure, a honey bee exposed concurrently to thiamethoxam had lower catalase levels than the control.

Also, Nie et al.[59] found that neonicotinoids can damage mitochondria, and the damaged mitochondria subsequently release more ROS. Consequently, the expression of antioxidant genes decreases due to the increased oxidative stress caused by ROS (Such as GPX and SOD). Additionally, Farag et al.,[60] stated that

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while CAT gene expression remained unchanged, the SOD and glutathione S-transferase (GST) genes' hepatic expressions were reduced after exposure to thiacloprid compared with the control. The results demonstrated that artichoke extract supplementation significantly upregulated the expression of the CAT and GPX genes in groups receiving thiamethoxam. Löhr et al.[61] found that GPX gene expression was somewhat stimulated by artichoke leaf extract.

The histopathological examination revealed that the hepatic tissues of TMX-intoxicated group revealed a change in the normal hepatic cord architecture, which was replaced by an abundance of perivascular fibrous connective tissue, as well as an increase in the number of small bile ducts lined by epithelial cells with a high nuclear to cytoplasmic ratio, in addition to a lack of inflammatory cells and necrotic hepatocytes, biliary adenomatous hyperplasia, regenerative nodules walled by fibrous connective tissue and infiltrated and surrounded by inflammatory cells, diffuse hepatic necrosis with shrunken, hypereosinophilic cytoplasm and pyknotic or karyorrhectic nucleus infiltrated with few leukocytic infiltrations.

Normal histological appearance of the hepatic parenchyma was observed in both the artichoke and control groups. Similarly, these findings are consistent with an earlier study confirming the ameliorative effect of artichoke in rat liver, which exhibited only a mild degree of lymphocyte infiltration compared to the control.[43] While, Seoudi and Saleh[62] revealed that artichoke reduced the histopathological abnormalities caused by CCl4-induced hepatic toxicity in rats.

Conclusion

In summary, we hypothesized that TMX may have caused liver injury in chickens by generating oxidative and nitrogenous stress and by altering gene expression. However, the administration of artichoke extract protects chickens from TMX toxicity by igniting internal antioxidant defenses and restoring disrupted gene expression.

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Data availability

All relevant data are available in the manuscript and its supporting information files.

Acknowledgments

The researchers are very grateful to the Faculty of Veterinary Medicine, Mansoura University, Egypt, and Animal Health Research Institute for providing a suit place to achieve this study.

Funding statement

All authors were paid for this publication, there was not any external funding.

Conflicts of interest

The authors have no conflict of interest to declare regarding this investigation.

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References

1. Khaldoun Oularbi H, Richeval C, Lebaili N, Zerrouki-Daoudi N, Baha M, Djennas N, *et al*. Ameliorative effect of vitamin C against hepatotoxicity induced by emamectin benzoate in rats. Human & Experimental Toxicology 2017;36(7):709—717. doi: 10.1177/0960327116661022.
2. Borsuah JF, Messer TL, Snow DD, Comfort SD, Mittelstet AR. Literature review: global neonicotinoid insecticide occurrence in aquatic environments. Water. 2020;12(12):3388. doi: 10.3390/w12123388.
3. Costas-Ferreira C, Faro LRF. Neurotoxic effects of neonicotinoids on mammals: what is there beyond the activation of nicotinic acetylcholine receptors? —A systematic review. International Journal of Molecular Sciences. 2021;22(16):8413. doi: 10.3390/ijms22168413.
4. Habotta OA, Ateya A, Saleh RM, El-Ashry ES. Thiamethoxam-induced oxidative stress, lipid peroxidation, and disturbance of steroidogenic genes in male rats: palliative role of *Saussurea* lappa and *Silybum marianum*. Environmental Toxicology. 2021;36(10):2051—2061. doi: 10.1002/tox.23322.
5. Zaefarian F, Abdollahi MR, Cowieson A, Ravindran V. Avian liver: the forgotten organ. Animals. 2019;9(2):63. doi: 10.3390/ani9020063.

doi: 10.22201/fmvz.24486760e.2025.1285
Vol. 12 | 2025

6. Manokhina AA, Dorokhov AS, Kobozeva TP, Fomina TN, Starovoitova OA. Varietal characteristics of Jerusalem artichoke as a high nutritional value crop for herbivorous animal husbandry. Applied Sciences. 2022;12(9):4507. doi: 10.3390/app12094507.
7. Cornescu GM, Panaite TD, Soica C, Cismileanu A, Matache CC. Jerusalem artichoke (*Helianthus tuberosus* L.) as a romising dietary feed ingredient for monogastric farm animals. Applied Sciences. 2023;13(23):12748. doi: 10.3390/app132312748.
8. Jimenez-Escrig A, Dragsted LO, Daneshvar B, Pulido R, Saura-Calixto F. *In vitro* antioxidant activities of edible artichoke (*Cynara scolymus* L.) and effect on biomarkers of antioxidants in rats. Journal of Agricultural and Food Chemistry. 2003;51(18):5540—5545 doi: 10.1021/jf030047e.
9. Kaur N, Gupta AK. Applications of inulin and oligofructose in health and nutrition. Journal of Biosciences. 2002;27:703—714. doi: 10.1007/BF02708379.
10. Radwan NL, Abdo ZMA, Hassan RA. Effect of feeding artichoke leaves meal on productive and reproductive performance of Mandarah hens. International Journal of Poultry Science. 2007;6(11):826—834. doi: 10.3923/ijps.2007.826.834.
11. Edenz F, Paarkhurrst R. CS influence on performance of broilers in conventional and cage rearing environments. Poultry Science. 2001;15(7):146—150.
12. Kleessen B, Elsayed N, Loehren U, Schroedl W, Krueger M. Jerusalem artichokes stimulate growth of broiler chickens and protect them against endotoxins and potential cecal pathogens. Journal of Food Protection. 2003;66(11):2171—2175. doi: 10.4315/0362-028X-66.11.2171.
13. Wang M, Simon JE, Aviles IF, He K, Zheng Q-Y, Tadmor Y. Analysis of antioxidative phenolic compounds in artichoke (*Cynara scolymus* L.). Journal of Agricultural and Food Chemistry. 2003;51(3):601—608. doi: 10.1021/jf020792b.
14. Abdo ZMA, Radwan NL, Selim NA. The effect of artichoke leaves meal on the utilization of dietary energy for broiler chicks. International Journal of Poultry Science. 2007;6(12):973—982. doi: 10.3923/ijps.2007.973.982.
15. Gul ST, Ahamd I, Saleemi MK, Ahmad M, Ahmad L, Khan A. Toxico-pathological effects of thiamethoxam on hemato-biochemical and productive performance of commercial laying Hens. Pakistan Veterinary Journal. 2020;40(4):449—454. doi: 10.29261/pakvetj/2020.052.
16. Mirderikvandi M, Kiani A, Khaldari M, Alirezaei M. Effects of artichoke (*Cynara scolymus* L.) extract on antioxidant status in chicken thigh meat. Agricultural and Food Sciences. 2016;10(1):73—81. doi: 10.22059/IJVM.2016.57054.
17. Coles MA, Brown DF. "Staphaurex" negative, methicillin resistant *Staphylococcus aureus*. Journal of Clinical Pathology. 1986;39(12):1365. doi: 10.1136/jcp.39.12.1365.
18. Onunkwor DN, Udokwu IU, Ekundayo EO, Ezenyilimba BN, Omumuabuike JN, Ezeoke FC. Serum biochemical assay of broiler chickens administered water containing various medicinal plant leaf methanol extract. Nigerian Journal of Animal Production. 2022(Mar 8);49(2):95—100. doi: 10.51791/njap.v49i2.3466.

doi: 10.22201/fmvz.24486760e.2025.1285
Vol. 12 | 2025

19. Sapan CV, Lundblad RL, Price NC. Colorimetric protein assay techniques. Biotechnology and Applied Biochemistry. 1999(Apr 29);(2):99—108. doi: 10.1111/j.1470-8744.1999.tb00538.x.
20. Doumas BT, Watson WA, Biggs HG. Albumin standards and the measurement of serum albumin with bromcresol green. Clinica Chimica Acta. 1971;31(1):87—96. doi: 10.1016/0009-8981(71)90365-2.
21. Pundir CS, Kumar P, Jaiwal R. Biosensing methods for determination of creatinine: a review. Biosensors and Bioelectronics. 2019(Feb 1);126:707—724. doi: 10.1016/j.bios.2018.11.031.
22. Ohkawa H, Ohishi N, Yagi K. Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. Analytical Biochemistry. 1979;95(2):351—358. doi: 10.1016/0003-2697(79)90738-3.
23. Beutler E, Yeh MK. Erythrocyte glutathione reductase. Blood. 1963;21(5):573—585. doi: 10.1182/blood.V21.5.573.573.
24. Aebi H. Catalase *in vitro*. Methods in Enzymology 1984;105:121—126. doi: 10.1016/S0076-6879(84)05016-3.
25. Weydert CJ, Cullen JJ. Measurement of superoxide dismutase, catalase and glutathione peroxidase in cultured cells and tissue. Nature Protocols. 2010;5:51—66. doi: 10.1038/nprot.2009.197.
26. El-Deep MH, Asser M, Shabaan M, Eid Y, Sayed M. Glutathione stimulates liver anti-oxidants related genes and reduces hepatic dysfunction induced by dietary mycotoxins in laying hens. Egyptian Poultry Science Journal. 2016;36(2):389—407. doi: 10.21608/epsj.2016.34561.
27. Chen D, Jiang X, Hong Y, Wen Z, Wei S, Peng G, *et al.* Can chest CT features distinguish patients with negative from those with positive initial RT-PCR results for coronavirus disease (COVID-19). AJR American Journal Roentgenology. 2021;216(1):66—70. doi: 10.2214/AJR.20.23012.
28. Lu X, Whitaker B, Sakthivel SKK, Kamili S, Rose LE, Lowe L, *et al.* Real-time reverse transcription-PCR assay panel for Middle East respiratory syndrome coronavirus. Journal of Clinical Microbiology. 2014;52(1):67—75. doi: 10.1128/jcm.02533-13.
29. Wang J, Zhang Y, Wang J, Liu L, Pang X, Yuan W. Development of a TaqMan-based real-time PCR assay for the specific detection of porcine circovirus 3. Journal of Virological Methods. 2017;248:177—180. doi: 10.1016/j.jviromet.2017.07.007.
30. Pfaffl MW. A new mathematical model for relative quantification in real-time RT–PCR. Nucleic Acids Research. 2001;29(9):e45. doi: 10.1093/nar/29.9.e45.
31. Al-Sultan SI, Gameel AA. Histopathological changes in the livers of broiler chicken supplemented with turmeric (*Curcuma longa*). International Journal of Poultry Science. 2004(Apr 15);3(5):333—336. doi: 10.3923/ijps.2004.333.336
32. Hussain R, Ghaffar A, Abbas G, Jabeen G, Khan I, Abbas RZ, *et al.* Thiamethoxam at sublethal concentrations induces histopathological, serum biochemical alterations, and DNA damage in fish (*Labeo rohita*). Toxin Reviews. 2022;41(1):154—164. doi: 10.1080/15569543.2020.1855655.
33. Avcı G, Kupeli E, Eryavuz A, Yesilada E, Kucukkurt I. Antihypercholesterolaemic and antioxidant activity assessment of some plants used as remedy (*sic.*) in Turkish folk medicine. Journal of Ethnopharmacology. 2006;107(3):418—423. doi: 10.1016/j.jep.2006.03.032.

doi: 10.22201/fmvz.24486760e.2025.1285
Vol. 12 | 2025

34. Rezazadeh A, Ghasemnezhad A, Barani M, Telmadarrehei T. Effect of salinity on phenolic composition and antioxidant activity of artichoke (*Cynara scolymus* L.) leaves. Research Journal of Medicinal Plants. 2012;6(3):245—252. doi: 10.3923/rjmp.2012.245.252.
35. Salekzamani S, Ebrahimi-Mameghani M, Rezazadeh K. The antioxidant activity of artichoke (*Cynara scolymus*): a systematic review and meta-analysis of animal studies. Phytotherapy Research. 2019;33(1):55—71. doi: 10.1002/ptr.6213.
36. Lattanzio V, Kroon PA, Linsalata V, Cardinali A. Globe artichoke: a functional food and source of nutraceutical ingredients. Journal of Functional Foods. 2009;1(2):131—144. doi: 10.1016/j.jff.2009.01.002.
37. Ben Salem M, Ben Abdallah Kolsi R, Dhouibi R, Ksouda K, Charfi S, Yaich M, *et al.* Protective effects of *Cynara scolymus* leaves extract on metabolic disorders and oxidative stress in alloxan-diabetic rats. BMC Complementary and Alternative Medicine. 2017;17(1):328. doi: 10.1186/s12906-017-1835-8.
38. El-Boshy M, Ashshi A, Gaith M, Qusty N, Bokhary T, AlTaweel N, *et al.* Studies on the protective effect of the artichoke (*Cynara scolymus*) leaf extract against cadmium toxicity-induced oxidative stress, hepatorenal damage, and immunosuppressive and hematological disorders in rats. Environmental Science and Pollution Research. 2017;24:12372—12383.
39. Elhamalawy OH, Al-Anany FS, El Makawy AI. Thiamethoxam-induced hematological, biochemical, and genetic alterations and the ameliorated effect of *Moringa oleifera* in male mice. Toxicology Reports. 2022;9:94—101. doi: 10.1016/j.toxrep.2021.12.012.
40. Hataba A, Keshta AT, Mead HMI, El-Shafey N. Hematological, biochemical and histological alterations induced by oral administration of Thiamethoxam and Acetamiprid in male rats. Biochemistry Letters. 2014;10(1):113—125. doi: 10.21608/blj.2014.63858.
41. Colak E, Ustuner MC, Tekin N, Colak E, Burukoglu D, Degirmenci I, *et al.* The hepatocurative effects of *Cynara scolymus* L. leaf extract on carbon tetrachloride-induced oxidative stress and hepatic injury in rats. SpringerPlus. 2016;5(1):1—9. doi: 10.1186/s40064-016-1894-1.
42. Heidarian E, Rafieian-Kopaei M. Protective effect of artichoke (*Cynara scolymus*) leaf extract against lead toxicity in rat. Pharmaceutical Biology. 2013;51(9):1104—1109.doi: 10.3109/13880209.2013.777931.
43. Zaker-Esteghamati H, Seidavi A, Bouyeh M. Effect of *Cynara scolymus* and its derivatives on broilers: an updated review. Animal Biotechnology. 2021;32(5):656—662. doi: 10.1080/10495398.2020.1737097.
44. Gul ST, Khan A, Ahmad M, Anwar MF, Khatoon A, Saleemi MK, *et al.* Effect of sub-lethal doses of thiamethoxam (a neonicotinoid) on hemato-biochemical parameters in broiler chicks. Toxin Reviews. 2018;37(2):144—148. doi: 10.1080/15569543.2017.1336731.
45. Bekhaled I, Benalia A, Mehida H, Meziani S, Tarfaoui L, Djjebar AA, Mai AH, Bensaid I, Demmouche A. Evaluation of the acute toxicity of dandelion (*Taraxacum officinale*) roots. Journal of Drug Delivery and Therapeutics. 2020;10(3):159—163. doi: 10.22270/jddt.v10i3.4093.
46. Valko M, Leibfritz D, Moncol J, Cronin MTD, Mazur M, Telser J. Free radicals and antioxidants in normal physiological functions and human disease. The

doi: 10.22201/fmvz.24486760e.2025.1285
Vol. 12 | 2025

International Journal of Biochemistry & Cell Biology. 2007;39(1):44–84. doi: 10.1016/j.biocel.2006.07.001.

47. Saad-Hussein A, Ibrahim KS, Abdalla MS, El-Mezayen HA, Osman NFA. Effects of zinc supplementation on oxidant/antioxidant and lipids status of pesticides sprayers. Journal of Complementary and Integrative Medicine. 2019;17(1):20190001. doi: 10.1515/jcim-2019-0001.
48. Jameel M, Jamal K, Alam MF, Ameen F, Younus H, Siddique HR. Interaction of thiamethoxam with DNA: hazardous effect on biochemical and biological parameters of the exposed organism. Chemosphere. 2020;254:126875. doi: 10.1016/j.chemosphere.2020.126875.
49. Ezeji EU, Onwurah INE. Biochemical effects of dichlorvos pesticide on the liver of poultry birds (*Gallus domestica*). American Journal of Biochemistry. 2017;7(2):23–26. doi: 10.5923/j.ajb.20170702.02.
50. Küçükgergin C, Aydın AF, Özdemirler-Erata G, Mehmetçik G, Koçak-Toker N, Uysal M. Effect of artichoke leaf extract on hepatic and cardiac oxidative stress in rats fed on high cholesterol diet. Biological Trace Element Research. 2010;135:264–274. doi: 10.1007/s12011-009-8484-9.
51. Refaie AA, Ramadan A, Sabry NM, Khalil WKB, Mossa A-TH. Synthetic insecticide fipronil induced over gene expression, DNA and liver damage in female rats: the protective role of fish oil. Egyptian Journal of Chemistry. 2021;64(5):2325–2336. doi: 10.21608/ejchem.2021.58506.3264.
52. Chen Q, Zhang M, Shen S. Effect of salt on malondialdehyde and antioxidant enzymes in seedling roots of Jerusalem artichoke (*Helianthus tuberosus* L.). Acta Physiologiae Plantarum. 2011;33:273–278. doi: 10.1007/s11738-010-0543-5.
53. Duzguner V, Erdogan S. Acute oxidant and inflammatory effects of imidacloprid on the mammalian central nervous system and liver in rats. Pesticide Biochemistry and Physiology. 2010;97(1):13–18. doi: 10.1016/j.pestbp.2009.11.008.
54. Laurindo LF, Santos ARdOd, Carvalho ACAd, Bechara MD, Guiguer EL, Goulart RdA, *et al.* Phytochemicals and regulation of NF-kB in inflammatory bowel diseases: an overview of *in vitro* and *in vivo* effects. Metabolites. 2023;13(1):96. doi: 10.3390/metabo13010096.
55. El Euony OI, Elblehi SS, Abdel-Latif HM, Abdel-Daim MMA, El-Sayed YS. Modulatory role of dietary *Thymus vulgaris* essential oil and *Bacillus subtilis* against thiamethoxam-induced hepatorenal damage, oxidative stress, and immunotoxicity in African catfish (*Clarias garipenus*). Environmental Science and Pollution Research. 2020;27:23108–23128. doi: 10.1007/s11356-020-08588-5.
56. El Okle OS, El Euony OI, Khafaga AF, Lebda MA. Thiamethoxam induced hepatotoxicity and pro-carcinogenicity in rabbits via motivation of oxidative stress, inflammation, and anti-apoptotic pathway. Environmental Science and Pollution Research. 2018;25:4678–4689. doi: 10.1007/s11356-017-0850-0.
57. Yang Y, Yu Q, Zhang C, Wang X, He L, Huang Y, *et al.* Acute thiamethoxam exposure induces hepatotoxicity and neurotoxicity in juvenile Chinese mitten crab (*Eriocheir sinensis*). Ecotoxicology and Environmental Safety. 2023;249:114399. doi: 10.1016/j.ecoenv.2022.114399.

doi: 10.22201/fmvz.24486760e.2025.1285
Vol. 12 | 2025

58. Coulon M, Schurr F, Martel A-C, Cougoule N, Bégaud A, Mangoni P, *et al.* Influence of chronic exposure to thiamethoxam and chronic bee paralysis virus on winter honey bees. PLoS One. 2019;14(8):e0220703. doi: 10.1371/journal.pone.0220703.
59. Nie Z-W, Niu Y-J, Zhou W, Kim Y-H, Shin K-T, Cui X-S. Thiamethoxam inhibits blastocyst expansion and hatching via reactive-oxygen species–induced G2 checkpoint activation in pigs. Cellular Signalling. 2019;53:294—303. doi: 10.1016/j.cellsig.2018.08.014.
60. Farag MR, Zizzadoro C, Alagawany M, Abou-Zeid SM, Mawed SA, El Kholy MS, *et al.* In ovo protective effects of chicoric and rosmarinic acids against Thiacloprid-induced cytotoxicity, oxidative stress, and growth retardation on newly hatched chicks. Poultry Science. 2023;102(4):102487. doi: 10.1016/j.psj.2023.102487.
61. Löhr G, Deters A, Hensel A. *In vitro* investigations of *Cynara scolymus* L. extract on cell physiology of HepG2 liver cells. Brazilian Journal of Pharmaceutical Sciences. 2009;45:201—208. doi: 10.1590/S1984-82502009000200003.
62. Seoudi DM, Saleh EM. Assessment of hepatoprotective and apoptotic efficacy of *Cynara scolymus* leaf extract. International Journal of Biosciences. 2018;12(1):300—314. doi: 10.12692/ijb/12.1.300-314.