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TRIBULUS TERRESTRIS METHANOLIC EXTRACT MODULATES SPIROTETRAMAT-INDUCED LIVER AND KIDNEY TOXICITY IN DOMESTIC PIGEONS (*COLUMBA LIVIA DOMESTICA*)

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ABSTRACT

This research aimed to examine the protective effect of *Tribulus terrestris* (TT) methanolic extract against Spirotetramat-induced (SPT) liver and kidneys toxicity in adult domestic pigeons. Thirty male pigeons weighing 309.20 ± 14.41g were divided equally into six groups and were treated orally as follows: (CT) was used as the control, the SPT group received 15 mg/kg BW/day of SPT, the TT100 and TT50 groups were administered 100 and 50 mg/kg BW/day of TT, respectively, in addition to (SPT+ TT100) and (SPT + TT50) groups. After ten consecutive weeks of treatment, pigeons were sacrificed, and their livers and kidneys were weighed and examined. Plasma was also analyzed for hepatic and nephrotic markers represented by alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), total proteins, urea, creatinine, glucose, and uric acid. The results showed that SPT administration induced a significant increase in liver and kidney weights, and plasma ALT, AST, GGT activities. The biochemical markers revealed increases in total proteins, urea, creatinine, glucose, and uric acid levels. However, the co-treatment of TT with SPT has restored liver and kidney weight, ALT, AST, GGT, and all other examined biochemical parameters. The histopathological examination showed necrotic and remarkable alterations in the liver and kidney tissues of the SPT group. However, combined treatment has reduced the hepatic and renal tissue injury induced by SPT alone. The present study demonstrated that TT possesses potential cytoprotective effects against hepato-nephrotoxicity caused by SPT.

Keywords: *Tribulus terrestris*, Spirotetramat, pigeons, liver, kidney

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INTRODUCTION

The liver and kidneys have complex structures where various metabolic activities occur, making them the target organs for multiple chemicals such as drugs and xenobiotics (Cataudella *et al*., 2012). Hepatotoxicity and nephrotoxicity induced by pesticides have been observed in albino rats (Benjamin *et al.,* 2006) and male albino mice (Arfat *et al*., 2014). It is known that pesticides can cause cirrhosis, steatosis, hepatic fibrosis, and inflammation in the liver (Cataudella *et al*., 2012). However, the nephrotoxicity is characterized by lower urine concentration, tubular proteinuria, decreased ammonium excretion, reduced creatinine clearance, diminished glomerular filtration rate, increased serum urea and creatinine, and provoked morphological changes of kidney tissues (Chinnala *et al*., 2017).

SPT a novel insecticide derivative of tetronic acid, is being developed to control scales and aphids (Zhang *et al*., 2020). SPT effects on the non-target animals have been studied, in which Yin *et al*. (2014) demonstrated that sub-lethal doses of SPT were mildly harmful to Chinese toad tadpoles. Wu *et al*. (2012) demonstrated that SPT might be absorbed and converted into metabolite residues in various organs and tissues. Liu (2011) reported that SPT had reduced rat weight and damaged hepatic and sexual organs. Furthermore, SPT increased acid phosphatase activity in rats, but decreased alkaline phosphatase and carboxyl esterase activity *in vivo*. Chen (2018) showed that SPT administration retarded the development of zebrafish embryos, induced oxidative stress, and reduced the activity and expression of target Acetyl CoA carboxylase, fatty acid synthesis, and sterol regulatory element associated genes. The findings obtained by González-marín *et al*. (2021) showed that Movento® 240SC insecticide is a genotoxic agent in *D. melanogaster* ovaries because it increased the genotoxic parameters (tail length, tail moment, and tail

intensity) in cell nuclei of *D. melanogaster.* According to Zhang *et al*. (2015), SPT can cause low and moderate levels of DNA damage in earthworm coelomocytes and may represent possible biochemical and genetic toxicity to earthworms. A previous study showed that the mRNA levels of the genes related to lipid metabolism were significantly altered by the insecticides Spirodiclofen, Spiromesifen and SPT (Zhang *et al*., 2019).

Herbal extracts are widely used to treat various diseases since they are natural, generally safe, and have little or no adverse effects (Kumar and Singh, 2015). TT is a medicinal plant belongs to Zygophyllaceae family. The species is distributed in the south Europe, north Australia, Africa, and south Asia. In traditional medicine, various components of TT were used to treat hypertension, coronary artery disorders, diabetes, hyperlipidemia, and fungal infections (Phillips *et al*., 2006). Furthermore, TT has been found to have diuretic, lithontriptic, aphrodisiac, and antibacterial properties (Al-bayati and Al-mola, 2008). The pathogenesis of most diseases has been linked to a free radical-mediated process. Oxidative damage caused by free radicals may be avoided by using antioxidants such ascarotenoids, ascorbic acid, tocopherols, and other plants compounds (Kamashi *et al*., 2004). Moreover, according to recent research, TT extract possesses apoptotic inhibitory, antioxidative, and vasodilator effects (Kavitha *et al*., 2011), as well as the ability to protect renal epithelial cells from damages caused by oxalates and ethylene glycol intake (Kamboj *et al*., 2011). Also, Kavitha *et al*. (2011) revealed the hepatoprotective and antioxidant properties of TT against Acetaminophen-induced toxicity in fresh-water fish. In addition, free radical scavenging activity, secondary metabolites, trace elements, amino acids, and proteins contained in TT could protect hepatocytes against hazardous chemicals in several different ways (Kavitha *et al*., 2011). Previous studies have shown TT as the most effective ameliorative treatment against Atrazine herbicide-induced hepatotoxicity (Nimavathi *et al*., 2021a). Abubaker and Khalid, (2016) showed that the TT extract had a substantial nephroprotective effect. It has also significant hepatoprotective activity due to its ability to scavenge generated free radicals and stimulate antioxidant enzyme production and the down-regulation of pro-inflammatory markers released after liver tissue damage (Ali *et al*., 2018).

So far, pigeons have not yet been used as a biological model to investigate the effects of SPT on the liver and kidney markers. This study aims to evaluate the hepatoprotective and nephroprotective activity of TT methanol extract against SPT-induced toxicity in adult male pigeons *Columba livia domestica.*

MATERIALS AND METHODS

Chemicals: The SPT (Movento®, 150 OD, CAS No. 203313-25-1, purity 98.5%) was supplied by Bayer Crop Science (Germany), and the other analytical grade reagents were purchased from Setif laboratories Ltd., Setif, Algeria. Though this study used a dose of 15 mg/kg/day of SPT, whose LD50 for birds is above 2000 mg/kg (Maus, 2008), and The SPT insecticide concentration was prepared on an LD50 basis according to toxicology methods (Weil, 1952).

Plant material and extraction method: The dry TT aerial parts (1.5 kg) were bought from a medicinal herbs market (Setif-Algeria, January 2021). The plant sample was identified (by the botanist Dr Sakhraoui Nora), and then powdered by home mixer. One kg of powder was dissolved in a hydro-methanolic solution (80%) for 24 hours to produce the methanolic extract. The extract was subjected to a paper filter type Whatman N°.1 to obtain a separate solution. The latter, was evaporated by a vacuum evaporator (RE-100 Pro) at 45°C to obtain a final solid residue. At the treatment time, the solid residue was dissolved in distilled water in order to prepare two fresh doses of 50 and 100 mg/kg dry weight.

Animals: Thirty male domestic pigeons weighing 309.20 ± 14.41 g were obtained from Sikkda, northeast Algeria. Five birds were acclimated in each polypropylene cage of 90x90x90 cm for two weeks in the animal house of Biological Faculty at 23 ± 2 °C and 50 ± 10% humidity, with adequate aeration and standard photoperiod. Pigeons were given free access to a standard diet and tap water.

Experimental protocol: Thirty male pigeons were divided into equal six groups (n=5) and were treated orally for ten consecutive weeks as follows (Table 1).

Table 1. Experimental protocol of pigeons' treatment for ten consecutive weeks.

Group	n	Period (week)	Treatment (by oral)
Control	5	10	Distilled water
SPT	5	10	Spirotetramat (15 mg/kg. BW/day).
TT 100	5	10	*T. terrestris* (100 mg/kg. BW/day).
TT 50	5	10	*T. terrestris* (50 mg/kg. BW/day).
SPT+TT 100	5	10	Spirotetramat (15 mg/kg. BW/day) combined with *T. terrestris* (100 mg/kg. BW/ day).
SPT+TT 50	5	10	Spirotetramat (15 mg/kg BW/day) combined with *T. terrestris* (50 mg/kg BW/day).

After ten weeks of treatment, pigeons were sacrificed, and then 3 ml of blood were collected from each pigeon. After the centrifugation procedure, the obtained plasma was stored at 4°C until biochemical analysis.

Livers and kidneys were quickly removed from the body, washed with isotonic saline and weighed before they were fixed in 10 % formalin to be used later for the anatomo-histopathology study.

Measurements

Assessment of liver and kidneys mass: Relative liver and kidney weights were calculated according to the following formula: Relative organ weight (g/100 g) = [Total organ weight (g)/Final body weight (g)] × 100

Determination biochemical parameters: The enzymatic activities of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and gamma-glutamyl transpeptidase (GGT) were determined in plasma using previously published techniques (Edwards *et al*., 1995). The estimation of total proteins, urea, creatinine clearance, glucose, and uric acid was realized by using standard diagnostic kits (Medi Screen kit, France).

Histopathology examination: The fixed liver and kidney specimens were put in cassettes and placed into a vacuum tissue processor that operated automatically (ASP 300 S, Leica Biosystems, Nussloch, Germany). Samples were immersed and blocked in paraffin wax before being sectioned using a microtome (RM 2125 RTS, Leica Biosystems, Nussloch, Germany) to obtain thin sections of 3µm. Sections were stained with Mayer's hematoxylin solution and treated with the eosin-phloxine solution before being mounted on slides (Prophet *et al.*, 1994).

Statistical Analysis: GraphPad Prism version 9.2.0 (GraphPad Software, LLC, CA, USA) was used for statistical analysis. The mean ± standard deviation (SD) of five animals was applied. One-way analysis of variance (ANOVA) has been used to compare data from various groups, followed by Tukey's multiple comparison tests for inter-group comparisons. All findings were considered statistically significant at $P < 0.05$.

RESULTS

Liver and kidney relative weights: Liver and kidney weight data were illustrated in Figure (1). A significant increase ($P < 0.001$) in the relative livers and kidney means weights of SPT treated pigeons was noted. However, the relative organ weights of TT groups were not significantly different from those of the control pigeons. The SPT+TT co-treatments were significantly lower compared to SPT group.

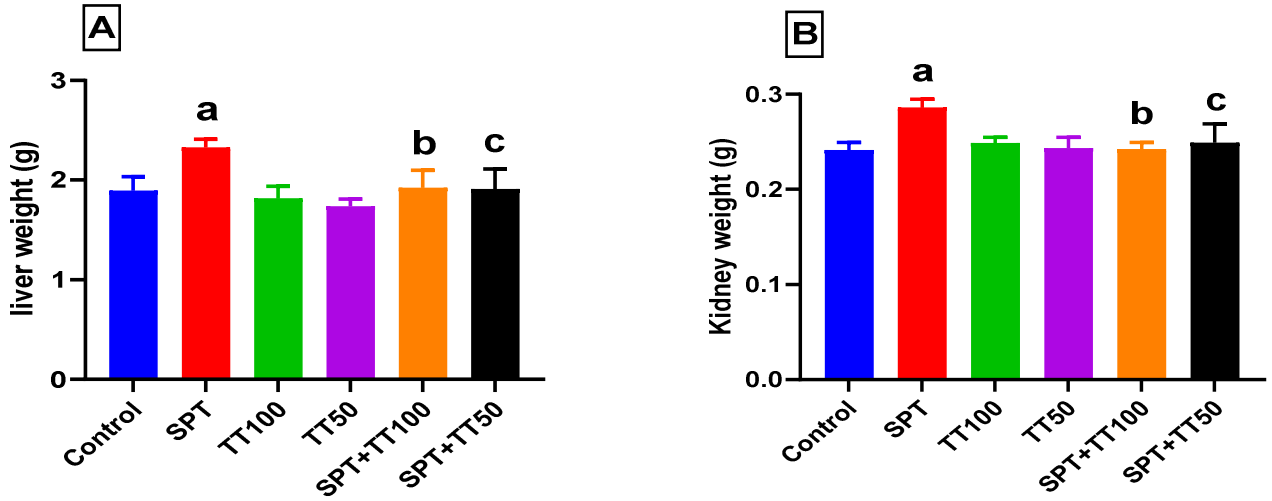

Fig 1. The effect of SPT and TT on relative weight (Mean ± SD) of liver (A) and kidney (B) of male pigeons after ten consecutive weeks. SPT: Spirotetramat (15 mg/kg.BW/day), TT100: *T. terrestris* (100 mg/kg BW/day), TT50: T. terrestris (50mg/kg BW/day). a, difference between control and SPT; b, difference between SPT and SPT + TT100; c, difference between SPT and SPT + TT50.

Plasma Enzymatic: Fig. 2 reports the mean values of the various biochemical parameters of domestic's pigeons *Columba livia domestica* treated with SPT and TT for 70 days.

Data revealed a significant increase in the enzymatic activities of AST, ALT and GGT in the SPT treated pigeons. Nevertheless, compared to the control, no significant difference was observed in the activities of these enzymes in pigeons treated with the TT extract (TT100 and TT50) alone or in combination with the insecticide SPT.

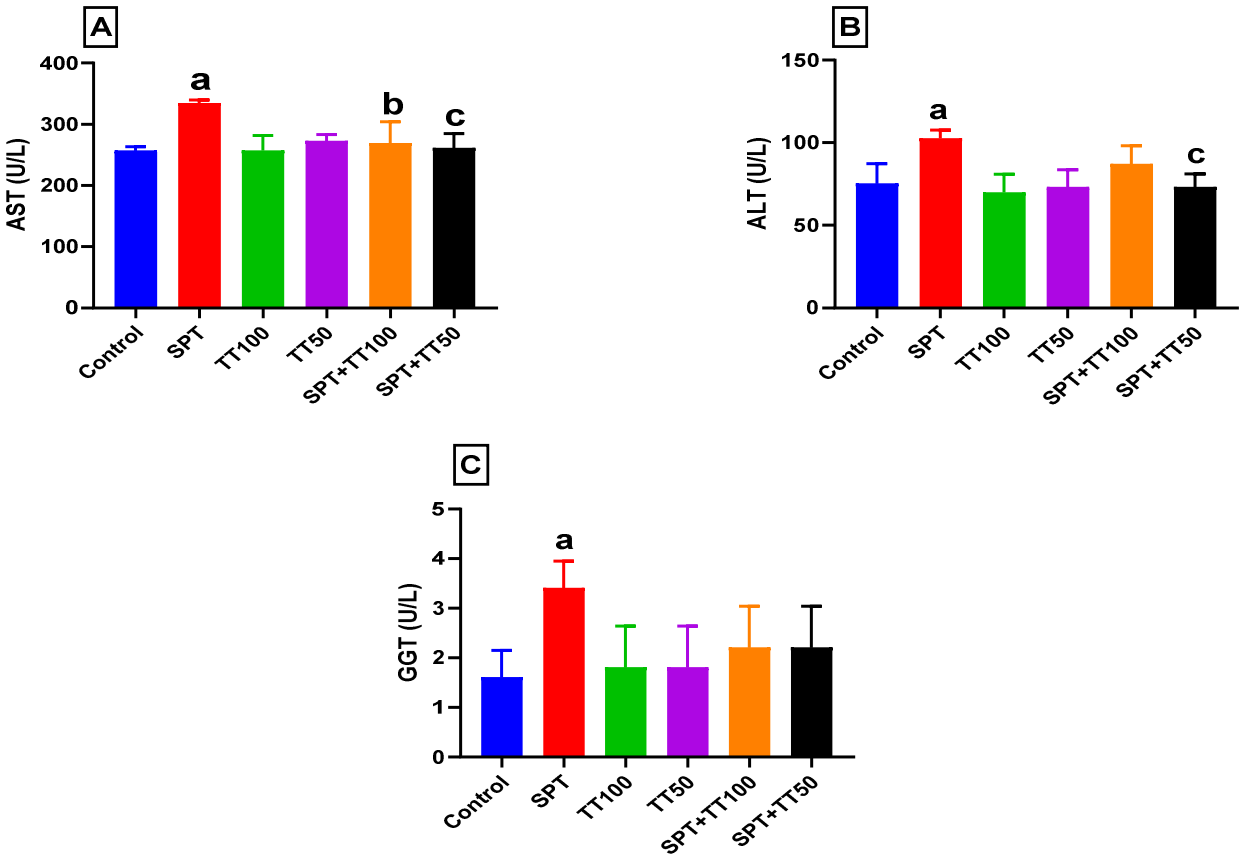

Fig. 2. The effect of SPT and TT on plasma AST (A), ALT (B), and GGT (C) activities (Mean ± SD) of male pigeons after ten consecutive weeks. SPT: Spirotetramat (15 mg/kg BW/day), TT100: *T. terrestris* (100 mg/kg BW/day), TT50: *T. terrestris* (50 mg/kg BW/day). a, difference between control and SPT; b, difference between SPT and SPT + TT100; c, difference between SPT and SPT + TT50.

Plasma biochemical markers: Fig. 3 demonstrates changes in plasma urea, creatinine, acid uric, glucose, and total proteins' levels after 10 weeks of TT and SPT treatments. The obtained results showed a significant increase in urea and creatinine concentration in the SPT-treated group compared to the control. Compared to the control, the extracts of TT alone did not change the levels of plasma parameters, but the co-treatments have significantly decreased urea (SPT+TT100), uric acid (SPT+TT50), and glucose (SPT+TT100 and SPT+TT50) levels, while, total proteins' concentration was significantly raised in both groups (SPT+TT100 and SPT+TT50).

Histopathological examinations:

Liver: The hepatic histological sections of different groups of pigeons treated for ten consecutive weeks were presented in Fig. 4. The hepatocytes and other hepatic cells in the control group showed compact and regular structure and were organized systematically (Fig. 4-a). The SPT exposed group revealed a partially distorted liver histo-architecture, inflammation and necrosis in hepatocytes at the central vein, and significant vascular and sinusoidal congestion with widespread degenerative alterations. In addition, periportal regions showed high numbers of infiltrated mononuclear cells, and the sinusoids and central veins were severely congested (Fig. 4-b). Liver alterations caused by SPT were improved by TT co-administration. Liver sections in the SPT+TT-treated groups exhibited significant recovery with persistent moderate hydropic degeneration and localised mild congestion. There was also residual portal moderate inflammatory infiltration, although no sinusoidal dilatation or necrosis was seen (Fig. 4-c and 4-d). The (SPT+TT) groups showed some areas of fibrous dilation, with no fibrosis or mild congestion, and the architecture was preserved (Fig. 4-e and 4-f).

Kidney: The histological sections of the control group revealed regular kidney histology with glomerulus, tubules, capillaries, and Bowman's capsule (Fig. 5-a). On the other hand, the regions of the cortex containing renal corpuscles and related tubules showed more severe alterations in the SPT-exposed pigeons (Fig. 5-b). Also, the SPT group showed remarkably degenerated glomeruli, Bowman's capsules and the related tubule

structures, with glomeruli shrinking, tubular dilation, and an increased congestion (Fig. 5-b). However, treatment with SPT+TT notably reduced the inflammatory signs and led to a general improvement in kidney histology (Fig. 5-c and 5-d). In addition, there was moderate localised hydropic degeneration of tubular epithelial cells, the glomeruli exhibited increased cellularity, and the stroma showed minimal congestion and limited lymphocytic infiltration in the SPT+TT-treated groups (Fig. 5-e and 5-f).

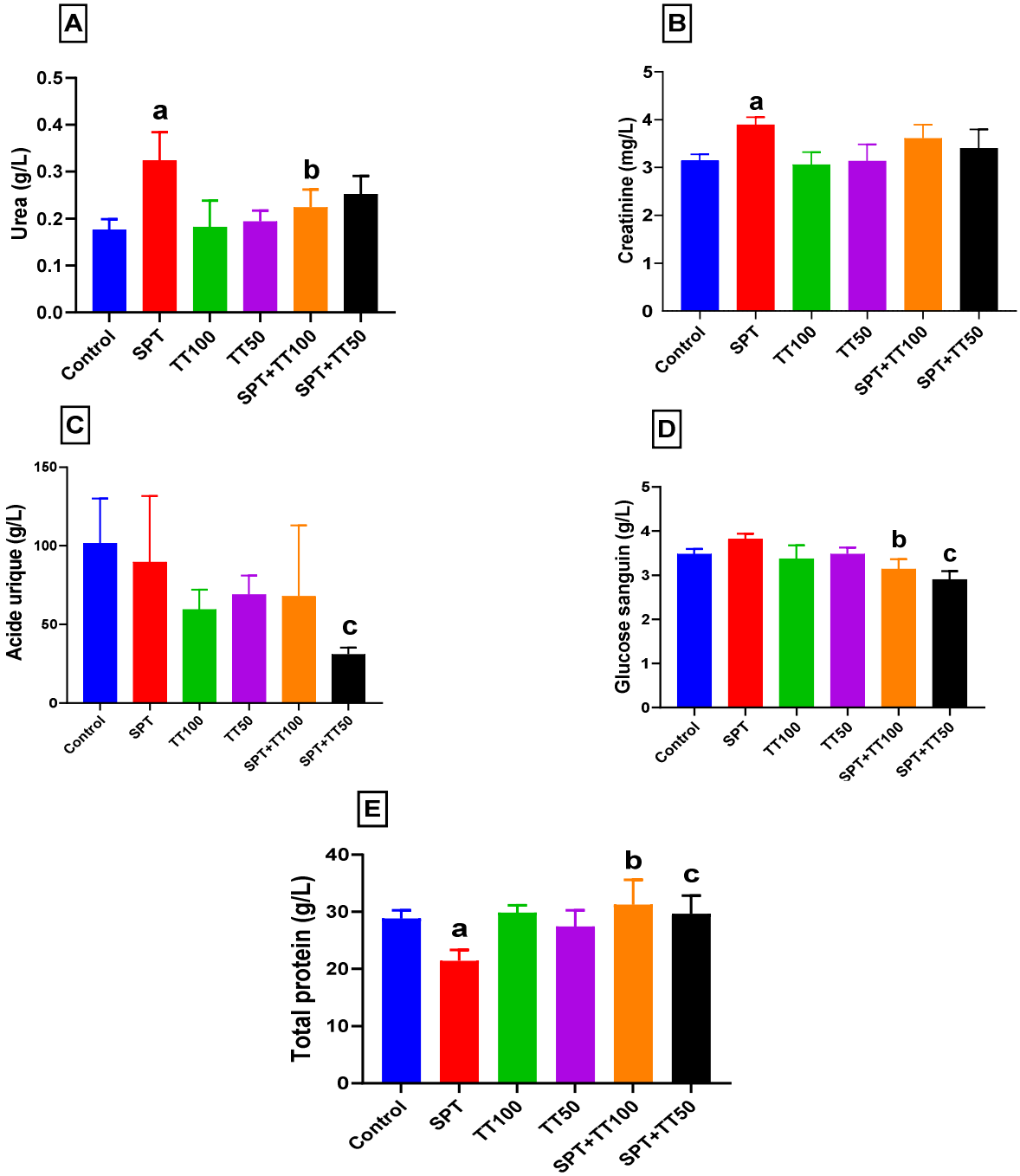

Fig. 3. The effect of SPT and TT on plasma urea (A), creatinine (B), uric acid (C), glucose (D), and total proteins' (E) concentrations (Mean ± SD) of male pigeons after ten consecutive weeks. SPT: Spirotetramat (15 mg/kg BW/day), TT100: *T. terrestris* (100 mg/kg BW/day), TT50: *T. terrestris* (50 mg/kg BW/day). a, difference between control and SPT; b, difference between SPT and SPT + TT100; c, difference between SPT and SPT + TT50.

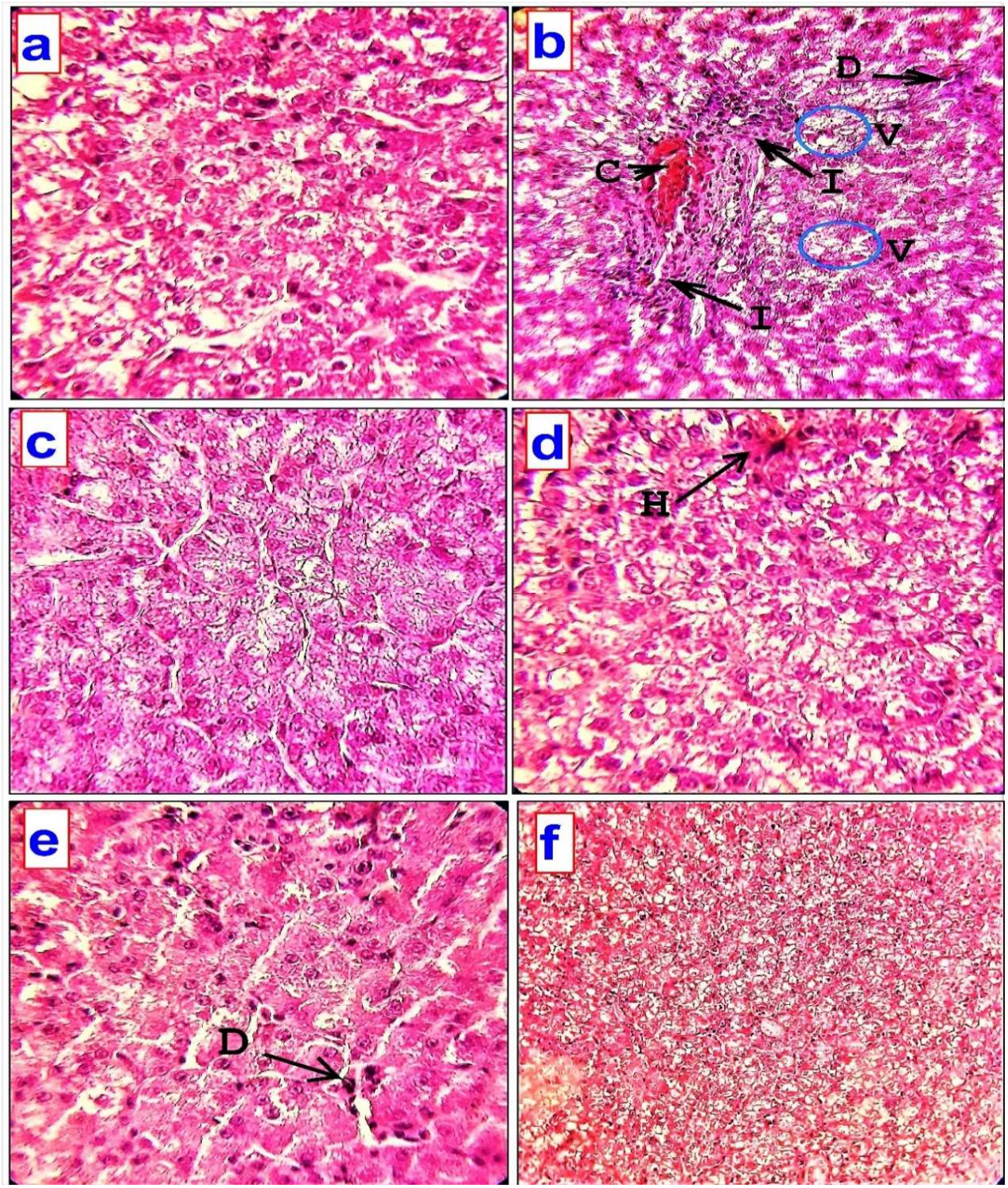

Fig. 4. Hepatoprotective effect of TT in SPT-intoxicated male pigeons treated for ten consecutive weeks. (a)*:* **Control group shows normal morphology.** (b)*:* **SPT-treated group shows portal infiltration with inflammatory cells [I] and degeneration of hepatocytes [D] and congestion of central vein [C] and cytoplasmic vacuolization [V].** (c) **and** (d)*:* **TT-treated gills show the normal architecture of tissue section with some hemorrhage [H]. SPT+TT-Treated groups show some degeneration of hepatocytes [D] and mild congestion, and the architecture was preserved (e and f). Magnification x40 (d) and magnification x10 (a, b, c, e, and f).**

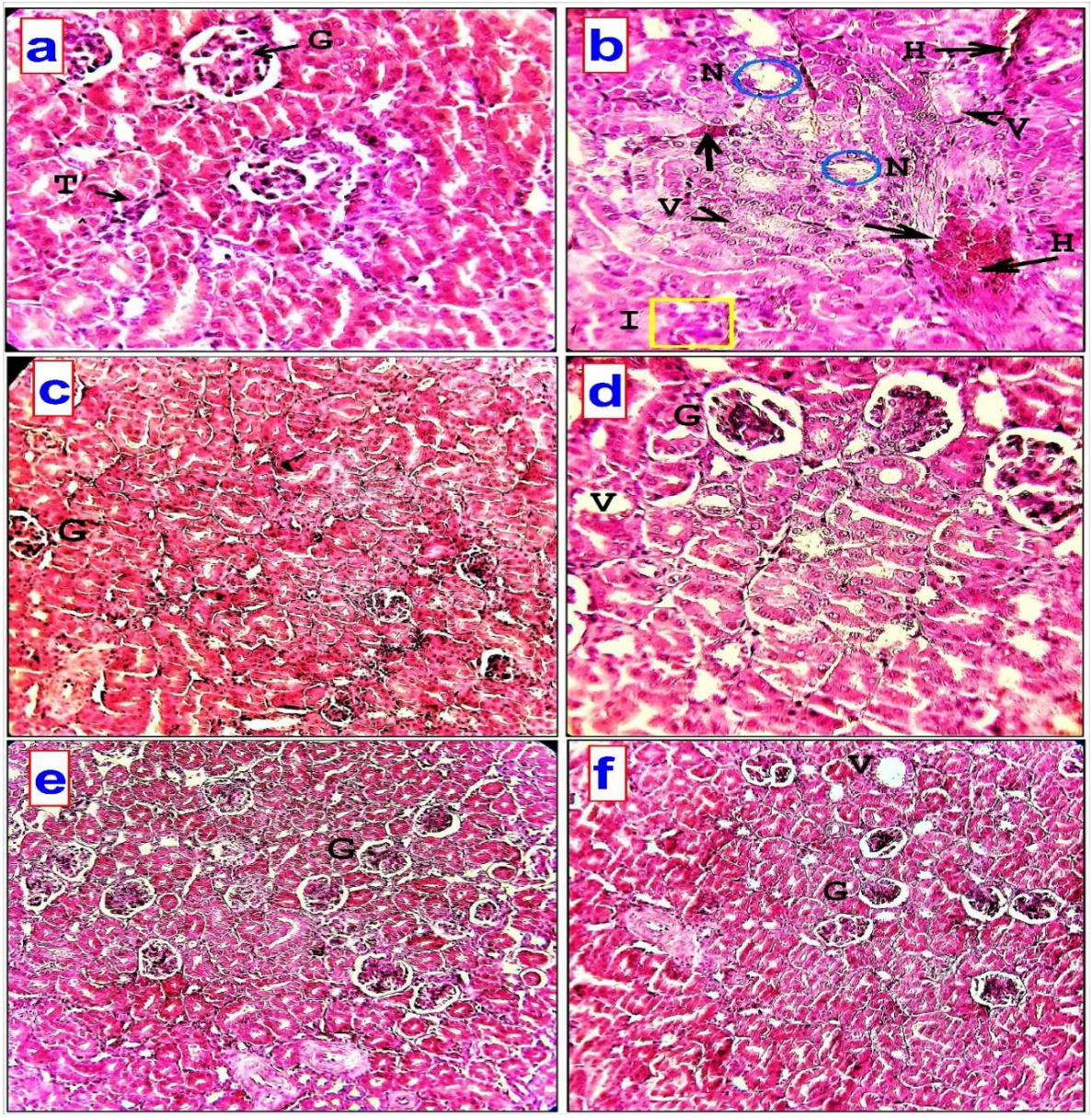

Fig. 5. Nephroprotective effect of TT in SPT-intoxicated male pigeons treated for ten consecutive weeks. (a): Control group shows normal morphology of the glomerular [G] and tubules [T] at the cortex. (b): SPT-treated group shows glomerular with inflammatory [I], focal necrosis (N) of renal tubules associated with hemorrhage [H], and vacuolation [V] of tubular epithelium. (c) and (d): TT-treated groups, show a typical architecture of tissue section with some vacuolization [V]. (e) and (f): SPT+TT-treated groups, show near-normal architecture with very mild cloudy swelling of tubular epithelium and some vacuolization [V]. Magnification x40 (a, b and d) and magnification x10 (c, e, and f).

DISCUSSION

Hepato-renal dysfunction is one of the most significant inevitable elements during the disposition of drugs or xenobiotics (Cepa *et al*., 2018). Pesticides may cause organ toxicity, oxidative tissue damage, endocrine disruption, and reproductive toxicity (Gaikwad *et al*., 2015). According to literature reviews, free radical-mediated oxidative stress is responsible for pesticide toxicity and other chemicals (Abdollahi *et al*., 2004). SPT is a new foliar systemic tetramic acid insecticide that is effective against sucking insects, including aphids, psyllids, and whiteflies (Frank and Lebude, 2011).

The present study showed an increase in liver relative weights after 10 weeks of exposure to SPT. These results are in accordance with Abolaji *et al*. (2017),

who observed that co-exposure of rats to the pesticides Chlorpyrifos and Carbendazim reduced weight gain and altered relative kidney weights. In addition, similar results are obtained by Shakeel *et al*. (2020) after applying the insecticide Chlorpyrifos, which can cause a significant increase in the absolute and relative weights of the liver. In addition, the study of Silini *et al*. (2022) about the two pesticides Deltamethrin, Abamectin and their mixture and the results of Slımanı *et al*. (2021) in the pigeon (*Columba livia domestica)* treated with the fungicide Thiram showed an increase in the relative weights of liver and kidney. According to Mccormack (2009), blood carries toxins to organs like the liver and kidney after pesticide exposure, in which the kidney was found as a target organ in rats at mid and high doses and the liver at the highest dose. The enlargement of the liver in exposed birds was a strong indication of SPT hepatotoxicity (Shakeel *et al*., 2020).

The obtained results demonstrated that SPT administration to male rats has led to an elevation in the activities of ALT, AST, and GGT. Similar results were obtained by the study of Shakeel *et al*. (2020), who found a significant increase in ALT, AST and ALP in the serum of pigeons (*Columba livia domestica*) exposed to the insecticide Chlorpyrifos. Another study on the brain and liver of rock pigeons (*Columba livia domestica*) showed a significant increase in serum levels of alanine aminotransferase (ALT), lactate dehydrogenase (LDH) following exposure to the insecticide Imidacloprid (Abu Zeid *et al*., 2019). These results could be related to membrane leaking of these hepatic key enzymes as it was reported that hepatocyte destruction and necrosis had increased cell membrane permeability and so plasma amino-transferase activities (Arfat *et al.*, 2014). Moreover, ALT, AST, and GGT are essentiel indicators of liver failure and hepatotoxicity in patients (Abdel-Daim *et al.*, 2013; Rjeibi *et al*., 2016). SPT toxicity to rats perhaps provoked lipid membranes' peroxidation, as it was demonstrated that peroxides caused rapid alteration of the function and structure of membranes such as those of mitochondria, endoplasmic reticulum, and lysosomes, (Toughan *et al*., 2018). It was found that damaged or inflamed liver cells could liberate more metabolites and substances, including liver enzymes, into the blood (Nimavathi *et al*., 2021), hypothesing that the plasma elevation of these enzymes was proportionate to the degree of hepatocyte injury and necrosis (Ramaiah, 2007).

In this study, a decrease in the concentration of total plasma proteins after ten week oral exposure of pigeons to SPT may be an indication of liver dysfunction, since most blood proteins are synthesized in the liver (Yang and Chen, 2003); these findings may be the cause of protein synthesis disruption mainly albumin due to hepatocytes' impairment (Pahwa and Chatterjee, 1990). It was suggested that the reduction in total protein levels reported in the malathion-exposed rats may be related to a decrease in hepatocytes (Elzoghby *et al*., 2014). Our data showed a significant increase in relative kidney weight in SPT-treated pigeons, similar to the findings observed in mice intraperitoneally administered with a single dose of 45 mg/kg of Cisplatin (Kim *et al*., 2005). In the present study, plasma creatinine and urea were higher in pigeons received SPT for ten weeks that is probably linked to renal function alterations, where birds were unable to excrete these very toxic metabolites. Similar elevations in plasma creatinine and urea were observed with the Propoxur insecticide in pigeons (*Columba livia domestica*) (Azab *et al*., 2016) and the Thiram fungicide (Slimani *et al*., 2021) in the pigeon (*Columba livia domestica)*. In addition, Jayasree *et al*. (2003) found that day-old male broiler chicks given Deltamethrin (100 mg/kg feed) for 6 weeks had increased serum urea, possibly due to free radical damage. The current study's elevated blood urea and uric acid may be attributed to SPT-induced renal dysfunction and decreased glomerular filtration rate (Azab *et al*., 2016). As suggested by Kumar *et al*, (2011), reduced mitochondrial activity in mice intoxicated with the pesticide Chlorpyrifos, has induced excessive reabsorption in the proximal tubule, affecting urea, uric acid, and creatinine balance.

Actually, herbs are used for their preventive and curative benefits against liver disorders, because they have antioxidant activities against radicals generated mainly by xenobiotics (Hussein *et al.*, 2016). In the current study, TT co-administration with the SPT restored liver and kidney weight of male pigeons. Similar findings were recorded in rats, which demonstrated that TT supplementation to gentamycin-induced toxicity to rats has led to a reduction in kidney weight (Kilany *et al*., 2020). The protective effects of TT on SPT-exposed pigeons' liver and kidney relative weights may be due to its ability to counteract SPT-generated free radicals.

Our liver function tests suggested that TT-treated pigeons were protected against SPT-induced liver damage by normalizing AST, ALT, and GGT levels due to the presence of different components including high polyphenolic content and the excellent radical scavenging activities that protect cell membrane damage and reduce oxidative stress (Reshma *et al*., 2015). Similar findings were observed in mercury-treated mice (Sugunavarman *et al.*, 2010). Furthermore, TT was reported to protect rats against cyclosporine-induced nephrotoxicity (El-Beih *et al*., 2017) and freshwater fish from atrazine-induced hepatotoxicity (Nimavathi *et al.*, 2021b). Moreover, Cabrera *et al*. (2006) indicated that the powerful antioxidants properties of polyphenols may boost antioxidant enzyme production in cells. However, antioxidant activities of polyphenols in the TT extract may have kept plasma liver enzymes within the normal ranges (Eagappan *et al.*, 2015). The obtained results

suggested that TT preserved membrane integrity and reduced hepatic toxicity of pigeons treated with SPT.

Following SPT co-administration, plasma urea and uric acid levels decreased, while total protein levels increased, suggesting that TT-treatment improved renal function in pigeons. Previous studies demonstrated that oral administration of TT have decreased plasma creatinine and urea levels in streptozotocin-induced diabetic rats (Amin *et al*., 2006). Similar results were demonstrated in metronidazole-treated mice (Kumari and Singh, 2015), ethylene glycol-treated rats (Saxena and Argal, 2015), and cadmium-treated rats (Kumar and Singh, 2016).

Our findings suggest that TT's nephroprotective effect may be linked to reduced renal oxidative stress. TT extract has been demonstrated to reduce renal epithelial damage, inflammation, and glomerular architecture in oxalate-induced rats (Raoofi *et al*., 2015).

According to our data, supplying TT to SPT-exposed pigeons-maintained plasma glucose almost within physiological ranges. Previous studies indicated similar results as that of Li *et al*. (2002), where TT's saponin decreased blood glucose in alloxan-induced diabetic rats, and that of Azam *et al*. (2019) on diabetic mice supplemented with TT methanolic extracts at a dose of 50 mg/kg body weight after 4 and 6 hours of treatment. In addition, the combination of TT and *Andrographis paniculata*, as well as Amaryl®, have significantly improved the abundance of islet cells against atrophy and degeneration, specifically in the β-cell area (Istiak *et al*., 2018).

In the current study, histological examination indicated that exposure to SPT revealed distorted liver and kidney histo-architecture. Similar findings were reported by Falcón *et al.* (2013), who proved that the insecticide SPT might cause liver and kidney damage in male Wistar rats. Like most pesticides, SPT also causes alterations in hepatic and renal tissues. Likewise, histological degenerations of Imidacloprid, Chlorpyrifos (Arfat *et al*., 2014; Deng *et al*., 2016), Thiram fungicide (Slimani *et al*., 2018), and Cypermethrin (Berkani *et al.*, 2022). Moreover, SPT was found to injure zebrafish gonadal development through histological inflammation and cell apoptosis (Zhang *et al*., 2020b). These changes in histoarchitecture of pigeons may be due to the toxic effects of SPT via the induction of ROS that can damage cell components.

On the other hand, TT reduced SPT-induced hepato-renal histological alterations in pigeons. In gentamicin-treated rats, TT supplementation decreased renal tubule damage, oxidative stress, and apoptosis (Harborne and Williams, 2000). Our data suggest that TT's components may protect tissue damage. According to Choi *et al*. (2004), TT's antioxidant properties may regulate enzymes involved in cell division, proliferation, detoxification, inflammation, and immune responses. After reperfusion injury in rat cardiac muscles, TT extract reduced oxidative stress and cell death (Zhang *et al.*, 2010). Thus, plants' steroids saponins and flavonoids were demonstrated as the most bioactive phytoconstituents (Zheleva-dimitrova *et al*., 2012; Azhar *et al.*, 2020), and also the TT's antioxidant, anti-inflammatory, and anti-apoptosis activities might be used to treat degenerative disorders (Tian *et al*., 2019).

Conclusion: The current study has established that the oral administration of the pesticide SPT to male pigeons has disrupted most plasma markers and the histological architecture of liver and kidney after ten weeks consecutive exposure. On the other hand, the co-administration of TT methanolic extract with SPT has roughly reduced such toxicity, suggesting that this spontaneous herb could be used in the protection of hepato-renal toxicity against pesticides.

Authors contribution: AB, SS and MN contributed in the study design, experimental work and writing the manuscript. SH and AB contributed in statistical analysis. AB and SS performed the histopathological examination. AB and SS analyzed the sera and tissue samples. SA corrected the writing language of the manuscript. All authors interpreted the data and approved the final version.

Conflict of interest statement: The authors declare that there is no conflict of interest.

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