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Toxicological Investigation of Byleton (Triadimefon) Following Oral Administration in Nubian Goats (*Capra aegagrus hircus*), Sudan

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Abstract: Humans and animals in Sudan continuously ingest fungicides through their food, and their effects are pronounced. Triadimefon is a triazole Agro-fungicide for many cereals, fruits, and vegetables. The objective of this work is to evaluate the toxicity of Triadimefon. Are designed to investigate the hematological, immunological, and histopathological effects of Triadimefon on goats. Twelve healthy male Nubian goats were dosed orally with Triadmefon at rates of 500, 300, and 100 mg/kg/day; three goats were untreated (control) for twelve weeks. Dosed animals showed poisoning signs five minutes post dosing, death occurred within 6- 24 hrs. in animals dosed with 500 mg/kg/day. After 4 hrs., animals dosed with 300 and 010 mg/kg/day recovered. Gross lesions observed in the brain, lungs, heart, liver, kidneys, and digestive tract were slight to moderate congestions and /or hemorrhages. The liver showed accentuation of the lobular markings, and the center of the lobule was the palest. Kidneys showed slight degenerative foci with a yellowish color. Heart was flabby. In lungs, some of the bronchioles contained acidophilic homogeneous material and /or lymphocytes and detached epithelial cells, while in the liver, there were hepatocyte cytoplasmic vacuolations. The kidneys' glomeruli either shrank or disappeared, or were infiltrated with lymphocytes. In all dosed groups, values of Packed Cell Volume and Hemoglobin

decreased significantly ($p<0.001$ and $p<0.01$) respectively, while value of Mean Corpuscular Hemoglobin Concentration increased significantly ($p<0.001$). The serum urea concentration and Glutamate Oxaloacetate Transaminase activity values were high ($p<0.001$). Significant decrease in serum Na ($p<0.001$) and Mg ($p<0.05$-0.01) was observed. The study on Triadimefon toxicity to Nubian goats has shown clear clinical, histopathological, hematological, and immunological changes.

Keywords: Triadimefon, oral dose, Toxicity, Nubian goats.

Introduction

Triadimefon, a systemic fungicide belonging to the azole group, was first registered in Sudan in 1980 (Plant Protection Directorate, 1998). Its chemical formula is C14H16ClN3O2 and it is systematically named 1-(4-chlorophenoxy)-3,3-dimethyl-1-(1H-1,2,4-triazol-1-yl) butan-2-one. Both Triadimefon and its primary metabolite, triadimenol, are known for their persistence in plant materials and soils, exhibiting low mobility and minimal bioaccumulation in fish and animal fats (FAO/WHO, 1979).

In humans, Triadimefon poisoning can manifest as nausea, excitation, and drowsiness (Bayer, 1985). Synergistic effects have been observed when Triadimefon is combined with other pesticides. For instance, a mixture of Triadimefon and Propiconazole at lower individual doses (50 mg/kg each) proved more toxic and rapidly fatal in Nubian goats than higher individual doses (100 mg/kg) of either fungicide alone, suggesting drug interaction (Tahir and Nour, 2009). Similarly, mixtures with other pesticides have shown synergistic effects on embryonic development (Wang *et al*., 2020).

Triadimefon is a zebrafish (Danio rerio) known neurotoxicant. Studies in rats revealed dose-dependent hyperactivity (100–200 mg/kg), rapid onset of motor activity, and recovery (Crofton *et al*., 1988). Higher doses (100–300 mg/kg) induced arousal stereotypies, including repetitive sniffing, head bobbing, pacing, and self-mutilation (Moser and MacPhail, 1989). Other neurobehavioral effects included handling-induced convulsions, altered reflexes, sensory reactivity changes, hypothermia, and body weight loss (Moser and MacPhail, 1989). Its effects in rats resemble those of psychomotor stimulants, increasing fixed-interval response patterning, motor activity, and producing stereotypes at high doses (Allen and MacPhail, 1993). Triadimefon and

triadimenol specifically inhibit dopamine uptake in rodents (Walker and Mailman, 1996), a mechanism that may contribute to their neurobehavioral effects. Notably, among 14 pesticides, only Triadimefon and triadimenol consistently induced hyperactivity in male Long Evans rats (Crofton, 1996), suggesting a rigid structure–activity relationship for this specific neurotoxic effect.

Chronic exposure to Triadimefon in mice (Mus musculus), rats (Rattus norvegicus), and dogs led to dose-related increases in liver weights and elevated serum hepatic alkaline phosphatase and transaminase activities (FAO/WHO, 1986). While enzymatic induction was reversible in rats upon cessation of exposure, mice exhibited significant histopathological changes, including hyperplastic liver nodules, at the highest dose tested (1800 ppm) (FAO/WHO, 1986). Triadimefon is known to bind to hepatic cytochrome P-450 and acts as a modest inhibitor of microsomal enzyme activities (FAO/WHO, 1986).

In rats, corn fodder containing Triadimefon (0.6%) caused body mass loss in females, and at higher doses (1600 and 6400 mg/kg fodder), decreased transmural electrical potential differences in the gastric mucosa (Jonderko *et al*., 1990). Triadimefon has been shown to alter spleen weights (Berman et al., 1995). The lowest effective dose for systemic toxicity was found to be within 3–56% of the acute LD_{50} and 1–30% for repeated administration (Berman *et al*., 1995).

The U.S. Environmental Protection Agency classified Triadimefon as a "possible human carcinogen" (Class C) based on limited animal evidence (US EPA, 1997). Experimental evidence suggests its potential for liver carcinogenicity in rodents, as it induced preneoplastic lesions in the liver of rats (Hakoi *et al*., 1992). It has also been linked to an increase in thyroid follicular cell tumors in treated rats and liver adenomas in both sexes of two strains of treated mice (US EPA, 1996).

Studies in timed pregnant rats showed that Triadimefon caused maternal toxicity, slight developmental toxicity, and delayed parturition (dystocia) (Menegola *et al*., 2013). It is suggested that azoles, including Triadimefon, act as teratogens in rats through a common mode of action, necessitating their grouping for risk assessment (Narotsky and Kavlock, 1995). High doses of azole drugs like ketoconazole can inhibit adrenocortical steroid and testosterone synthesis, potentially leading to gynecomastia in male humans (Hayes, 1985).

Triadimefon poses significant reproductive and developmental risks to aquatic life. Zebrafish embryos exposed to Triadimefon exhibited severe morphological malformations, including craniofacial defects, absent mandibles, hypoplastic pharyngeal arches, massive pericardial edemas, abnormal heart shapes, bradycardia, and inhibited or absent blood circulation (Liu *et al*., 2017; Zoupa and Machera, 2017). Furthermore, Triadimefon and its enantiomers demonstrate endocrine-disrupting effects on lizards (Eremias argus) by sensitively affecting sex steroid hormones and steroidogenic-related genes (Li *et al*., 2017). Its presence in surface waters and impact on hormonal pathways can disrupt tadpole development and metamorphosis (Zhang *et al.*, 2018), leading to adverse effects on the aquatic population and even ecosystem levels (Hou *et al*., 2022).

The objective of this work is to evaluate the toxicity of Triadimefon.

Hypothesis:

No prior detailed toxicity studies in goats, especially Nubian goats, which may have different metabolic or physiological responses. Based on previous toxicological data in other species and the chemical nature of Triadimefon, it is reasonable to hypothesize that oral administration of Byleton may cause detectable toxic effects in Nubian goats. These effects are expected to manifest as changes in clinical signs, alterations in blood biochemistry (such as liver and kidney function markers), and histopathological lesions in major organs. Consequently, this will affect public health due to the pesticide residue reaching humans when consuming meat and milk from grazing animals.

Materials and Methods:

Twelve healthy Nubian goats (*Cappara aegagrus hicus*) 5-6 months old and weighing 8.5-12 kg, were divided randomly into 4 groups, each of three goats; one group was undosed (control). All goats were fed on forage sorghum (Abu-70), *Sorghum vulgare*, and provided water *ad libitum.* Goats in groups 1, 2, and 3 received doses by drench of Bayleton agro-fungicide at the rate of 100 mg/kg /day, 100 mg/kg/day of Tilt, and 100 mg/kg/day. The Bayleton was obtained from the Khartoum Pesticide Market. Drenching continued until the animals died or were slaughtered. Postdosing sampling of blood was taken on day 1, 3, 7, 14, 21, 28, 42, 56, 77, 98, and 120. Additional samples were taken from animals in moribund condition. Samples from the brain, spinal cord, heart, lungs, liver, spleen, kidneys, abomasum, omasum, and small intestine were obtained from dead or slaughtered animals and immediately preserved (Table 1).

Table 1: Dose and animal fate in Nubian goats poisoned with Triadimefon

Group	Animal No.	Sex	Initial weight (kg)	Final weight (kg)	Dose (mg/day)	Fate of the animal
Group 1	1.	Female	12	12	500	died after 6 hrs.
	2.	Male	9	9	500	died after 1 day.
	3.	Male	7	7	500	died after 1day.
Group 2	4.	Male	9	8	300	died after 18 days.
	5.	Male	8.5	7	300	died after 15 days.
	6.	Male	8	8	300	died after 18 days.
Group 3	7.	Male	7	6	100	slaughtered after 12 weeks.
	8.	Female	7.5	7	100	slaughtered after 12 weeks.
	9.	Female	7.5	6	100	slaughtered after 12 weeks.
Group 4	10.	Male	9	11	0.00	slaughtered after 12 weeks.
	11.	Female	9	11	0.00	slaughtered after 12 weeks.
	12.	Male	8	10	0.00	slaughtered after 12 weeks.

Clinical and Hematological Investigations:

Tested animals were closely observed for clinical signs and behavior. Body weight changes were recorded weekly. Dead or slaughtered animals underwent postmortem examination, and lesions were recorded. Fresh blood was investigated for haemoglobin concentration (Hb), packed cell volume (PCV), red blood cells (RBC) count, white blood cells (WBC) count, mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), and mean corpuscular haemoglobin concentration (MCHC) (Dacie and Lewis, 1991). Serobiochemical analysis includes Glutamic-Oxaloacetic Transaminase (GOT), total protein, and total urea were determined using a commercial kit (Plasmatec laboratory products Ltd., England). Serum concentration of calcium (Ca), magnesium (Mg), sodium (Na), potassium (K), copper (Cu), iron (Fe), manganese (Mn), and zinc (Zn) was determined using an atomic absorption spectrophotometer (PERKIN - ELMERT 2380, Germany). Tissue samples for histopathological studies were prepared according to Mahaney (1983). The sections were stained by Mayer's double staining method (Haematoxylin and Eosin, H & E). Photography of sections was by light microscope (Leitz DIALUX 20, LEITZ WESTZLAR 513467, Germany) fitted with camera (WILD 11, Wild Heerburg, Switzerland).

Statistical analysis:

Data from the treated and non-treated groups of animals were analyzed using Student's t-test (Byrkit, 1987).

Results

Clinical signs:

Oral doses of Triadimefon and animal fate are summarized in Table 1. Animals in groups 1, 2 and 3 showed five minutes postdosing salivation, grinding of teeth, frothing (Figure.1), muscle tremor especially of the hind limbs, tail fagging, frequent urination and defecation. Twenty minutes later, poisoned animals in group 1 showed depression, weakness in the hind limbs, incoordination, and became recumbent, and death occurred at 6- 24 hrs. After 4 hrs of the first dose, animals in groups 1 and 2 recovered. After the second dose, the previously mentioned signs were mild, but they were more aggressive, knocking heads with each other and against hard objects. On day 7, the fecal color was yellowish in group 1. The animals of groups 2, 3, and 4 died or were slaughtered in weeks 2-12. The loss in body weight was not significant in groups 1 and 2.

Postmortem lesions:

These lesions are summarized in Table 2. Gross lesion observed in the brain, lungs, heart, liver, kidneys and digestive tract (abomasum, omasum and intestine) were slight to moderately congested and /or hemorrhagic. Both trachea and lungs contained froth, specially when excised. The liver showed accentuation of the lobular markings and the center of the lobule was the palest part, particularly in group 1. The kidneys showed slight degenerative foci with a yellowish colour. The heart was flabby and slightly congested in group1 and with slight hydropericardium in group 3. The urinary bladder was distended with urine without obstruction of the urinary tract.

Table 2 Postmortem lesions in Nubian goats poisoned with Triadimefon

Organ	Lesions	Groups			
		1	2	3	4
Brain	Congestion	-	-	-	-
	Haemorrhage	+ +	+	+	-
Trachea	Froth	-	-	-	-
Lungs	Congestion	+	+	-	-
	Haemorrhage	+	+	+	-
	Oedema	+	+	+	-
	Emphysema	+	+	+	
Heart	Congestion	+	-	-	-
	Haemorrhage	-	-	-	-
	Flabbiness	+ +	+	+	-
Liver	Congestion	+	+	+	
	Haemorrhage	+	+	+	
	Fattychange /necrosis	+ +	+ +	+ +	-
Kidney	Congestion	+	+	+	-
	Haemorrhage	+	+	+	-
	Fattychange and/ or necrosis	+ +	+ +	+ +	-
Abomasum and omasum	Congestion	+	+	+	-
	Abomasitis	+	+	+	-
	Omasitis	+	+	+	-
Intestine	Congestion	+ +	+	+	-
	Haemorrhage	+	+	+	-
	Enteritis	+	+	+	-

+ + + severe ;+ + moderate; + slight ; - no lesions.

Histopathological findings:

Lungs: Some of the bronchioles contained acidophilic homogeneous materials and /or lymphocytes and detached epithelial cells (Photo 1) in group 1 animals. Peribronchiolar lymphocytic infiltration was seen in groups 2 and 3, and the bronchioles were slightly dilated. Some of the alveoli were ruptured and others contained RBC and /or lymphocytes mixed with homogenous acidophilic materials.

Liver: Severe to moderate hepatocytic cytoplasmic vacuolations were observed in Triadimefon -dosed animals, extending from the central zone to midzone and sometimes throughout the hepatic tissue (Photo 2). In group 1, the hepatocytic cytoplasmic vacuolation might extend into the portal tract. While in groups 2 and 3, it

was centrilobular, and the sinusoids were congested and severely dilated. Slight bile duct hyperplasia was seen.

Kidneys: In group 1 animal's glomeruli either shrank, demonstrating widening of Bowman's space with the tuft of glomeruli not filling it, or disappeared or infiltrated with lymphocytes. The proximal convoluted renal tubules showed severe hydrophilic vacuolations, and some of them underwent necrosis. In groups 2 and 3, the necrosis might occur individually, and some of the renal epithelial cells were detached into the lumen (Photo 3). There was congestion of renal blood vessels and medullary rays, and scattered small foci of RBC were also seen in the interstitial tissue. Some of the collecting ducts exhibited individual cell necrosis. Some of the medullary renal tubules contained RBC, while scattered inflammatory cells were also seen in the medullary interstitial tissue adjacent to the tubules.

Abomasum, Omasum, and Intestine: Slight mucosal and submucosal lymphocytic infiltration was seen in all Triadimefon -dosed groups. Group 3 animals showed slight intestinal mucosal hemorrhage and abomasum congestion.

Spleen: Slight hemosiderin deposits were seen in the goats of group 1.

Heart: Scattered foci of RBC and inflammatory cells were noticed between the cardiac muscle bundles (Photo 4).

Other organs: No significant histopathological changes were observed in the brain and spinal cord of the dosed animal. No lesions were observed in the goats of group 4.

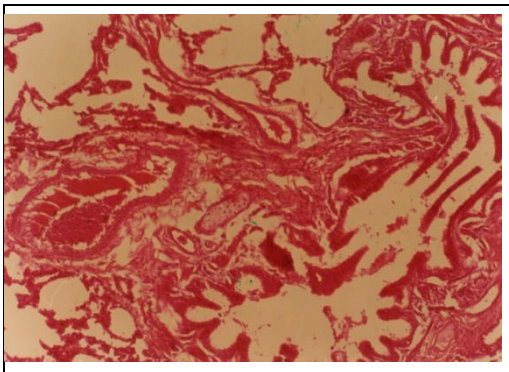	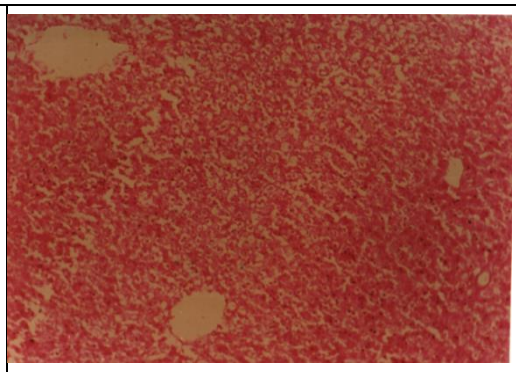
Photo 1 Section through lung showing bronchioles contained RBC, acidophilic material and detached epithelial cells (40XH&E).	Photo 2 Section through the liver showing necrosis and/or fatty cytoplasmic hepatocytic vacuolations (10XH&E).

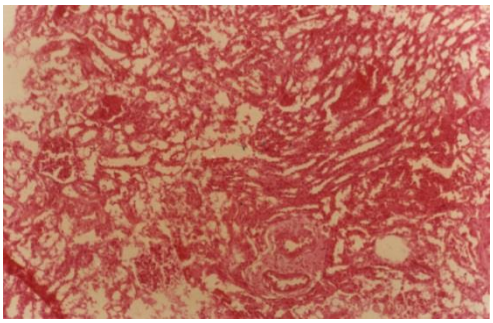	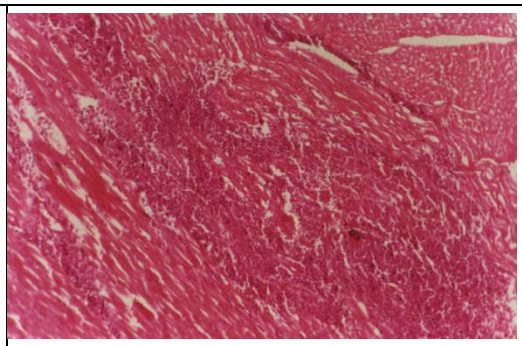
Photo 3 Section through the kidney of Nubian goat treated with Bayleton showing proximal convoluted tubules undergone hydrophilic vacuolation and the glumerular tuft were lobulated in addition congestion of the medullary rays(40XH&E).	Photo 4 Section through heart of Nubian goat treated with Bayleton, showing RBC and inflammatory cells between the cardiac muscle bundles (10XH&E).

Haematological findings:

The results of hematological parameters of different dosages and the control group are given in Table 3. In all dosed groups, the values of PCV and Hb decreased significantly ($p<0.001$ and $p<0.01$, respectively, while the value of MCHC increased significantly ($p<0.001$). The MCV value decreased significantly ($p<0.001$) in group 1. The value of RBC decreased significantly ($p<0.001$) and the values of MCH increased significantly ($p<0.001$) in groups 2 and 3. The values of WBC increased significantly ($p<0.05$) in group 6.

Table 3 Hematological findings for Nubian goats dosed with Triadimefon

Group	Parameter						
	RBC ($X10^3\mu l$)	PCV (%)	HB (gm/dl)	MCV (fl)	MCH (pg)	MCHC (gm/dl)	WBC (μl)
Group 1	12.532 ± 0.969 N.S.	20.50± 1.11 ***	7.49 ± 0.14 **	16.36 ± 1.49 ***	6.00 ± 0.05 N.S.	36.50 ± 0.87 ***	8.125 ± 1.638 N.S.
Group 2	9.900 ± 1.103 ***	21.60± 2.60 ***	7.46 ± 0.34 **	21.82 ± 3.62 N.S.	7.50 ± 0.80 ***	34.50 ± 3.38 ***	11.063± 1.379 *
Group 3	9.942 ± 1.772 ***	21.53± 2.73 ***	7.25 ± 0.59 **	21.66 ± 1.82 N.S.	7.30 ± 0.30 ***	33.7 ± 0.53 ***	9.619 ± 2.796 N.S.
Group 4 (control)	13.394 ± 0.63	26.28± 2.31	7.93 ± 0.34	19.62 ± 1.42	5.95 ± 0.53	30.20 ± 2.17	9.271 ± 1.783

* = $p<0.05$; ** = $p<0.01$; *** = $p<0.001$; N.S. not significant.

Serobiochemical findings:

Values of some serum constituents of the experimental and control groups are shown in Table 4. In group 2, the post-dose values of total protein were significantly low ($p<0.001$). The serum urea concentration and GOT activity values were high ($p<0.001$) in all Bayleton-poisoned groups, compared to the control group values. Significant decreases in serum Na ($p<0.001$) and Mg ($p<0.05$-0.01) were recorded in goats of groups 1 and 2, respectively. In group 1, the Zn value decreased ($p<0.05$). No significant changes were recorded in serum concentrations of Ca, K, Cu, and Fe in any of the dosed animals when compared with values recorded in the control group.

Table 4 Serobiochemical findings for Nubian goats dosed with Triadimefon

	GOT	GOT I.U.	To. protein g/100ml	Urea mg/ 100ml	Ca mg/ 100 ml	Na mg/ 100 ml	K mg/100 ml	Cu µg/ml	Fe µg/ml	Mn µg/ml	Zn µg/ml
Group 1	8900 ± 011 * * *	7.07 ± 0.85 N.S.	40.17 ± 0.82 * * *	10.48 ± 1.76 N.S	0.75 ± 0.03 *	336.70 ± 8.0 N.S	11.15 ± 123 N.S	1.06 ± 0.17 N.S.	1.06 ± 0.02 N.S	0.19± 0.09 N.S.	0.77± 0. 01 *
Group 2	62.38 ±15.76 * * *	5.48 ± 0.33 * *	46.67 ± 6.65 * **	10.27 ± 1.07 N.S	0.79 ± 0.12 *	331.7 ±15.3N.S	10.61 ± 0.47 N.S.	1.34 ± 0.34 N.S.	1.60± 0.03 N.S.	0.16 ± 0.03 N.S.	0.91± 0.11 N.S.
Group 3	65.36 ± 5.77 * **	7.58 ± 2.46 N.S.	38.30 ± 6.67 * **	10.22 ± 1.10 N.S	0.90 ± 0.11 *	348.0 ±16.3 N.S	10.16 ± 0.61 N.S.	0.94 ± 0.13 N.S.	1.64 ± 0.09 N.S.	0.15 ±0.03 N.S.	1.09 ±0.12 N.S.
Group 4	21.00 ± 0.30	7.68 ± 0.86	17.48 ± 1.67	10.19± 0.79	0.96 ± 0.16	358.50 ± 11.7	10. 48 ± 0.89	0.98 ± 0.02	1.42 ± 0.05	0.15± 0.02	0.97 ± 0.11

* = $p<0.05$; ** = $p<0.01$; *** = $p<0.001$; N.S. not significant.

Discussion

The present study has shown that a single oral dose of 500 mg/kg/day of Triadimefon is fatal to Nubian goats within 24 hours; the dosed animals showed some clinical signs, goats were aggressive, knocking heads with each other and against hard objects after dosing. This behavior may be linked to the role of Triadimefon in inhibiting dopamine uptake, as discussed by Crofton et al. (1989), Walker and Mailman (1996), and Perkins et al. (1991), which plays an important role in neurobehavioral effects. It has also been stated that Triadimefon and methylphenidate have discriminative stimulus properties (Perkins *et al*., 1991). Furthermore, studies showed that the effect of Triadimefon on the behavior of rats is similar to that of a psychomotor stimulant (Allen and MacPhail,

1993). The mechanism of action of drugs that stimulate the central nervous system (CNS) is largely unknown, whether directly or indirectly (Bowman *et al*., 1974). Triadimefon has also been shown to inhibit spatial learning and impair spatial reference memory, with associated decreases in hippocampal retinoic acid concentration in rats (Xi *et al*., 2018; Holden *et al*., 2018). However, the power and precision of muscle function are governed by the central cortical areas, basal ganglia, and cerebral regions. Generally speaking, basal ganglia are stimulated by acetylcholine and inhibited by dopamine (Sukker *et al*., 1998).

Acute poisoning in humans by propiconazole and prolonged inhalation of its vapor may irritate the throat and nasal passages, and cause CNS effects like headache, dizziness, confusion, and nausea, and if swallowed, abdominal pain, nausea, gastritis, breathing difficulty, or diarrhea may occur (U.S. Department of Agriculture, 1999). It is estimated that azoles, used as human drugs, inflict toxicity. For example, ketoconazole causes gastrointestinal disturbance, anemia, and hyponatremia; miconazole produces nausea, headache, and abdominal pain; and fluconazole causes liver toxicity (Rang and Dale, 1991).

Unlike the adrenal medulla, the adrenal cortex and its secretions are essential for life (Bowman et al., 1974). After bilateral adrenalectomy, there is a loss of appetite, rapid weight loss, and pronounced diuresis. This is followed by hypothermia, reduced basal metabolic rate, concentrated blood with increased urea and potassium levels, dramatic sodium loss in the urine, renal failure, severe muscular weakness, and ultimately death (Bowman *et al*., 1974).

The results of this study revealed that different oral doses of Triadimefon in Nubian goats were associated with decreases in RBC, PCV, and Hb, while MCV values fluctuated, indicating either microcytic or macrocytic anemia without clinical jaundice. RBC reductions were within the normal range (13.000–9.680 $\times 10^6/\mu l$) in Nubian goats estimated by Ibrahim (1992). It is found that human triazoles exert a hemolytic effect in humans (Doeglas, 1979). PCV concentrations were low in all treated animals. At low and prolonged doses (300, 100, and 20 mg/kg/day), no consistent trend in PCV was observed. However, the PCV value depends on two factors: the plasma volume in the blood and the mass of red cells (Anderson, 1984). In this study, red cell mass and Hb were low, especially at the high dose of 500 mg/kg/day of Bayleton. These factors, along with hemorrhage and organ congestion observed at postmortem and histology, play a major role in reducing RBC and Hb values. Leucopenia occurred at high doses,

suggesting that Triadimefon may have an immunosuppressive effect similar to benzene, sulphonamides, antithyroid, and glucocorticoid drugs in humans (Anderson, 1984). Triadimefon did not affect WBC count at any dose. The leukocytosis observed at low and repeated doses of the fungicide is attributed to inflammatory lesions in various tissues, such as the lungs, liver, and kidneys.

In the present study, the significant increase in serum urea and GOT levels is indicative of hepatorenal disorder caused by Triadimefon. Histopathological changes in the kidney and liver tissues confirmed this effect. According to FAO/WHO (1979), chronic feeding of mice, rats, and dogs with triadimenol produced a dose-related increase in liver weight, accompanied by elevated serum hepatic alkaline phosphatase and transaminase activities. It is stated that after four days of treatment with Triadimefon, male CD-1 mice showed a significant reduction in serum cholesterol, which is an early sign of liver dysfunction. This may be causally associated with later pathological changes, including cell death, increased cell proliferation, and tumor formation (Martin *et al.*, 1985). For Triadimefon-treated mice, a dose of 500 ppm led to significant weight reduction at five weeks, and the high dose of 1800 ppm showed weight reductions compared to controls at weeks 9, 12, and 13 (Martin *et al*., 1985).

Such elevation of Ca^{2+} and Mg^{2+} is accompanied by clinical disorders and renal insufficiency (Blood and Radostits, 1989). On the contrary, hypocalcemia recorded in this study is attributed to abomasitis (Ammerman et al., 1971). The hypomagnesemia observed may be due to loss of appetite, resulting in rumen dysfunction (Tomas and Potter, 1976). The primary site of magnesium absorption in ruminants is usually the rumen (Tomas and Potter, 1976).

Conclusion: Triadimefon exposure in Nubian goats caused severe clinical, hematological, and histopathological changes, indicating systemic toxicity. These findings have important **public health implications** as pesticide residues from grazing animals could enter the human food chain through meat and milk, posing risks of chronic toxicity. From a **food safety** perspective, the results highlight the need for strict monitoring of fungicide residues in animal products. In **animal husbandry**, such toxicity could compromise animal health, productivity, and economic value, underscoring the importance of regulating agrochemical use in grazing areas. For **veterinary practice**, the study highlights the importance of early recognition, diagnosis, and management of pesticide poisoning in livestock. From a **pesticide regulation** perspective, these results call for stricter control of agrochemical application

in grazing areas, enforcement of maximum residue limits, and promotion of safer alternatives to protect animal and human health.

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Ethical approval:

The ethical approval for this study was obtained from the Ethics Committee of the College of Veterinary Medicine, **Sudan University of Science and Technology** (**SUST)**, Khartoum State, Sudan.

Conflict of interest

The authors state that they have no competing interests.

Availability of data:

All data and histopathological slides are available in the Department of Archeology, University of Khartoum.

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