



Original Research Article

Histopathological Changes in the Liver and Kidney of Albino Mice on Exposure to Insecticide, Dimethoate

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ABSTRACT

Keywords

Dimethoate,
Histopathology,
Liver,
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mice

The pesticides are one of the most potentially harmful chemicals liberated in the environment in an unplanned manner. Dimethoate is widely used as a potent pesticide in many countries and has been shown to produce some adverse health effects. The present study was undertaken to investigate the toxic effects of the organophosphorous pesticide, dimethoate on some organs of mice (liver and kidney). The Dimethoate was administered at the doses of 14mg/kg and 28 mg/kg. Treated mice groups showed many Histopathological changes in the liver, There were congestion blood vessels, hemorrhage, infiltration, vasodilatation, hydropic changes, fatty changes and hypertrophy. Meanwhile, kidney showed some changes including Glomerular Degeneration, Tubular Degeneration, Hemorrhage, Infiltration, Hydropic Changes, Tubular Cast, Tubular Widened Lumen, Glomerular Shrinkage and Compressed Blood Vessel. The results of this study confirmed that dimethoate seriously deteriorates some organ in Digestive system (liver and Kidney) of Albino mice.

Introduction

A great proportion of acute poisoning cases are caused by exposure to pesticides, especially organophosphate (OP) compounds. The primary mechanism of action of OP pesticides is based on inhibition of the acetylcholinesterase (AChE) enzyme Hazarika *et al.* (2003). Once AChE has been inactivated, acetylcholine (ACh) accumulates throughout the nervous system, resulting in overstimulation of muscarinic and nicotinic receptors. Signs and symptoms of OP poisoning can be divided into three broad categories, as muscarinic, nicotinic, and central nervous system effects.

management of severe poisoning is difficult, requiring intensive care and use of atropine and oxime cholinesterase reactivators (Eddleston *et al.*, 2005).

The toxicity of organophosphorus insecticides results in negative effects on many organs and systems such as the liver, kidney, nervous system, immune system and reproductive system (Kossmann *et al.*, 1997; Nagymajtenyi *et al.*, 1998; Gomes *et al.*, 1999; Aly and El-gendy, 2000; Mansour and Mossa, 2011). Several mechanisms of the organophosphorous toxicity have been

proposed, including through inhibition of acetylcholinesterase, leading to accumulation of acetylcholine and subsequent activation of cholinergic, muscarinic and nicotinic receptors (Ecobichon,1996). immunotoxicity (Galloway and Handy, 2003). Furthermore, organophosphorus insecticides exert their biological effects through electrophilic attack on the cellular constituents of hepatic and brain tissues (Samanta and Chainy, 1995) with simultaneous generation of reactive oxygenspecies (Sharma *et al.*, 2005a).

Toxicity of organophosphorus insecticides used compounds against human and animals were always evaluated by assessment of such biochemical parameters alterations and histopathological changes in tissues and organs (Ghanem *et al.*, 2006; Massoud *et al.*, 2010). Kidney is one of the targets organs of experimental animals attacked by organophosphorous compounds (Sivapiriya *et al.*, 2006; Mansour and Mossa, 2010).

Dimethoate,(IUPAC name O, O-dimethyl S-N-methyl carbamoyl methyl phosphorodithioate) is widely used against a broad range of insects and mites and is also used for indoor control of houseflies. The extensive use of Dimethoate poses a health hazard to animals and humans because of its persistence in soil and crops (WHO) and International Program on Chemical Safety (IPCS), 1996 ; Rose and Hodgson, 2004).

Dimethoate classified as moderately hazardous (kidd, *et al.*, 1991; IPCS and WHO, 2001). the oral dose of dimethoate is biotransformed to its oxygen analogue Omethoate, which is the active form, by hydrolysis of the methyl ester group and removal of the methyl-amido group (IPCS and WHO, 1991). Omethote is considerably

more toxic than dimethoate(IPCS and WHO, 2001).

U. S. Environmental Protection Agency (USEPA) has registered Dimethoate a systemic organophosphate insecticide but interim in 2006 it released reregistration eligibility decision (IRED) document for dimethoate in accordance with FQPA requirements. Moreover, there is lack of evaluating the toxicity of organophosphorus pesticides such as Dimethoate low concentration levels near the environmental level (Singh *et al.*, 2009).

Dimethoat Epoisoning is usually block neuromuscular transmission in both animals and humans (De-bleecker *et al.*, 1993).

Recent studies have shown that acute and sub chronic exposure to dimethoate alters the antioxidant status and the histology of liver , brain and testes of rat (Sayim, 2007b; Astiz *et al.*, 2009; Saafi *et al.*, 2011) and human erythrocytes (Gargouri *et al.*, 2011).The liver is the primary organ involved in xenobiotic metabolism and is a major target organ for chemical and drugs. Hepatotoxicity is therefore an important endpoint in the evaluation of the effect of a particular xenobiotic. Clinical Chemistry and histopathology evaluations are commonly used methods for detecting organ –specific effect related to chemical exposure (Travlos *et al.*,1996).

Few studies have been made on the histopathological effects of dimethoate (Thangavel, 1994 and Persis, 2001) in animals. Moreover, dimethoate induce hyperglycemia and cause various toxic effects on rat pancreas following acute, sub chronic and chronic exposure (Hagar and Fahmy, 2002; Kamath and Rajini, 2007; Kamath *et al.*, 2008).

The present study aimed to investigate the histopathological effects of the organophosphorous pesticide dimethoate that is extensively used in some agricultural areas in Yemen on some organs of laboratory animals.

Materials and Methods

Chemicals

Dimethoate(40% EC) O,O-dimethyl s-(n-methyl carbamoylmethyl) phosphorodithioate (IUPAC).is an organophosphorous pesticide with a chemical formula :



Trade name: cygon, cekuthoatedimet, dicap, devigon, perfokthion, Fosfamed, ferkethion, roxion, rego, afidox, rogodial, rogodan, trimetion and sevigor .It has a stomach action and a cholinesterase inhibitor. it is of low persistence in the soil, water and environment with half-lives of 4-16 days, may disappear from open waters due to microbial action or chemical degradation as photolysis and evaporation (USEPA, 2000a). was introduction by cheminovaco .baef-group. the acute oral LD₅₀ for mice used in the present study is 140 mg/kg according to WHO (2001). has classified dimethoate as “moderately hazardous.”Dimethoate was dissolved and diluted to the required doses using distilled water.

Design of experiment

A total of 45 adult male swiss albino mice strain *Musmusculus domestic* were used in the experiment animals were divided into three groups (each of 15 mice) .The first group was served as control group, and

received 0.2 ml of distilled water. The second group was given oral dose equivalent to 1/10 LD₅₀ (14 mg/kg b.w.) of dimethoate every other day (total of 30 treatments) while the third group given oral high dose equivalent to 1/5 LD₅₀ (28 mg/kg b.w.) of dimethoate alone every other day (Total of 30 Treatments). The experimental animals were maintained in the animal house on daily observations and well fed by mouse chaw under good conditions of ventilation and at room temperature of 24-25c, relative humidity of 50±150c and a normal photoperiod of 12 hours/day. All animals were housed in plastic cages made by London plastic/north kentldl and given standard diet and water *ad libitum* throughout the study.

Histopathological studies

After terminal the experiment all mice were necropsied. The liver was removed, washed in normal saline, fixed in bouin’s fluid while the kidney fixed instantaneously in 10% formalin for 24 hours. The liver washed in ethyl alcohol 70%, while the kidney washed in tap water, dehydrated in ascending grades of ethanol, cleared in xylene, embedded in paraffin wax (melting point of 50-56 c), Paraffin sections were cut at 6µm thicknesses using a rotary microtome, the sections were stained with harris haematoxylin and eosin. Observation were made using a light microscope and photographs were taken with an automatic photo micrographic system.

Results and Discussion

Histopathological changes in liver

The histopathological examination of the liver sections in the control untreated Mice group showed a normal histological picture. The central vein lies at the centre of the

lobule surrounded by the hepatocytes with strongly eosinophilic granulated cytoplasm, and distinct nuclei. In addition, between the strands of hepatocytes the hepatic sinusoids are exhibited as shown in (Fig.1a).

The liver of Mice treated with (1/10 the LD₅₀) of dimethoate showed that there were liver congestion and infiltration (Fig.1b), vasodilatation and congestion (Fig.1c) and hydropic changes (Fig.1D). Moreover, liver section of Mice in this group treated with high dose (1/5 the LD₅₀) of dimethoate showed Infiltration and congestion (Fig.2e), liver hemorrhage (Fig.2f), vasodilatation and congestion (Fig.2g), fatty changes (Fig.2h) and hypertrophy (Fig.2i).

Histopathological Alterations in kidney

Histopathological examination photomicrographs of the kidney sections in the control group showed a renal corpuscle and renal tubules, proximal convoluted tubules and distal convoluted tubules. further, the Glomerulus, urinary space and Bowman's capsule were noticed as shown in (Fig.3a).

The kidney of Mice Dimethoate inistrated with (1/10 the LD₅₀) of dimethoate showed Glomerular Degeneration (Fig.3b), Tubular Degeneration (Fig.3c), Hemorrhage(Fig.3d), Infiltration(Fig.3e), Hydropic Changes (Fig.3f),Tubular Cast (Fig.3g),Tubular Widened Lumen And Tubular Degeneration (Fig.3h) and Glomerular Shrinkage (Fig.3i). Photomicrographs for kidney sections of Mice given a high dose equivalent to 1/5 LD₅₀ of either dimethoate showed Glomerular Degeneration (Fig.4a), Hydropic Changes (Fig.4b), Tubular Degeneration (Fig.4c),Tubular Widened Lumen(Fig.4d) and Compressed Blood Vessel(Fig.4e).

The histopathological changes in the liver

The histopathological examination results in this study demonstrated that 30-day the oral intake exposure of Mice to dimethoate at the tested dose equivalent to 1/10 LD₅₀ resulted in degenerative changes in the liver including congestion blood vessels, infiltration, vasodilatation and hydropic changes, Also liver section of Mice in this group treated with high dose (1/5 the LD₅₀) of dimethoate showed congestion blood vessels, infiltration, hemorrhage, vasodilatation, fatty changes and hypertrophy.

The liver is well known target organ of the toxic impact regarding its function in biotransformation and excretion of xenobiotics (Roganovic and Jordanova,1998).

These results are agreement with many authors; Selmanoglu and Akay (2000) who reported similar histopathological changes including mononuclear cell infiltration, congestion, hydropic degeneration and hepatocellular damage in the liver of male rats treated with dimethoate, endosulfan and carbaryl. Also, Sharma *et al.* (2005b) who found that a 30-day exposure of male rats to technical grade dimethoate at doses of 6 and 30 mg/kg caused portal inflammation, centrizonal congestion and focal hepatocyte necrosis in the liver of rats. (Sayim, 2007a ; Gokcimen *et al.*, 2007; Elhalwagy *et al.*, 2008 and Muthuviveganandave *et al.*, 2011) Suggested that may occur hemorrhage, inflammatory cell infiltration.

Organophosphate insecticides are known to induce various histopathological changes in the liver tissues (Goel *et al.*, 2005; Gokcimen *et al.* 2007; Sayim, 2007a).

Earlier studies have shown that acute and sub chronic exposure to dimethoate alters

the antioxidant status and the histology of liver and brain in rats (Sharma *et al.*, 2005a, 2005b; Sayim, 2007b).

The evidences of liver damage like cord disarray hypertrophy and disintegration of hepatocytes showing different sizes of nuclei, lymphocytic infiltration, in addition to sinusoidal blood congestion and hemorrhage was also reported by (Persis and Kalairasi, 2001).

Previous studies have shown that acute and sub-chronic exposure to Dimethoate alters the antioxidant status and the histology of liver and induce hepatic lipid peroxidation in mice (Sivapiriya *et al.*, 2006) and rats (Sharma *et al.*, 2005b ; Kamath *et al.*, 2008 and Heikal *et al.*, 2011).

Also These results are Consistent with Choudhary *et al.*, (2003) whom revealed that the treatment with endosulfan, 10 mg/kg/day in rats causes liver damage which includes dilation of sinusoidal spaces with irregular nuclear shape, degenerative changes includes binucleated cells, hypertrophy of hepatocytes and lymphocytic infiltration in the central vein.

The histopathological changes in the kidney

The histopathological examination photomicrographs of the kidney tissues in mice treated with the tested dose of dimethoate, (equivalent 1/10 LD₅₀) resulted in Histological changes in the Kidney including Glomerular Degeneration, Tubular Degeneration, Hemorrhage, Infiltration, Hydropic Changes, Tubular Cast, Tubular Widened Lumen and Glomerular Shrinkage. While, the photomicrographs of kidney sections in mice treated with the oral dose (equivalent 1/5 LD₅₀) of dimethoate showed that there were some histopathological alterations in kidneys of

treated mice including Glomerular Degeneration, Hydropic Changes, Tubular Degeneration, Tubular Widened Lumen and Compressed Blood Vessel. These results are agree with Khogali *et al.*, (2005) in mice treated with dimethoate 40 EC. The microscopic changes observed in test kidneys are (in all the groups of experimental mice), degeneration of parenchymatous cells of renal tubules, glomerular atrophy and haemorrhages .

Also The results in this study agree with the findings of Kerem *et al.*, (2007) and Afshar *et al.*, (2008) they reported kidney damage such marked tubular dilation, hydropic degeneration in tubular lining epithelium, moderate congestion and hemorrhage in the cortical male Wistar rats exposed some organophosphate pesticides.

Tubular degeneration, glomerular atrophy, leucocytic infiltrations and congestion of renal blood vessels were noticed during deltamethrin – intoxication in kidneys of male wistar rats (Sakr and Al-Amoudi, 2012).

It appeared results of Al-Sharqi *et al.*, (2012) noticed large haemorrhagic areas, lobulated glomeruli, congested blood vessels, degenerative changes and infiltration of inflammatory cells in kidneys of insecticide (actara) treated mice.

Conclusion

The present findings clearly demonstrate that dimethoate is capable of inducing dose-dependent histopathological changes in the liver and kidney of the exposed mice. According to these results, it is suggested that systemic insecticide like dimethoate exposure might cause hazardous effects, especially at high doses, to man and environment.

Fig.1 Photomicrograph of the liver sections of mice treated with **14 mg/Kgb.w** of Dimethoate (H&E Stain X 650) . **(a)**: Control liver showing normal hepatocytes architecture with normal central vein(CV), hepatic cells (HC) sinusoids (S) and Kupffer Cells (KC). **(b)**: liver congestion (CON) and infiltration (INF).**(c)**: vasodilatation and congestion (VAS and CON). **(d)**: hydropic changes (H.C)

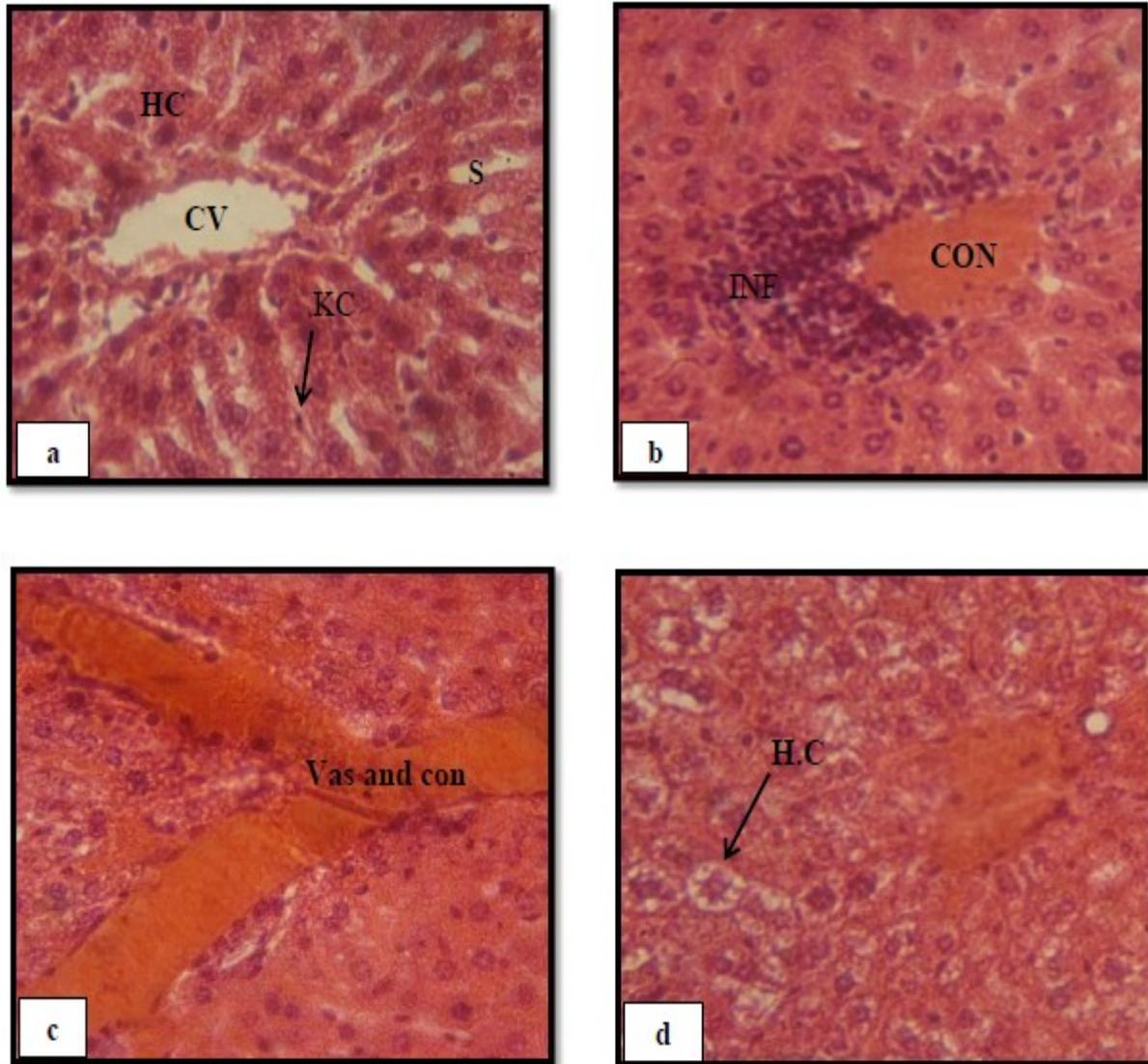


Fig.2:Photomicrographofthe liver sections of mice treated with **28 mg/Kg b.w** of Dimethoate (H&E Stain X 650). **(e):** Infiltration(**INF**) and congestion(**CON**). **(f):** liver hemorrhage(**HE**). **(g):**vasodilatation and congestion (**VAS and CON**).**(h):**fatty changes(**FC**). **(i):**hypertrophy (**HY**).

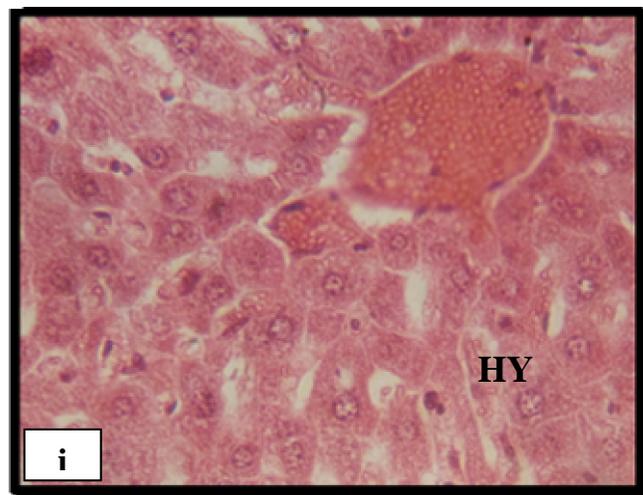
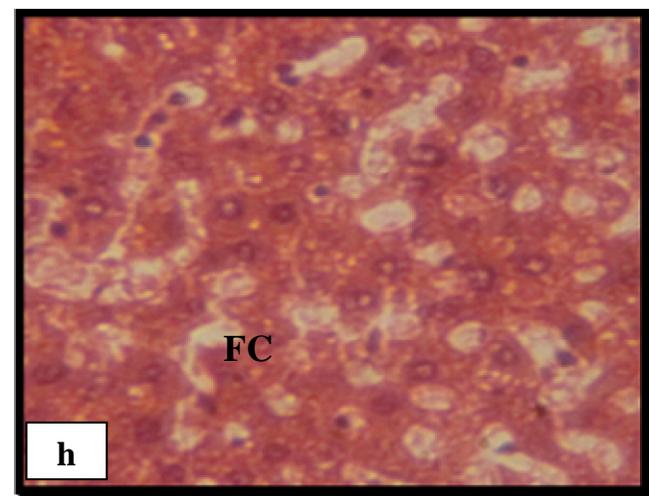
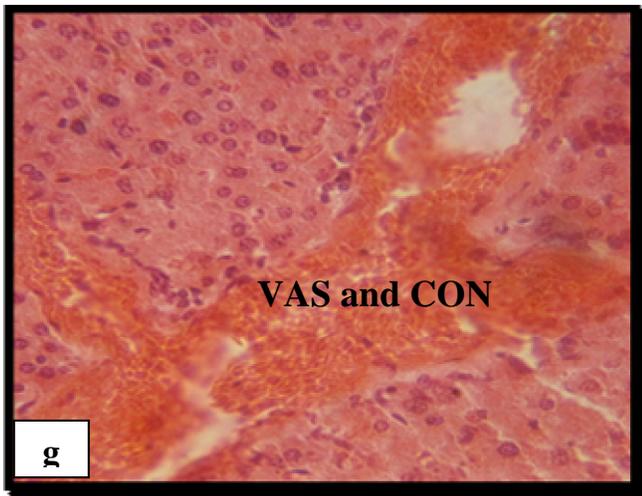
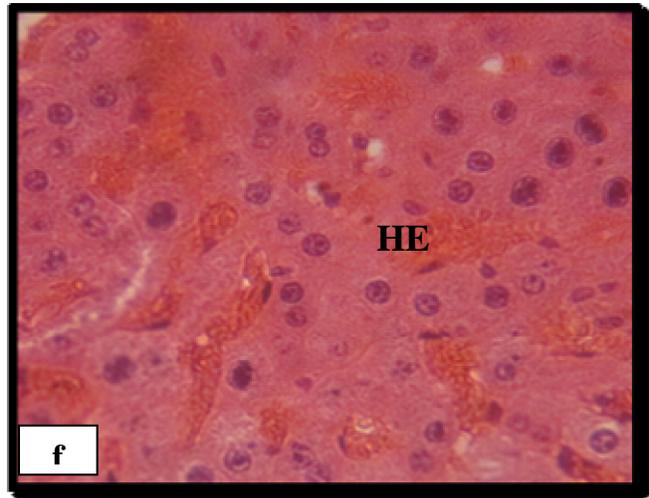
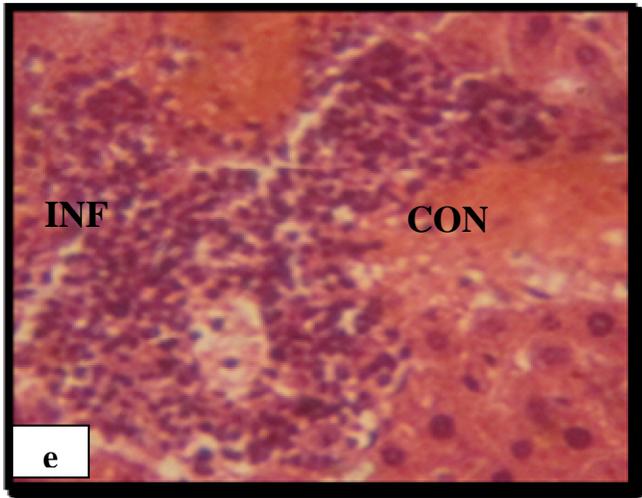
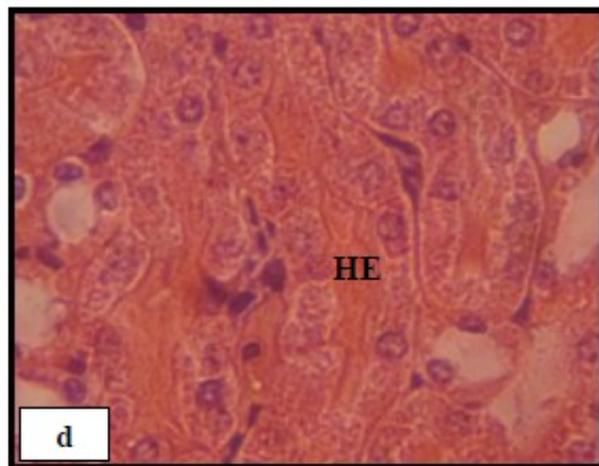
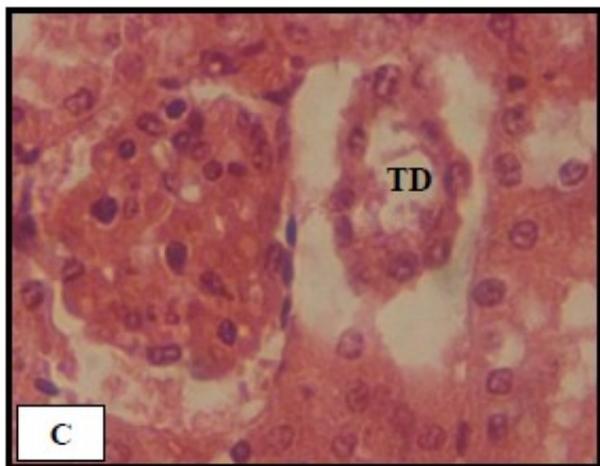
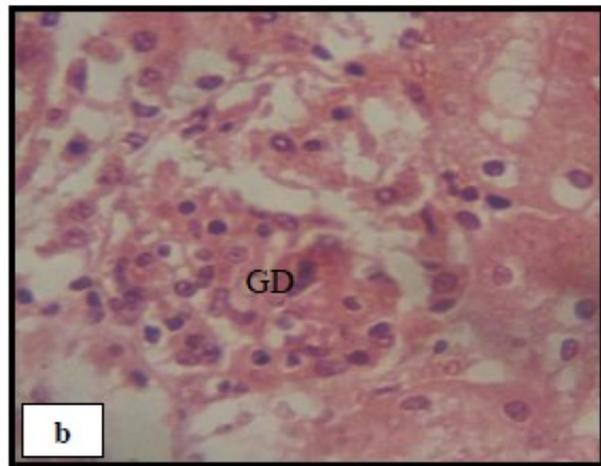
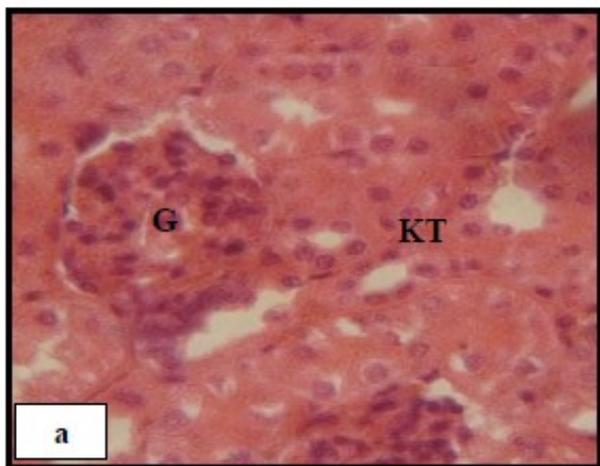


Fig.3: Photomicrograph Of The Kidney Sections Of Mice Treated With 14 Mg/Kg B.W Of Dimethoate (H&E Stain X 650). (a): Control Kidney Showing Normal Glomerulus(G)And Normal Kidney Tubules (KT). (b): Glomerular Degeneration (GD).(c): Tubular Degeneration (TD). (d): Hemorrhage(HE). (e): Infiltration(IFN). (f): Hydropic Changes (H.C). (g): Tubular Cast (TC). (h):Tubular Widened Lumen(TWL) And Tubular Degeneration (TD). (i): Glomerular Shrinkage (GS).



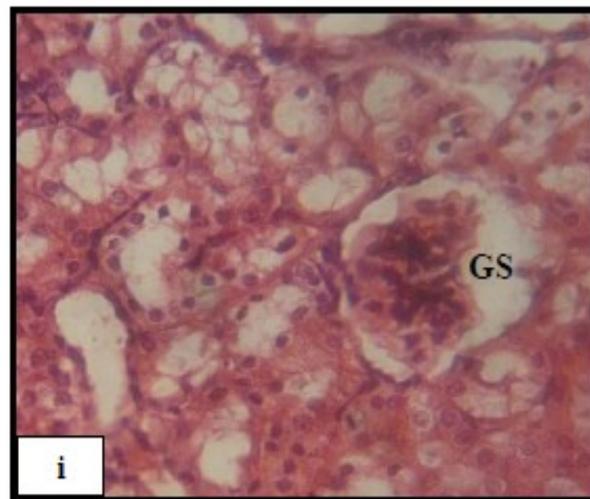
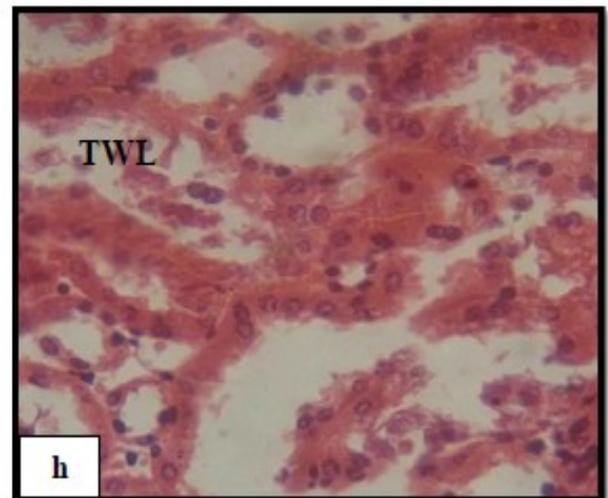
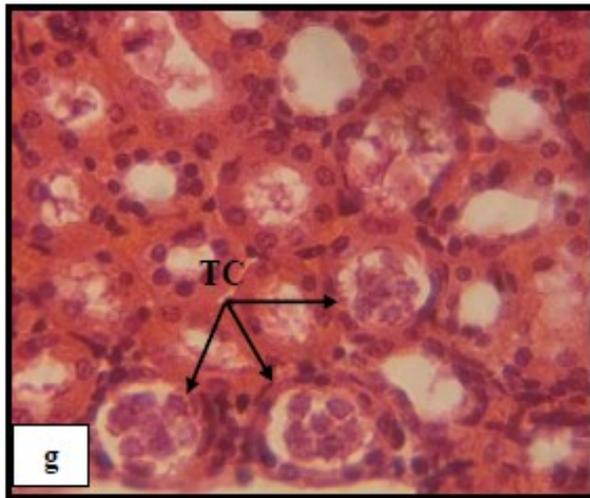
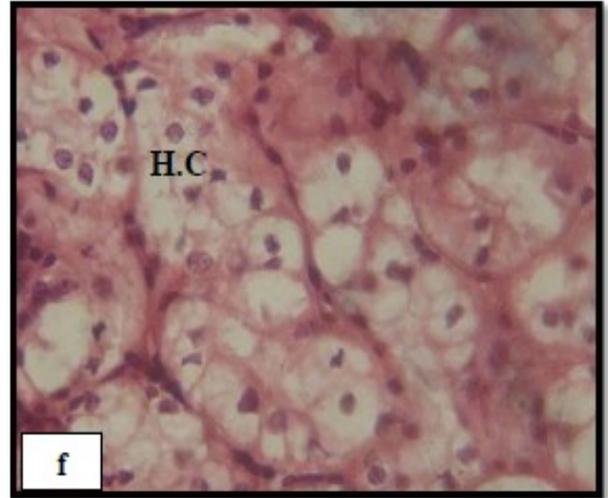
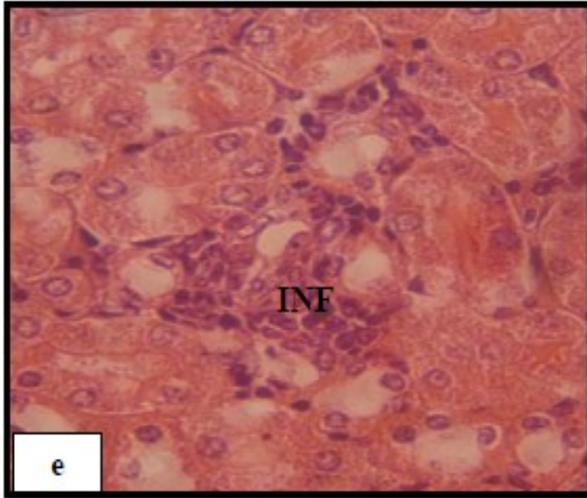
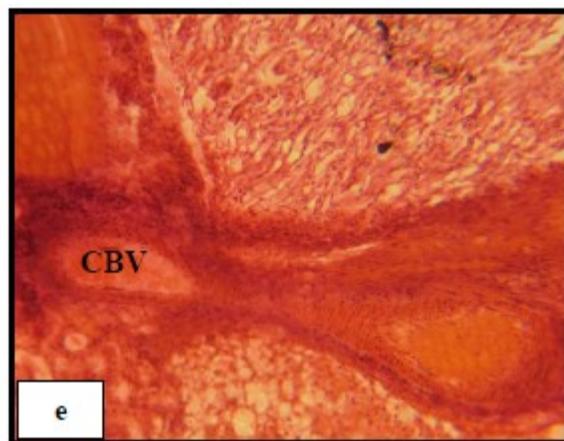
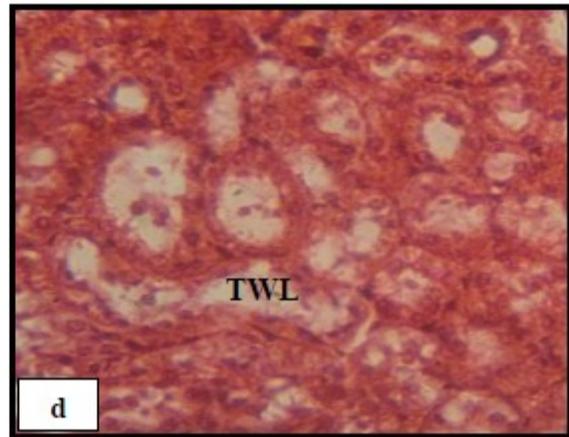
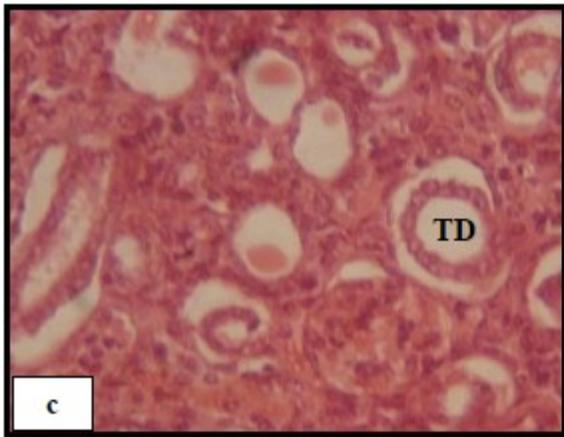
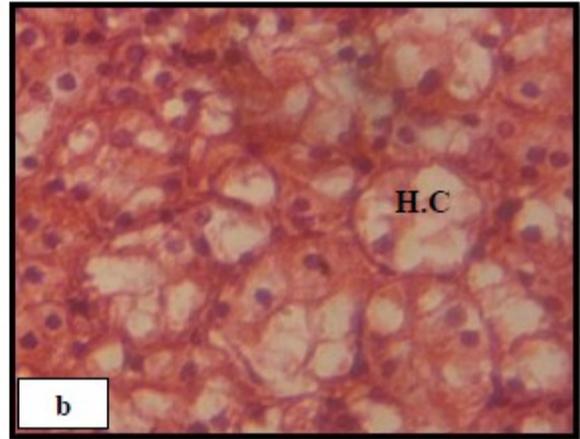
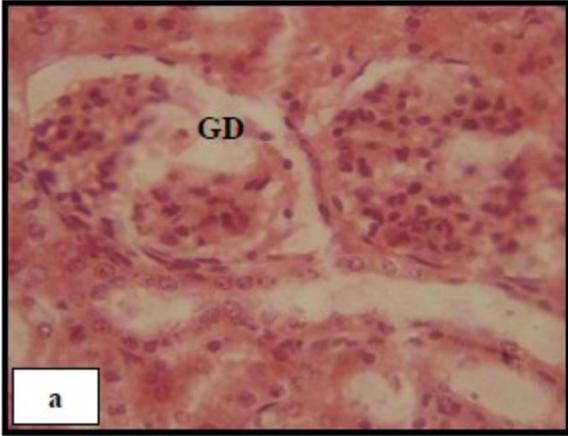


Fig.4: Photomicrograph Of The Kidney Sections Of Mice Treated With **28 mg/Kg B.W** Of Dimethoate (H&E Stain X 650). **(a):**Glomerular Degeneration(**GD**).**(b):** Hydropic Changes (**H.C**). **(c):**Tubular Degeneration (**TD**). **(d):** Tubular Widened Lumen (**TWL**) .**(e):** Compressed Blood Vessel (**CBV**)



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