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Clinicopathological and Toxocological Studies on the Effect of Vanadium Pentoxide as Anticarcinogenic

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ABSTRACT

Vanadium (V) is a heavy metal and trace element. It is believed to be a novel anticarcinogenic agent. It helps in the protection against the cancer induced by dimethylbenzantheracene (DMBA), adenocarcinoma in female-albino rats. One hundred and five female rats were divided into four gps. Gp.(1), 15 rats, was the negative control. Gp.(2), 30 rats, was orally intubated by vanadium pentoxide (0.05mg/kg B.wt for 150 days), Gp.(3), 30 rats, was orally given DMBA(100mg/kg B.wt, the dose was divided into 4 weekly applications, dissolved in corn oil.. Gp.(4) , 30 rats, was orally given vanadium (0.05mg/kg B.wt for 150 days). Four weekly oral doses of DMBA, dissolved in corn oil were given after one month from the start of vanadium which continued for 150 days. Blood samples were collected from the retroorbital venous plexus for hematological and biochemical studies after 90, 120 and 150 days from the beginning of the experiment. Specimens were taken at the same time from the liver, kidneys, lungs, spleen, mammary glands, oviduct and ovaries for histopathological examination after sacrifice of the rats.

Vanadium pentoxide, at a very low dose (0.05mg/kg B.wt), induced mild alterations in the hematological and biochemical parameters besides reversible hepatic and renal lesions. Vanadium enhanced the elevation of antioxidants as catalase enzyme (CAT), superoxide dismutose ((SOD) and glutathione (GSH).Vanadium protected the female albino rats against the mammary gland adenocarcinoma, induced by the chemical carcinogen (DMBA).The polycyclic aromatic hydrocarbon (DMBA) can induce adenocarcinoma in the mammary glands of the female albino rats.

INTRODUCTION

Vanadium is a heavy metal which is found at low levels in the air, water, and food. Most people are exposed to vanadium, mainly through food. Vanadium reaches the environment, mainly from its natural sources and from the burning of fuel oils *(1)*.

DMBA (9,10 – Dimethyl - 1,2 - benzanthracene) is polycyclic aromatic hydrocarbon (PAH) compound found in tobacco smoke. It is a potent carcinogen *(2)*.

Exposure to high levels of vanadium can cause harmful health effects *(1)*.

Scibior et al (3) evaluated the effect of vanadium on certain hematological parameters in rats, given sodium metavanadate (SMV) at a concentration of 0.125 mg V/mL for 6 weeks. The exposure to vanadium led to a significant decrease in the RBC count, Hb concentration, MCV, and MCH values.

Vanadyl sulfate was administered by gavage at a dose of 100 mg/kg.Bwt. The serum AST, ALT and alkaline phosphatase activities besides the urea and creatinine levels were not significantly changed after 60 days of treatment *(4)*.

Fifty day old female Sprague-Dawley rats, were treated with 7, 12 diemthylbenz (a) anthracene (DMBA 0.5 mg /100gm body weight) as a single tail-vein injection in an oil emulsion. Vanadium (ammonium monovanadate) at a concentration of 0.5 ppm was added to the drinking water and given ad libitum to the experimental group immediately after the carcinogen treatment and continued until the termination of the study (24 weeks). It was found that the vanadium treated animals

showed a substantial protection against DMBA-induced mammary carcinogenesis. There was a significant reduction in the incidence, total number, multiplicity and size of palpable mammary tumors with delaying in the mean latency period of tumor appearance following vanadium supplement, compared with the DMBA control *(5)*.

Rats were orally orally four doses of 0.5% DMBA solution (1ml/rat) at weekly intervals. The rats were sacrificed after 4 weeks of DMBA administration. There was a significant decrease in the antioxidant enzymes catalase (CAT) and superoxide dismutase (SOD) when compared with the controls. The increased lipid peroxidation was accompanied by a significant decrease in the level of the total reduced glutathione (GSH). The results of the study indicated that the alteration of the circulatory antioxidant status was more prominent in the orally infused rats with DMBA.

Female albino rats were treated with 7,12-dimethyl benzanthracene (DMBA with 25 gm./kg.Bwt orally/rat). There was an increase in the mitochondrial lipid peroxidation (in the mammary gland and liver) accompanied by high malondialdehyde (MDA) levels along with lowered activities of the mitochondrial enzymic antioxidants (superoxide dismutase, catalase) and reduced glutathione (GSH) after 28 days. Mammary gland carcinoma was detected after 28 days on ,12-dimethyl benz-anthracene (DMBA 25 mg./kg.Bwt. orally/rat).

MATERIAL AND METHODS

A-Experimental Animals

One hundred and five female albino rats weighing 150-200 gm, were obtained from the Laboratory Animal's Farm, Faculty of Vet. Med. Zagazig University, and divided into four experimental groups.

Group (1):15 rats were kept without treatment as normal control.

Group (2):30 rats were daily orally given vanadium pentoxide (0.05mg/kg B.wt.) for 150 days.

Group (3):30 rats were intubated with DMBA (100mg/kg B.wt. dissolved in corn oil) The dose was given to each rat on 4 times with one-week interval to induce cancer.

Group (4): 30 rats were daily given vanadium pentoxide (0.05mg/kg B. Wt.) as a prophylaxis for 150 days. After one month from the beginning of the experiment, the rats were given 4 weekly doses of DMBA, dissolved in corn oil .

B-Chemical substances

1) Vanadium pentoxide

It is the pentavalent state of vanadium as a yellow- red crystalline powder *(8)*. It was obtained from Hanawa Extra Pure Reagent China. It was dissolved in distilled water and given by oral intubation (0.05 mg/ kg B.wt.) *(9)* for 30 days as a prophylaxis and continued for other 120 days until the end of the study (150 days).

2) 9,10-dimethyl-1,2-benzanthracene (DMBA)

It is a polycyclic aromatic hydrocarbon containing four aromatic rings. It was obtained from Sigma CO. *(10)*.

(1) Blood samples

The blood samples were collected from the retro-orbital venous plexus of rats. Few blood drops were collected on EDTA sodium, as anticoagulant, for hematological studies. Another blood sample was collected for serum separation and used for biochemical evaluation of the liver function, kidney function and tumor marker (CEA).

1-Hematological Techniques *(11)*

The total leukocytic count (TLC) was done using the improved Neubauer hemocytometer and Turkey's fluid Giemsa stained blood smears were prepareds and the differential leukocytic counts were performed, and the absolute counts were calculated for each type of leukocyte.

The serum total protein *(12)* and albumin *(13)* were determined. The serum globulin was calculated by subtracting the albumin from total protein. The serum alkaline

phosphatase (ALP) activity *(14)*, alanine aminotransferase (ALT) and the aspartate aminotransferase (AST) were also determined *(15)*. The serum bilirubin (total and direct) was estimated *(16)*. The indirect bilirubin was obtained by subtracting the direct bilirubin from total bilirubin.

Measurements of the antioxidant enzymatic activities

The catalase activity (CAT), superoxide dismutase (SOD) *(17)*, and malondialdehyde (MDA) *(18)* were determined.

Statistical analysis

Data analysis was carried with one way ANOVA model procedures of SAS *(19)*.

RESULTS AND DISCUSSION

The vanadium has been established as an essential element normally found as ultratrace element in the human body. It is ingested mainly with the diet *(20)*.

DMBA is one of the polycyclic aromatic hydrocarbon derived chiefly from petroleum and coal tar distillation which is distributed allover the environment. It has a potent carcinogenic effect *(2)*.

The present work revealed leukopenia manifested by neutropenia and lymphopenia in gp.(3) which was orally given DMBA for 90 days. The leukopenia became more pronounced with neutropenia, lymphopenia and eosinopenia after 120 day. The leukopenia was manifested by neutropenia and eosinopenia after 150 day from the beginning of the experiment. It may be attributed to the depression of the hematopoietic tissue by the polyaromatic hydrocarbon (PAH). The histopathological lesions showed leukocytic aggregations in the kidneys besides lymphoid depletion from the spleen which were cited previously *(21)*.

Gp.(4) showed a moderate leukopenia manifested by neutropenia and lymphopenia (90 and 120 days PT with V.). After 150 days the leukopenia was manifested by neutropenia, lymphopenia and monocytopenia which may be due to depression of the hematopoietic tissue as a result of exposure to the PAH. Microscopically,leukocytic aggregations were seen in the portal areas. The spleen showed mild lymphoid depletion of the white pulp.

Gp.(3) showed hypoproteinemia and hypoalbuminemia which may be due to renal and hepatic damage. Our results revealed hepatic hydropic degeneration and leukocytic infiltration in the portal areas. The kidneys showed focal interstitial leukocytic aggregations in the renal cortex. Some nephrons exhibited coagulative necrosis of some tubular epithelia.

The alkaline phosphatase (ALP) and ALT activities were not altered in gp.(2) suggesting that the vanadium did not impair the liver function. Our results are in consistent with the biochemical effects of vanadyl sulfate on liver functions of normal rats *(4)*.

The ALP was significantly elevated in gps (3 and 4),but with a lesser extent, in all periods, which may be due to biliary obstruction and/or hepatocellular necrosis as a result of the toxic metabolites of DMBA. Similar results were described in previous studies *(22, 23)*.

The elevated AST activity, in the vanadium treated rats, may be due to mild toxic effects on several organs like heart, kidneys, intestine and hepatic tissue *(11)*. The microscopic picture supports the above findings as the liver showed mild reversible changes, mainly cloudy swelling. The elevated activities of the ALT and AST in gp.(3), throughout the experiment, could be due to hepatic damage. DMBA altered the liver function as revealed by the increase in tissue marker enzymes, besides the ALT and AST *(6)*. Microscopically, the hepatic cells suffered degenerative changes, mainly hydropic degeneration. The ALT activity was moderately elevated after 150 days from the start of the experiment.

Gp (3) revealed a significant increase in the total bilirubin level throughout the experiment. Meanwhile, the direct and indirect bilirubin levels were significantly elevated after 150 days. Such findings suggest

hemolysis due to poisoning by the DMBA on the erythrocytes besides intrahepatic cholestasis. Microscopically, the liver showed numerous newly formed bile ductules (cholestasis). The spleen showed golden yellow pigments (hemosiderosis) in the red pulp. Such findings get along with the significant elevation of the bilirubin. Gp.(4) showed a significant increase of the direct bilirubin after 90 days. This may be a result of hemolysis and cholestasis due to the toxic effect of the DMBA. The Increased AP in this group gets along with the above mentioned results.

The creatinine level was increased in gp.(3), during the experimental period. This elevation may be due to damaged glomeruli, as the toxic metabolites of DMPA are mainly excreted via the kidneys. The creatinine level was moderately elevated (gp.4) after 120 days which reflected the role of vanadium in protecting the kidneys against the toxic effect of the DMBA. Microscopically, some glomeruli showed proliferated and hyalinized mesangial cells and contracted tufts in gp.(4) which may be responsible for the creatinine elevation.

Our results showed a highly significant increase in the carcinoembryonic antigen (CEA) in group (3) which indicated the occurrence of carcinogensis because the neoplastic cells are stimulated to synthesize oncofetal antigen (CEA). Group (4), which received concomitant doses of V and DMBA, illustrated the role of vanadium in the protection against cancer, as the level of the CEA was low in this group. These findings suggest that the supplement of vanadium at a dose of 0.5 ppm effectively suppressed the formation of DNA 'comets' thereby indicating its nongenotoxicity at this particular dose. The potential role of vanadium chemopreventic mechanism in limiting the neoplastic transformation is defined in a model of experimental hepatocarcinogenesis in rats *(24)*. The acimar basement membrane was broken in gp.3 with tendency of the neoplastic cells to invade the stroma (invasive adenocarcinoma) These cells showed malignancy features. The rats which were given V ,as a protective agent against DMBA, (gp4) showed proliferated cells with intact basement membrane, and edematous stroma (adenoma). The activities of the antioxidants (catalase, reduced glutathione and superoxide dismutase) were significantly increased in the vanadium treated rats (gp.2). The activities of the catalase and GSH were elevated after 90 days of V- treatment in gp (4) then decreased at the end of the experiment. This may be due to the exhaustion of the antioxidants in the detoxification and removal of the reactive intermediates (end product of DMBA) by the action of cytochrome P450, one of phase I enzymes which acts on DMBA to produce the intermediate BAH which was suggested to produce the cancer *(25)*.

It could be concluded that vanadium stimulated phase II enzymes which helped to inhibit the formation of electrophiles and catalyze their conversion to inactive conjugates making them more water soluble and readily excreted. It is the cellular balance between phase I activating enzymes and phase II detoxifying enzymes which may contribute a the risk of developing cancer. Therefore, an elevation of catalase, GSH and SOD indicates an increase in the systemic ability to detoxify the electrophilic compounds including carcinogens.

Table 1. Changes in leukogram (mean values± SE) 90 , 120 and 150 day from the beginning of the experiment in all gps.

Parameters / Groups	TLC (10^3/µl)	Absolute differential count (cell /µl) (90 days)					Absolute differential count (cell /µl) (120 days)					Absolute differential count (cell /µl) (150 days)				
		Neut.	Seg.neut.	Lymph.	Esoino.	Mono.	Neut.	Seg.neut	Lymph.	Eosino.	Mono.	Neut.	Seg.neut	Lymph.	Eosino.	Mono.
(1) Control	a 6.54 ±0.21	a 3636.3 ±14.03	a 248.52 ±1.76	a 2118.9 ±10.82	a 248.52 ±3.21	a 287.76 ±2.95	a 3636.3 ±14.03	a 248.52 ±1.76	a 2118.9 ±10.82	a 248.52 ±3.21	a 287.76 ±2.95	a 3636.3 ±14.03	a 248.52 ±1.76	a 2118.9 ±10.82	a 248.52 ±3.21	a 287.76 ±2.95
(2) V2O5	a 6.28 ±0.18	a 3466.5 ±12.06	a 238.64 ±2.57	a 2147.76 ±9.90	a 175.84 ±2.86	a 251.36 ±3.21	a 3319.68 ±16.96	ab 212.16 ±1.97	a 2196.48 ±12.17	a 224.64 ±2.01	a 287.04 ±2.87	a 3476 ±24.33	a 252.8 ±2.63	a 2199.36 ±11.64	ab 176.96 ±2.29	ab 214.88 ±1.78
(3) DMBA	c 4.10 ±0.26	c 1877.8 ±11.66	a 196.8 ±5.68	b 1681 ±13.13	a 131.2 ±2.72	a 213.2 ±5.45	c 1556.6 ±9.22	c 94.12 ±1.03	b 1600.04 ±7.27	b 130.32 ±0.54	a 238.92 ±1.84	c 1792 ±6.71	b 134.4 ±2.20	a 2213.12 ±4.13	b 116.48 ±2.17	ab 224 ±2.29
(4) V2O5+ DMBA	b 5.16 ±0.18	b 2848.33 ±12.45	a 196.08 ±1.46	b 1744.08 ±7.59	a 185.76 ±3.32	a 185.75 ±2.59	b 2427.6 ±9.89	b 152.32 ±2.25	b 1685.04 ±10.96	a 257.04 ±2.79	a 238 ±3.46	b 2872.8 ±12.91	b 202.16 ±2.51	b 1840.72 ±5.25	a 244.72 ±6.26	b 159.6 ±3.91
F-test	**	**	N.S	*	N.S	N.S	**	**	*	*	N.S	**	*	*	*	*

Means within the same column with different superscripts, are significantly different (at $p \leq 0.05$).
N.S: non- significant. *: significant. **: highly significant.

Table 2. Changes in the liver function tests (mean values± SE) 90 day from the beginning of the experiment in all gps.

Parameters / Groups	Total protein (gm/dl)	Albumin (gm/dl)	Globulin (gm/dl)	ALP (KAU/dl)	ALT (U/ml)	AST (U/ml)	Bilirubin (mg/dl)		
							Total	Direct	Indirect
(1) Control	a 7.14 ±0.19	a 4.45 ±0.25	a 2.69 ±0.10	c 11.11 ±0.40	b 19.85 ±0.81	bc 28.67 ±1.26	b 0.49 ±0.03	b 0.26 ±0.03	bc 0.22 ±0.06
(2) V2O5	a 6.95 ±0.37	ab 4.12 ±0.13	a 2.83 ±0.27	c 10.64 ±0.68	b 23.90 ±1.12	b 30.35 ±1.47	b 0.47 ±0.03	b 0.20 ±0.02	ab 0.27 ±0.04
(3) DMBA	b 5.93 ±0.12	b 3.74 ±0.10	a 2.19 ±0.07	a 17.40 ±0.62	a 29.75 ±3.36	a 41.85 ±2.60	a 0.62 ±0.02	b 0.26 ±0.01	a 0.36 ±0.03
(4) V2O5+ DMBA	a 6.79 ±0.31	a 4.30 ±0.15	a 2.29 ±0.27	b 13.02 ±0.57	b 18.76 ±0.40	c 24.64 ±1.16	b 0.47 ±0.01	a 0.34 ±0.01	c 0.12 ±0.01
F-test	*	*	N.S	**	*	**	*	*	*

Means within the same column with different superscripts, are significantly different (at P≤ 0.05).

N.S: non- significant. *: significant. **: highly significant.

Table 3. Changes in liver function tests (mean values± SE) 120 day from the beginning of the experiment in all gps.

Parameters / Groups	Total protein (gm/dl)	Albumin (gm/dl)	Globulin (gm/dl)	ALP (KAU/dl)	ALT (U/ml)	AST (U/ml)	Bilirubin (mg/dl)		
							Total	Direct	Indirect
(1) Control	a 7.14 ±0.19	a 4.45 ±0.25	a 2.69 ±0.10	c 11.11 ±0.40	b 19.85 ±0.81	c 28.67 ±1.26	b 0.49 ±0.03	a 0.26 ±0.03	a 0.22 ±0.06
(2) V2O5	ab 6.37 ±0.26	ab 3.86 ±0.23	a 2.51 ±0.26	c 11.81 ±0.79	b 23.63 ±2.23	b 33.72 ±1.46	b 0.45 ±0.01	a 0.23 ±0.01	a 0.21 ±0.02
(3) DMBA	c 5.02 ±0.27	b 3.10 ±0.30	a 1.92 ±0.32	a 18.36 ±0.94	a 41.55 ±0.61	a 40.36 ±0.90	a 0.64 ±0.07	a 0.31 ±0.03	a 0.33 ±0.08
(4) V2O5+ DMBA	b 5.98 ±0.38	ab 3.70 ±0.20	a 2.27 ±0.52	b 14.18 ±0.53	b 23.94 ±1.36	c 26.66 ±1.04	b 0.49 ±0.03	a 0.31 ±0.02	a 0.18 ±0.04
F-test	*	*	N.S	**	**	**	*	N.S	N.S

Means within the same column with different superscripts, are significantly different (at P ≤ 0.05).

N.S: non- significant. *: significant. **: highly significant.

Table 4. Changes in liver function tests (mean values± SE) 150 day from the beginning of the experiment in all gps.

Parameters / Groups	Total protein (gm/dl)	Albumin (gm/dl)	Globulin (gm/dl)	ALP (KAU/dl)	ALT (U/ml)	AST (U/ml)	Bilirubin (mg/dl)		
							total	Direct	Indirect
(1) Control	a 7.14 ±0.19	a 4.45 ±0.25	a 2.69 ±0.10	b 11.11 ±0.40	c 19.85 ±0.81	b 28.67 ±1.26	b 0.49 ±0.03	bc 0.26 ±0.03	b 0.22 ±0.06
(2) V2O5	a 6.80 ±0.19	a 4.26 ±0.25	a 2.54 ±0.26	b 11.96 ±0.69	bc 20.93 ±1.16	b 27.15 ±1.03	b 0.47 ±0.02	c 0.20 ±0.01	ab 0.27 ±0.02
(3) DMBA	b 5.38 ±0.42	b 2.77 ±0.32	a 2.61 ±0.46	a 21.50 ±0.81	a 34.16 ±1.64	a 38.20 ±2.31	a 0.77 ±0.03	a 0.37 ±0.02	a 0.40 ±0.04
(4) V2O5+ DMBA	ab 6.25 ±0.52	a 4.10 ±0.21	a 2.15 ±0.36	a 19.91 ±1.57	b 23.98 ±1.40	b 26.93 ±1.09	b 0.55 ±0.02	ab 0.33 ±0.01	b 0.22 ±0.02
F-test	*	*	N.S	**	**	**	**	**	*

Means within the same column with different superscripts, are significantly different (at $P \leq 0.05$).
N.S: non- significant. *: significant. **: highly significant.

Table 5. Changes in some renal function tests (mean values± SE) 90, 120 and 150 day from the beginning of the experiment in all gps.

Time	90 days		120 days		150 days	
Parameters / Groups	Urea (mg/dl)	Creatinine (mg/dl)	Urea (mg/dl)	Creatinine (mg/dl)	Urea (mg/dl)	Creatinine (mg/dl)
(1) Control	b 39.70 ±1.63	b 0.71 ±0.04	b 39.70 ±1.63	c 0.71 ±0.04	b 39.70 ±1.63	c 0.71 ±0.04
(2) V2O5	a 47.20 ±1.72	b 0.67 ±0.07	a 48.83 ±1.81	c 0.67 ±0.04	b 45.80 ±3.62	c 0.77 ±0.03
(3) DMBA	a 49.19 ±2.45	a 1.42 ±0.14	a 48.22 ±2.46	a 1.51 ±0.09	a 54.75 ±2.21	a 1.70 ±0.07
(4) V2O5+ DMBA	a 47.67 ±2.23	b 0.93 ±0.02	a 47.40 ±1.20	b 0.95 ±0.02	b 44.21 ±1.46	b 0.95 ±0.06
F-test	*	**	*	**	*	**

Means within the same column with different superscripts, are significantly different (at $P \leq 0.05$).
*: significant. **: highly significant.

Table 6. Changes in carcinoembryonic antigen (CEA ng/ml) (mean values± SE) 90, 120 and 150 day from the beginning of the experiment in all gps.

Time	90 days	120 days	150 days
Parameters / Groups	CEA (ng/ml)	CEA (ng/ml)	CEA (ng/ml)
(1) Control	b 0.2 ± 0.0003	c 0.2 ± 0.0003	c 0.2 ± 0.0003
(2) V2O5	b 0.2 ± 0.0003	c 0.2 ± 0.0003	c 0.2 ± 0.0003
(3) DMBA	a 0.42 ± 0.01	a 0.59 ± 0.01	a 0.79 ± 0.04
(4) V2O5+DMBA	b 0.2 ± 0.0003	b 0.34 ± 0.01	b 0.43 ± 0.0003
F-test	**	**	**

Means within the same column with different superscripts, are significantly different (at $P \leq 0.05$).
**: highly significant.

Table 7. Changes in the antioxidant activities (mean values± SE) 90, 120 and 150 day from the beginning of the experiment in all gps.

Parameters / Groups	Changes in the antioxidant activities (Mean ± SE)											
	(90 days)				(120 days)				(150 days)			
	CAT (µM/L)	SOD (µg/gm)	GSH (µM/gm)	MDA (µM/L)	CAT (µM/L)	SOD (µg/gm)	GSH (µM/gm)	MDA (µM/L)	CAT (µM/L)	SOD (µg/gm)	GSH (µM/gm)	MDA (µM/L)
(1) Control	c 174.62 ±10.84	b 0.14 ±0.04	c 59 ±7.84	a 2.34 ±0.15	b 174.62 ±10.84	a 0.14 ±0.04	b 59 ±7.84	a 2.34 ±0.15	b 174.62 ±10.84	b 0.14 ±0.04	b 59.00 ±7.84	b 2.34 ±0.15
(2) V2O5	bc 206.52 ±11.40	ab 0.17 ±0.02	ab 98 ±4.60	a 1.90 ±0.20	a 236.63 ±27.77	a 0.18 ±0.01	a 131.50 ±16.27	a 2.03 ±0.13	a 259.15 ±39.15	a 0.32 ± 0.02	a 125.25 ±3.42	bc 1.9 ±0.11
(3) DMBA	a 243.60 ±0.45	b 0.15 ±0.02	a 111.50 ±8.38	a 2.28 ±0.19	c 128.08 ±8.09	a 0.09 ±0.01	b 79.75 ±15.39	a 2.81 ±0.22	c 109.42 ±12.22	b 0.06 ±0.009	b 49 ±4.24	a 3.07 ±0.20
(4) V2O5+ DMBA	ab 195.85 ±7.37	a 0.25 ±0.02	bc 76.25 ±6.96	a 2.52 ±0.30	a 217.80 ±25.96	a 0.14 ±0.06	ab 94.25 ±9.49	a 2.68 ±0.38	a 261.03 ±6.97	a 0.27 ±0.03	a 118.5 ±2.59	b 2.03 ±0.13
F-test	*	*	*	N.S	**	N.S	*	N.S	**	**	**	**

Means within the same column with different superscripts, are significantly different (at $P \leq 0.05$).
N.S: non- significant.
*: significant.

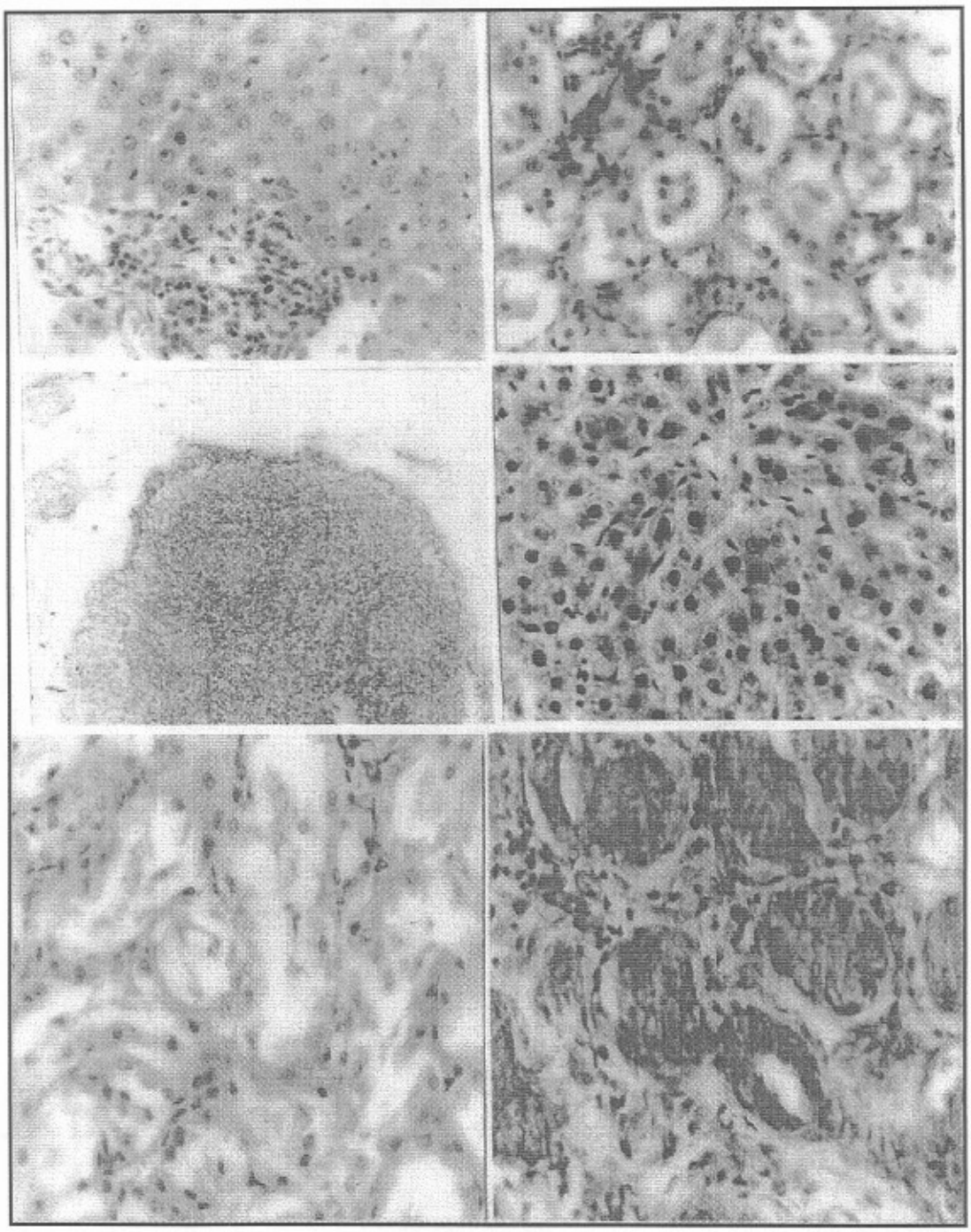

Fig.(1) Gp. (2). Liver showing portal lymphocytic aggregation and cloudy swelling of the hepatic cells (H & E., X1200).

Fig.(2) Gp. (2). Kidney showing cellular and hyaline casts inside the lumina of some renal tubules in the renal cortex (H & E., X1200).

Fig.(3) Gp. (2). Spleen showing lymphoid depletion of the white pulp and edema (H & E., X 300).

Fig.(4) Gp. (3). Liver showing degenerative changes and apoptosis of the hepatic cells with hyperplastic kupffer's cells (H & E., X 1200).

Fig.(5) Gp. (3). Kidney showing coagulative necrosis of some renal tubules (H & E., X1200).

Fig.(6) Gp. (3). Mammary gland showing invasive adenocarcinoma (H & E., X1200).

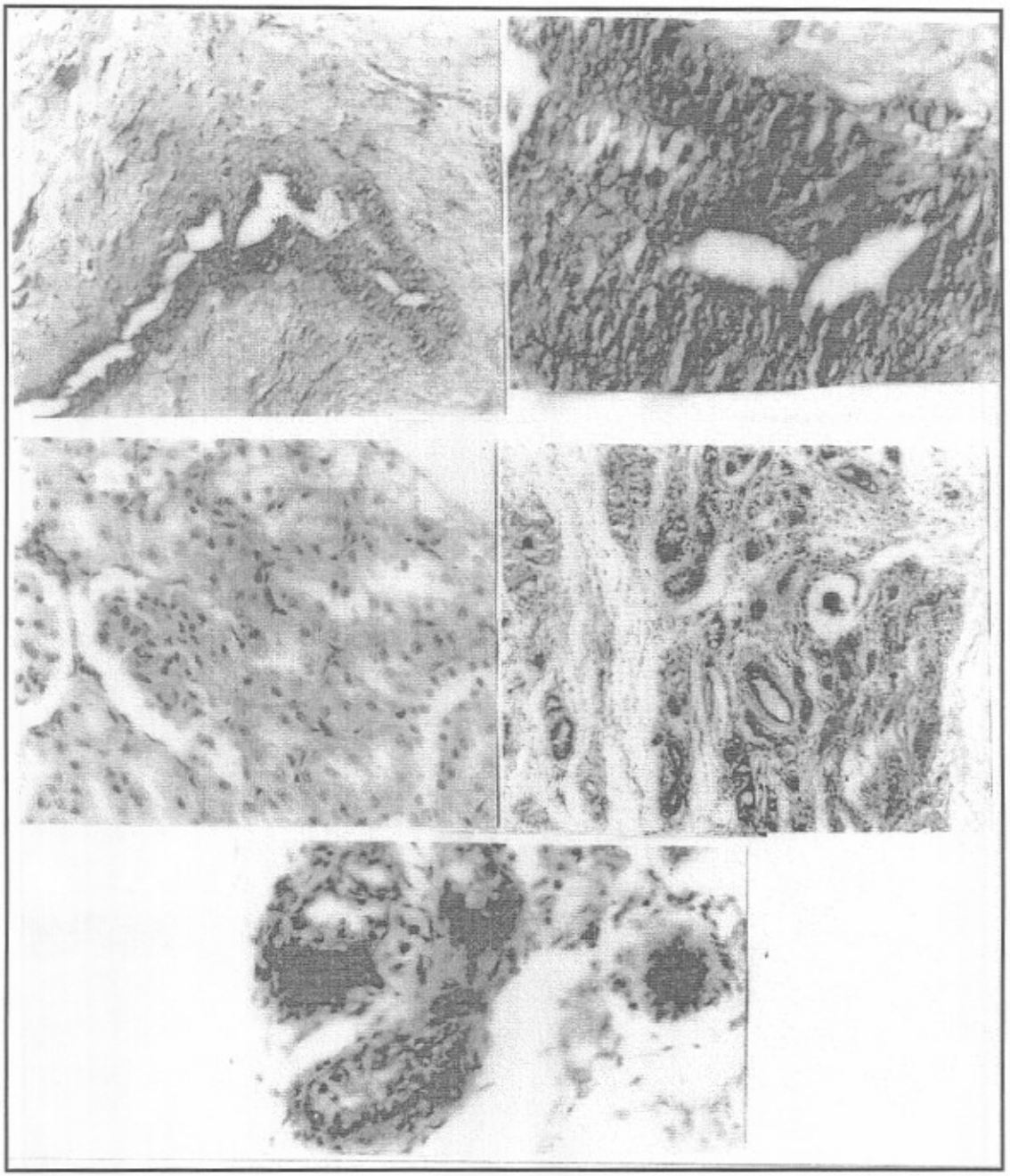

Fig.(7) Gp. (3). Mammary gland showing duct carcinoma (H & E.,X300).

Fig.(8) Gp.(3). A high power of Fig. (7) to show the duct lumen occupied by several rows of large vesicular hyperchromatic nuclei with mitotic activities (H & E., X1200).

Fig.(9) Gp.(4). Kidney showing nephrosis and proliferated mesangium with contracted glomerular tufts (H & E., X1200).

Fig.(10)Gp.(4). Mammary gland showing proliferated acinar epithelium with intact basement membrane (adenoma) (H & E., X300).

Fig.(11)Gp.(4). A high power for Fig. (10) to show acini lined by more than one row of cuboidal epithelium within edematous stroma (H & E., X1200).

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الملخص العربي

دراسات باثولوجية إكلينيكية على تأثير خامس أكسيد الفاناديوم كمضاد للسرطان

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يعتبر الفاناديوم واحد من أهم ملوثات البيئة والتى تزايد وجودها نتيجة لازدياد التقدم الصناعي الذي أدى بدوره إلى زيادة نسبة تلوث الماء والهواء والتربة بالعناصر الثقيلة.

و لقد اعتقد مؤخرا ان الفاناديوم يعتبر وسيلة مبتكرة فى الحماية ضد حدوث السرطان الكيميائى نتيجة التعرض لبعض الكيماويات المسرطنة مثل ٩-١٠ داى ميثيل بنزانثراسين(DMBA) لذلك أجريت هذه الدراسة لاستبيان تأثير الفاناديوم على خلايا و كيمياء الدم و كذلك تأثيره على وظائف بعض الأعضاء الأخرى مثل الكبد ، الكلية،الرئتين،الطحال،الغدة الثديية،المبايض وقناة البيض. كما استهدفت الدراسة استبيان تأثير الفاناديوم كمضاد للسرطان الكيميائى.

استخدم لهذا البحث عدد ١٠٥ فأر من إناث الفئران البيضاء وقد تم تقسيمها إلى أربعة مجموعات:

المجموعة الأولى: مكونة من ١٥ انثى من الفئران البيضاء تركت كضابط للتجربة.

المجموعة الثانية: عبارة عن ٣٠ انثى من الفئران البيضاء أعطيت خامس أكسيد الفاناديوم(٠,٠٥ ملجم / كجم من وزن الجسم) عن طريق الفم يوميا لمدة ١٥٠ يوم.

المجموعة الثالثة: مكونة من ٣٠ انثى من الفئران البيضاء أعطيت المادة المسرطنة(DMBA) بعد مرور شهر من بداية التجربة (١٠٠ملجم / كجم من وزن الجسم) وقد قسمت الجرعة على ٤ مرات ومذوبة فى زيت الذرة (١ مل) عن طريق الفم أسبوعيا.

المجموعة الرابعة: مكونة من ٣٠ انثى من الفئران البيضاء أعطيت خامس اكسيد الفاناديوم(٠,٠٥ ملجم / كجم من وزن الجسم) عن طريق الفم يوميا وبعد مرور شهر من التجربة أعطيت المادة المسرطنة(DMBA بجرعة ١٠٠ملجم / كجم من وزن الجسم) وقد قسمت الجرعة على ٤ مرات ومذوبة فى زيت الذرة (١ مل) عن طريق الفم أسبوعيا مع استمرار إعطاء الفاناديوم يوميا طوال مدة التجربة (١٥٠يوم).

تم تجميع عينات الدم من المجموعات الأربعة السابقة على ثلاث فترات (بعد ٩٠-١٢٠-١٥٠ يوم) من بداية التجربة لاجراء التحاليل الدموية و البيوكيميائية. ثم ذبحت الفئران فى نفس المدد السابقة وتم اخذ عينات من كل من(الكبد- الكلية- الرئتين- الطحال- الغدة الثديية- قناة فالوب و المبايض) للفحص الباثولوجى. كذلك تم اخذ جزء من الكبد من كل مجموعة لقياس الإنزيمات المضادة للأكسدة مثل (CAT, SOD,GSH, MDA) .

واظهرت النتائج مايلى :-

أن استخدام خامس أكسيد الفاناديوم بجرعة صغيرة جدا (٠,٠٥ ملجم/كجم من وزن الجسم) يؤدى إلى بعض التغيرات الطفيفة في خلايا وكيمياء الدم وكذلك فى بعض أنسجة الأعضاء الأخرى مثل الكبد والكلية والطحال. يعمل الفاناديوم على زيادة الأنزيمات المضادة للأكسدة مثل(CAT, SOD, GSH). يمكن استخدام الفاناديوم للوقاية من السرطان الناتج من الكيماويات المسرطنة مثل (DMBA) بعد التحكم فى الزمن والجرعة المعطاة. يعتبر DMBA مركب حلقى أروماتى محدث للسرطان وخاصة فى الغدة الثديية فى إناث الفئران البيضاء.