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EFFECT OF GRADED LEVELS OF DIETARY OXALIC ACID ON GROWTH PERFORMANCE, PHYSIOLOGICAL RESPONSES AND HISTOLOGICAL ALTERATIONS IN New Zeland White RABBITS

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ABSTRACT

A total of 50 NZW rabbits (25 males + 25 females) of 2 months old were used to study the toxic effect of the mycotoxin oxalic acid (OA) on rabbits. The animals were fed on graded levels of OA (0-30% of the diet) for 2 months. Feed intake and conversion, retained OA in different animal tissues, and blood picture were determined.

The bodyweight gain of the treated animals proportionally decreased according to the dietary levels of OA. The decrease was significant beginning at 10% OA and more. The feed intake, generally, decreased by increasing the dietary level of OA. The decrease was significant, also, beginning from the level of 10% OA and more. The feed conversion tended to be bad proportionally with the OA-level in the diets, particularly (and significantly) at the highest 2 levels of OA. Increasing its dietary level increased OA intake. There were significant increases in kidney and liver weights and decreases in the carcass weights by feeding OA. There were significant increases in transaminases activity and cholesterol, creatinine, uric acid, and OA concentrations; and decreases in blood total protein levels. OA accumulation in the animal organs took the following-descending order: muscles, liver, and kidney. Male animals contained more OA than females. The histological examination confirmed that all alterations were happened only in the animals group fed on 30% OA. Their livers suffered from a mild congestion of the portal vein in the portal tract. The kidney showed a degeneration of the glomeruli, polymorphonuclear leucocytes infiltration, interstitial nephritis, and oxalate deposition.

The animals treated with the highest 2 levels (30 and 20% OA) reflected lower appetence for feed from the 3rd week of the contaminated feeding. These animals showed also stress symptoms. These symptoms tended to be severer by elongation of the feeding period, particularly at the highest level of the toxin. Therefore, the animals of this group fed on 30% OA died at the 6th week, whereas those fed on 20% OA died at the 7th week. The animals fed on 10% OA showed stress syndromes and bodyweight loss at the 8th week. The post-mortem (P.M.) test for the animals fed on 20% OA revealed presence of inflammation and congestion along the digestive system; blue spots on the esophagus, stomach and intestine; haemorrhagic patches on the stomach, intestine, liver, lungs and kidneys; pale lungs; enlarged-dark kidneys and liver; and whity crystalline precipitations (gout) in the stomach. The animals group fed on 30% OA reflected the same previous P.M. picture, but severer, with bleeding of the digestive system. The other animal groups were normal.

Results obtained of the present study refer to the toxicity signs of OA and therefore it is a must to avoid feeding small and mono-gastric animals on OA-rich plants.

Keywords: *oxalic acid, mycotoxin, rabbits, performance, biochemistry, and histology.*

INTRODUCTION

Since 1941 it was noticed that some fungal species were capable for producing large amounts of OA on moist straw. That means that OA is a mycotoxin. It is produced by *Aspergillus flavous* and *A. niger* (Gedek, 1983 and Blood and Radostits, 1989). Yet, it is also a phytotoxic organic acid which naturally presents in different plant substances as free acid or calcium oxalate (Nehring, 1972). OA is found in mouldy straw and silage (Clarke *et al*. 1981). It is also presented in plants and grasses as beet, halogeton (up to 34.5%), pigweed (12-30%), mangels (up to 12%) fat hen (8%) soursob (5.9%), rice straw (1.56%), and spinach (90 mg/kg dry matter) (Sharaf, 1974; Fricker, 1976; and Morton, 1977). A number of foods, particularly some fruits and vegetables, contain oxalates, notable among these being rhubarb, spinach, and strawberries. Some OA may be formed in the course of metabolism (Varley, 1978).

Oxalic acid is a myco-and phytotoxin with nephritic influence particularly by the mono-gastric animals (Gedek, 1974). It leads to some toxic symptoms. It accumulates calcium oxalate crystals in the kidneys and urinary tract (causing progressive nephrosclerosis in animals). It can increase animal susceptibility to idiosyncrasies (Sharaf, 1974 and Clarke *et al*., 1981).

Oxalates found in plants are highest at the leafy stage of growth and plants, which are normally not dangerous to stock, may become so at certain times of the year. Unfortunately, most oxalate-containing plants are very palatable to stock. Oxalates in plants are found in form of calcium, potassium, or sodium salts. Sodium and potassium oxalates (and acid oxalates) are soluble and absorbed, but calcium oxalate is insoluble and is not assimilated during digestion thus precipitates in the intestine and evacuates with the faeces (Sharaf, 1974). Soluble oxalates are largely detoxicated, being converted into carbonate and bicarbonate, which if produced in sufficient quantities may produce a severe alkalosis. If, however, a large enough quantity of oxalate is ingested some of it will be absorbed unchanged and thus lead to oxalate poisoning. Animals, which have become accustomed to oxalate pastures, can consume considerably large quantities without ill effect. The form in which oxalate (as acid oxalate ion or as oxalate ion) is present in the plant may be of importance (Clarke and Clarke, 1978). There are interactions between some mycotoxins. For instance there is synergistic effect between OA and ochratoxin-A (ONA) (Frank, 1978) as well as between OA and ONA and/or citrinin (Gedek, 1983).

The aim of this study was to investigate the effect of graded levels of dietary oxalic acid on the growth performance, physiological responses and histological alteration on rabbits.

MATERIALS AND METHODS

Fifty Newzealand white (NZW) rabbits (25 animals per sex) of 2 months old were used in this study. Rabbits were brought from El-Serw - Station, Damietta Governorate with an average bodyweight of 1.15 kg. The animals were divided into 5 similar treatment groups (5 males and 5 females each). All animals were fed for 2 weeks on OA-free diet; thereafter, each group was offered one of the 5 tested diets which contained 0, 5, 10, 20, and 30% OA-salt (Table 1). All dietary ingredients were bought from the local market, whereas oxalic acid from Al-Gomhoria Co. for Chemicals, Al-Mansourah. The experimental feeding lasted for 8 weeks.

Table 1:Composition and chemical analysis of the experimental diets.

Ingredients %	Experimental diets				
	Control	T_1 5%	T_2 10%	T_3 20%	T_4 30%
Barley	17.0	15.0	15.0	22.0	15.0
Wheat bran	25.0	20.0	15.0	20.0	15.0
Yellow corn	45.0	42.5	40.0	25.0	17.5
Soybean meal (44 %)	12.5	17.0	19.5	12.5	22.0
Oxalic acid	0.0	5.0	10.0	20.0	30.0
Premix*	0.5	0.5	0.5	0.5	0.5
Total	100	100	100	100	100
Chemical analysis of the diets (%):					
Dry matter	88.51	89.18	89.71	90.93	89.74
Crude protein	15.74	15.06	15.90	15.51	15.41
Ether extract	2.84	2.71	2.39	2.06	1.61
Ash	3.88	3.64	4.10	4.13	3.49
Calculated ME** kcal/kg	2527	2507	2542	2558	2530

*** Vitamins and minerals mixture (Pfizer).**
**** According to NRC (1984).**

The animals of each group were individually housed in wooden boxes and supplemented with plastic feeders and waterers. Two electric fluorescence tubes (120 cm, 40w) were used for illumination. Ventilation was offered. Litter of sawdust was used. Faeces were daily removed. All treatments were under identical environmental conditions. Ambient temperature and relative humidity were 23 $\pm$ 3ºC and 70 $\pm$ 5%, respectively. Dry mash and water were daily offered for *ad lib*. Before access of feed and water, live bodyweight was recorded weekly for each animal. Feed consumption was recorded too. Two animals per group were slaughtered after 2 months of the experimental feeding (or at the death if happened before the 8th week) for blood collection and organs weight.

Samples of muscles and organs were kept frozen for analysis and another samples were fixed in formalin for histopathological examination. All chemicals used were from the United Co. for Chemicals and Medical Preparations. Heparinized test tubes were used for for blood collection from the tested animals. The sera were separated by centrifugation for different analyses. Blood metabolites were calorimetric determined using commercial kits from Diamond diagnostics (France). Since total proteins, creatinine, urea, uric acid, transaminases, and cholesterol were analyzed according to the methods of Henry (1964), Henry (1974), Patton and Crouch (1977), Trinder (1969), Reitman and Frankel (1957), and Watson (1960), respectively. Oxalic acid was estimated according to the method of Pearson (1973). Routine chemical analysis was carried out using the official methods of analysis (AOAC, 1980). The technique of Drury and Wallington (1980) was used for preparing the specimens for the histological test. The obtained numerical data were statistically analyzed according to Snedecor and Cochran (1988) and Duncan (1955).

RESULTS

Bodyweight gains of the tested animals (males and females) are presented in Table 2. The analysis of variance showed significant ($P \leq 0.01$) differences among the treatment groups within either of males and females. The decrease in bodyweight gains was proportional to the level of the dietary OA.

Data of feed intake and feed conversion of both male and female rabbits are given in Tables 3 and 4, respectively. The analysis of variance confirms the highly significance ($P \leq 0.01$) among treatment groups within both sexes and for both parameters. The dietary OA-inclusion, generally, caused low feed intake, particularly and significantly at 10% OA and more. The opposite was true with feed conversion, since the presence of OA compared with the control in the rabbits diet led to high feed conversion value, especially at 30% and/or 20% OA. Female rabbits consumed less feed and converted it somewhat better than males.

Although the rabbits fed on 30% and 20% OA had lower longevity, since they died during the 6^{th} and 7^{th} week of the experimental feeding, respectively; they consumed more OA (Table 5) than the other animal groups. The increase in OA consumption was gradually correlated with its dietary level. Differences among treatment groups and between sexes were significant.

Data of relative weights of the different organs of male and female rabbits are presented in Table 6. It shows significantly higher weights of kidneys and liver and significantly lower carcass weight by feeding OA-including diets.

Biochemical analysis of blood sera from the tested animals revealed dysfunction of both liver and kidneys of the rabbit fed on diets included OA. Hence, there were significant elevations in the activity of both transaminases (GOT and GPT) and in the concentrations of either of

cholesterol, creatinine, uric acid and OA. Whereas the levels of serum total proteins were significantly decreased (Table 7).

Table 2:Effect of dietary OA on bodyweight gains ($\bar{x}$ ± SE) g of male and female rabbits (g/head/week).

Age in week	Dietary treatments				
	Control	Tr_1	Tr_2	Tr_3	Tr_4
Males:					
11th	202 ± 22.5	173 ± 18.9	185 ± 10.6	134 ± 22.8	125 ± 26.2
12th	174 ± 39.3	190 ± 10.6	140 ± 24.8	126 ± 19.5	120 ± 11.2
13th	166 ± 18.5	175 ± 10.0	133 ± 21.1	108 ± 16.1	115 ± 22.4
14th	182 ± 22.5	176 ± 16.4	125 ± 15.4	117 ± 7.60	109 ± 23.0
15th	172 ± 38.5	158 ± 14.4	143 ± 7.60	114 ± 17.8	83.0 ± 24.7
16th	160 ± 19.7	161 ± 11.4	102 ± 14.4	105 ± 27.0	---
17th	195 ± 17.5	169 ± 8.20	188 ± 11.5	---	---
18th	210 ± 18.7	156 ± 6.50	121 ± 12.9	---	---
Total gain (11th - 18th wks)	1460 ± 17.0^{aA}	1362 ± 11.3^{bAB}	1125 ± 30.2^{bc}	691 ± 11.0^{acB}	525 ± 16.4^{cC}
Females:					
11th	167 ± 35.9	157 ± 9.80	125 ± 20.3	110 ± 20.2	105 ± 12.8
12th	166 ± 33.1	180 ± 15.8	126 ± 13.4	115 ± 33.5	110 ± 15.0
13th	166 ± 21.3	165 ± 15.4	139 ± 10.8	118 ± 11.0	110 ± 5.70
14th	188 ± 27.8	180 ± 29.2	160 ± 10.6	102 ± 14.4	75.0 ± 7.40
15th	148 ± 30.5	142 ± 30.2	147 ± 2.70	122 ± 20.2	50.0 ± 8.10
16th	180 ± 24.9	177 ± 24.9	101 ± 4.20	87.0 ± 17.9	---
17th	185 ± 14.4	151 ± 14.3	149 ± 4.20	---	---
18th	160 ± 14.2	174 ± 18.5	143 ± 6.70	---	---
Total gain (11th - 18th wks)	1360 ± 13.5^{aA}	1328 ± 14.4^{abA}	1095 ± 18.4^{bAC}	649.0 ± 12.5^{bBC}	450.0 ± 26.7^{bB}

a-c and A-C: means in the same row not followed by the same small or capital letters significantly (P ≤ 0.05 or 0.01, respectively) differ.

Oxalic acid was found not only in the rabbit's blood, but it was also accumulated in rabbits muscles, liver, and kidney, in a descending level. Its level in these tissues was gradually elevated according to its dietary level (Table 8). Differences among treatment groups and between sexes were significant.

The liver of rabbits treated with OA up to 20% level showed no pathological changes; while at a dietary concentration of 30%, there was a mild congestion of the portal vein in the portal tract. Kidney or rabbits received OA at concentration till 20% showed no pathological findings, while at a level of 30% there was a degeneration of the glomeruli, polymorphonuclear leukocytes infiltration and showed a sign of interstitial nephritis. Also, there was deposition of oxalate crystals.

Generally, the rabbits fed on OA supplemented diets reflected lower appetences for feed from the 3rd week of the experiment and go on,

particularly by those fed on the highest levels (20 and 30%). These groups of animals showed also stress symptoms. By the continual feeding, these changes were severe in the same both groups, particularly among rabbits fed on 30% OA. At the 6th week of the experiment, all animals died by feeding on 30% OA-including diet; whereas those fed on the 20% level died later at the 7th week. At the 8th week the rabbits fed on 10% OA-supplemented diet reflected fatigue and bodyweight loss.

Table 3:Effect of dietary OA on feed consumption (x ± SE) g/head/week of both male and female rabbits.

Age in week	Dietary treatments				
	Control	Tr_1	Tr_2	Tr_3	Tr_4
Males:					
11th	735 ± 35.2	720 ± 35.5	765 ± 18.4	600 ± 17.0	605 ± 11.7
12th	650 ± 31.7	780 ± 38.3	610 ± 27.9	585 ± 23.4	550 ± 13.2
13th	610 ± 30.1	735 ± 31.7	570 ± 20.5	515 ± 20.8	555 ± 7.30
14th	700 ± 37.5	750 ± 27.8	510 ± 23.3	570 ± 32.7	525 ± 15.1
15th	740 ± 40.2	660 ± 25.1	575 ± 27.3	520 ± 18.8	390 ± 20.2
16th	675 ± 31.3	640 ± 25.8	450 ± 20.2	460 ± 13.5	---
17th	750 ± 26.7	700 ± 27.1	780 ± 19.5	---	---
18th	890 ± 22.2	625 ± 22.2	500 ± 17.1	---	---
Total (11th - 18th wks)	5750 ± 83.4^{A}	5610 ± 55.2^{A}	4760 ± 40.5^{aB}	3250 ± 52.8^{bB}	2625 ± 80.9^{bC}
Females:					
11th	610 ± 26.4	575 ± 19.0	680 ± 17.9	500 ± 7.70	515 ± 11.5
12th	650 ± 17.7	685 ± 13.7	500 ± 14.5	440 ± 13.4	525 ± 9.80
13th	630 ± 20.8	640 ± 17.4	560 ± 21.6	585 ± 15.8	530 ± 14.2
14th	615 ± 27.2	680 ± 15.8	640 ± 24.4	490 ± 13.9	375 ± 17.1
15th	585 ± 21.2	545 ± 26.3	510 ± 19.3	565 ± 19.4	270 ± 12.6
16th	645 ± 23.5	625 ± 20.8	440 ± 22.2	410 ± 15.2	---
17th	685 ± 27.2	995 ± 25.3	575 ± 31.8	---	---
18th	665 ± 17.8	705 ± 20.5	615 ± 26.7	---	---
Total (11th - 18th wks)	5085 ± 32.2^{aA}	5450 ± 56.9^{aA}	4520 ± 79.9^{bA}	2990 ± 68.2^{bB}	2215 ± 66.2^{bB}

a-b and A-C: means in the same row not followed by the same small or capital letters significantly (P ≤ 0.05 or 0.01, respectively) differ.

Table 4: Effect of dietary OA on feed conversion (x ± SE) g feed/g gain of male and female rabbits.

Age in Week	Dietary treatments				
	Control	Tr_1	Tr_2	Tr_3	Tr_4
Males:					
11th	3.81 ± 0.26	4.16 ± 0.31	4.14 ± 0.23	4.50 ± 0.21	4.86 ± 0.10
12th	3.74 ± 0.14	4.11 ± 0.34	4.35 ± 0.19	4.65 ± 0.19	4.60 ± 0.32
13th	3.68 ± 0.31	4.20 ± 0.30	4.29 ± 0.17	4.75 ± 0.35	4.83 ± 0.25
14th	3.85 ± 0.27	4.26 ± 0.33	4.08 ± 0.26	4.89 ± 0.27	4.81 ± 0.30
15th	4.06 ± 0.22	4.18 ± 0.19	4.02 ± 0.24	4.58 ± 0.31	4.71 ± 0.29
16th	4.22 ± 0.25	3.98 ± 0.27	4.41 ± 0.29	4.40 ± 0.37	---
17th	3.87 ± 0.31	4.14 ± 0.37	4.15 ± 0.20	---	---
18th	4.24 ± 0.24	4.00 ± 0.29	4.13 ± 0.33	---	---
Total (11th - 18th wks)	3.94 ± 0.12^{a}	4.13 ± 0.24^{a}	4.20 ± 0.19^{a}	4.63 ± 0.28^{abc}	4.76 ± 0.08^{b}
Females:					
11th	3.65 ± 0.14	3.68 ± 0.08	3.85 ± 0.30	4.92 ± 0.33	4.89 ± 0.29
12th	3.92 ± 0.23	3.81 ± 0.05	3.97 ± 0.23	4.00 ± 0.14	4.77 ± 0.34
13th	3.79 ± 0.18	3.89 ± 0.12	4.04 ± 0.19	4.98 ± 0.35	4.82 ± 0.22
14th	3.27 ± 0.13	3.77 ± 0.09	4.00 ± 0.27	4.78 ± 0.32	4.99 ± 0.19

15th	3.95 ± 0.27	3.83 ± 0.17	4.01 ± 0.14	4.62 ± 0.26	5.20 ± 0.39
16th	3.58 ± 0.21	3.52 ± 0.31	4.36 ± 0.22	4.74 ± 0.37	---
17th	3.70 ± 0.25	3.94 ± 0.26	3.91 ± 0.36	---	---
18th	4.15 ± 0.28	4.05 ± 0.35	4.30 ± 0.32	---	---
Total (11th - 18th wks)	3.75 ± 0.24^{aA}	3.81 ± 0.09^{aA}	4.06 ± 0.33^{a}	4.67 ± 0.16^{bB}	4.93 ± 0.29^{bB}

a-c and A-B: means in the same row not followed by the same small or capital letters significantly (P ≤ 0.05 or 0.01 , respectively) differ.

The P.M. test for the rabbits fed on 20% OA-included diet revealed presence of inflammation and congestion along the digestive tract; blue spots on the esophagus, stomach and intestine; haemorrhagic patches on the stomach, intestine, liver, lungs and kidneys; pale lungs; enlarged-dark kidneys and liver; and whity crystalline precipitations (gout) in the stomach. Moreover, the rabbits which fed on 30% OA-supplemented diet presented the same P.M. picture but with severity, besides the hemorrhage inside the digestive tract. The other groups of animals were normal.

DISCUSSION

Confirming the obtained results in the present research, it is worth mentioning that plants containing oxalate decrease the absorption of calcium (Sharaf, 1974). OA content of a number of tropical grasses is high and some deaths from oxalate poisoning have been recorded (Stobbs and Thompson, 1978). In range animals a high intake of oxalates in plants is most commonly associated with a high incidence of urinary oxalate calculi and hypocalcemia, particularly by monogastrics than ruminants. The ingestion of excess oxalate causes some gastrointestinal irritation, muscular weakness and paralysis. Continued ingestion of small amounts of oxalate may lead to renal damage (nephrosis) or to the development of urinary calculi (due to precipitation of oxalate crystals in the lumen of the renal tubules) and in horses to the development of nutritional secondary hyperparathyroidism. Up to 450 g of sodium oxalate given by mouth is required to produce fatal effects in horses. Heavy mortalities may occur in groups of animals which are not accustomed to grazing the toxic pasture. Acute oxalate poisoning reflects clinical signs including paresis, muscle tremor, staggering, recumbence, increased heart rate, and death in coma. Where in chronic cases there are renal damage, poor appetite, failure to grow, ascetics and anemia. The gross findings are deposition of crystals in the renal tubules and pelvis and even in the ureters and urethra, severe gastroenteritis, necrosis and inflammation of the epithelium of the oesophagus (Blood and Radostits, 1989).

The obtained results of the blood could be interpreted on light of the clinical chemistry (Merck, 1974; Varley, 1978; and Zilva and Pannall, 1983) as follows:

1. Transaminases activity increases in toxic hepatitis, which may be associated by liver cell damage, necrosis, obstruction of the large bile passages, cirrhosis, hepatic infiltra-tion, hemolytic anemia, and skeletal muscle trauma.

2. Increases in cholesterol occur in a number of conditions. Hypercholesterolemia is found most characteristically in nephrosis, obstructive jaundice, arteriosclerosis, cardiovascular disease, and dysglobulinemia.
3. Causes of low total protein concentration are overhydration, excessive loss of protein through the kidney in the nephritic syndrome (massive proteinuria), or through the intestine in protein-losing entropathy, malabs-orption (for peptic ulcer, enteritis, sprue and other steatorrhoeas), decreased formation of protein in the liver, increased catabolism of protein, hyperlipidemia, hemorrhage, and liver disease (cirrhosis). A reduction in the total protein is one of the causes of edema. This type of edema is often known as nephritic edema since it is found in nephrosis.
4. Creatinine concentration is normally lower in females than in males. Its levels increase in cases of kidney and heart insufficiencies (decompensation).
5. Blood urea level is depending on protein intake, endogenous protein metabolism, and urinary execution of urea. It increases in cases of kidney diseases, acute obstruction of the intestine, intoxication, and severe protein catabolism.
6. Uric acid belongs to, and is the end product of the metabolism of, the group of substances known as the purines. Increase in serum uric acid occurs when there is impaired renal function, and in most conditions in which the blood urea is raised. Though renal complications may well develop ultimately in chronic gout, apart from this no increase in blood urea should accompany the rise in uric acid in that condition. Arise is sometimes seen in pernicious anemia, kidney insufficient, acute gout, and hunger. A serious effect of hyperuricaemia is due to precipitation of urate in the kidney, leading to renal failure. In attacks of acute gouty arthritis, local factors are of more importance than the plasma urate levels. Gout may lead to permanent joint deformity. Pseudogout, while not a disorder of purine metabolism, produces a similar clinical picture to gout, since salts precipitate in joint cavities.

Table 5: Oxalic acid intake ($\bar{x}$ ± SE) g/head/week throughout the experimental period by male and female rabbits.

Age in Weeks	Dietary treatments			
	Tr_1	Tr_2	Tr_3	Tr_4
Males:				
11th	36.0 ± 1.14	76.5 ± 2.58	120 ± 4.32	181.5 ± 5.76
12th	39.0 ± 2.18	61.0 ± 3.22	117 ± 4.79	165.0 ± 6.43
13th	36.8 ± 3.11	57.0 ± 3.28	103 ± 4.07	166.5 ± 6.90
14th	37.5 ± 3.55	51.0 ± 3.80	114 ± 3.80	157.5 ± 5.75
15th	33.0 ± 3.80	57.5 ± 4.20	104 ± 5.10	117.0 ± 6.30
16th	32.0 ± 2.40	45.0 ± 3.80	92.0 ± 4.50	---
17th	35.0 ± 3.10	78.0 ± 3.70	---	---
18th	31.3 ± 2.30	50.0 ± 4.60	---	---
Total (11th - 18th wks)	280.6 ± 2.70^{aA}	476.0 ± 3.65^{aD}	650.0 ± 4.61^{bCD}	787.5 ± 6.23^{cBC}
Females:				
11th	28.8 ± 2.10	68.0 ± 3.30	100 ± 3.70	154.5 ± 4.60

12^{th}	34.3 ± 2.60	50.0 ± 2.90	88.0 ± 3.40	157.5 ± 4.10
13^{th}	32.0 ± 2.11	56.0 ± 3.02	117 ± 3.91	159.0 ± 4.66
14^{th}	34.0 ± 2.60	64.0 ± 3.50	98.0 ± 4.00	112.5 ± 4.90
15^{th}	27.3 ± 1.85	51.0 ± 2.20	113 ± 3.90	81.0 ± 3.45
16^{th}	31.3 ± 2.10	44.0 ± 2.70	82.0 ± 3.60	---
17^{th}	29.8 ± 1.70	58.5 ± 2.80	---	---
18^{th}	35.3 ± 3.40	61.5 ± 3.55	---	---
Total (11^{th} - 18^{th} wks)	252.8 ± 2.31^{aA}	453.0 ± 3.00^{aAB}	598.0 ± 3.75^{bB}	664.5 ± 4.34^{bC}

a-c and A-D: means in the same row not followed by the same small or capital letters significantly (P ≤ 0.05 or 0.01, respectively) differ.

Table 6: Effect of dietary OA on the relative weights (% of LBW) of organs for male and female rabbits after 8 weeks of the experimental period.

Organs	Dietary treatments				
	Control	Tr_1	Tr_2	Tr_3	Tr_4
Males:					
LBW, g	2610 ± 25.7	2512 ± 13.0	2275 ± 18.0	1841 ± 10.3	1675 ± 19.2
Kidneys	0.52^{aAC}	0.56^{abA}	0.65^{bC}	0.85^{bB}	1.00^{cB}
Liver	1.38^{aA}	1.67^{aA}	1.89^{a}	2.88^{abB}	3.46^{bB}
Lungs	0.81	0.92	0.92	1.09	1.31
Heart	0.25	0.24	0.26	0.31	0.35
Brain	0.24	0.25	0.26	0.30	0.32
Spleen	0.13	0.14	0.13	0.17	0.18
Head	5.36	5.69	5.50	6.25	7.16
Carcass	39.8^{aA}	39.4^{aA}	38.9^{C}	38.6^{bB}	37.7^{cB}
Females:					
LBW, g	2470 ± 26.2	2478 ± 10.0	2245 ± 13.2	1799 ± 23.8	1655 ± 26.5
Kidneys	0.52^{aA}	0.51^{aA}	0.58^{a}	0.77^{ab}	0.91^{bB}
Liver	1.33^{aA}	1.40^{aA}	1.70^{ac}	2.61^{bcB}	3.08^{bB}
Lungs	0.73	0.61	0.85	1.00	1.03
Heart	0.22	0.21	0.25	0.29	0.30
Brain	0.21	0.22	0.22	0.31	0.30
Spleen	0.13	0.12	0.13	0.18	0.18
Head	5.06	5.14	4.90	6.50	6.65
Carcass	39.5^{aA}	38.8^{aA}	38.0^{B}	37.5^{C}	36.5^{D}

a-c and A-D: means in the same row not followed by the same small or capital letters significantly (P ≤ 0.05 or 0.01, respectively) differ.

Table 7: Means ± standard errors of some blood serum metabolites of male(M) and female (F) rabbits fed on OA for 8 weeks.

Treat-Ment Group	Sex	GOT, u/l	GPT, u/l	Choles-terol, mg/dl	Total protein, g/dl	Creati-nine, mg/dl	Urea, mg/dl	Uric acid, mg/dl	Oxalic acid, g/dl
Control	M	10.0 ± 0.82^{aA}	12.0 ± 2.12^{A}	247.5± 9.19^{aA}	10.1 ± 0.17^{A}	0.48 ± 0.09^{A}	4.43 ± 0.71^{aA}	7.09 ± 0.37^{A}	---
	F	8.50 ± 2.12^{aA}	10.0 ± 2.83^{A}	236.0± 15.6^{aA}	10.1 ± 0.33^{A}	0.43 ± 0.06^{A}	4.88 ± 0.54^{A}	7.24 ± 0.30^{aA}	---
Tr_1	M	16.0 ± 4.24^{A}	14.5 ± 3.54^{A}	268.5± 13.4^{b}	9.16 ± 0.38^{aA}	8.84 ± 0.04^{E}	4.78 ± 0.53^{aA}	10.3 ± 0.44^{aA}	0.37 ± 0.10^{A}
	F	21.0 ± 2.80^{A}	12.0 ± 1.41^{A}	265.0± 16.3^{A}	9.51 ± 0.62^{A}	7.99 ± 0.21^{E}	5.16 ± 0.16^{A}	9.67 ± 0.13^{A}	0.97 ± 0.03^{A}
Tr_2	M	23.0 ± 5.66^{A}	21.0 ± 5.66^{A}	320.5± 16.3^{abc}	7.67 ± 0.15^{bC}	11.1 ± 0.08^{D}	5.82 ± 0.31^{A}	13.4 ± 1.65^{D}	2.14 ± 0.19^{D}
	F	23.0 ±	19.0 ±	295.5±	7.35 ±	10.7 ±	5.62 ±	12.3 ±	2.47 ±

		5.66^{A}	2.83^{A}	6.36^{bA}	0.03^{C}	0.64^{aD}	0.18^{A}	0.21^{bAC}	0.09^{D}
Tr_3	M	53.0 ± 8.49^{b}	59.5 ± 3.54^{B}	345.5± 31.8^{bc}	6.27 ± 0.16^{aB}	12.0 ± 0.19^{C}	6.53 ± 0.35^{b}	15.1 ± 1.82^{bAC}	3.40 ± 0.28^{C}
	F	46.5 ± 7.78^{b}	56.0 ± 2.83^{B}	338.5± 12.0^{bB}	6.25 ± 0.39^{B}	11.2 ± 0.88^{aC}	6.28 ± 0.16^{A}	15.4 ± 0.33^{BC}	3.53 ± 0.28^{C}
Tr_4	M	76.0 ± 7.41^{B}	64.5 ± 3.54^{B}	364.0± 24.0^{BC}	5.73 ± 0.22^{aB}	12.8 ± 0.23^{B}	8.60 ± 0.11^{cB}	20.4 ± 1.36^{cBC}	4.07 ± 0.09^{B}
	F	71.5 ± 6.36^{B}	59.5 ± 3.53^{B}	380.5± 10.6^{B}	5.96 ± 0.64^{B}	12.4 ± 0.43^{B}	9.07 ± 0.18^{B}	19.1 ± 1.69^{B}	4.24 ± 0.16^{B}

a-c and A-E: means in the same column and sex of animal scripted with variable small or capital letters significantly (P ≤ 0.05 or 0.01, respectively) differ.

Table 8: Oxalic acid contents ($\bar{x}$ ± SE % on fresh weight basis) of male (M) and female (F) rabbits fed on OA for 8 weeks.

Treatment group	Sex	Tissues		
		Muscles	Liver	Kidney
Control	M	---	---	---
	F	---	---	---
Tr_1	M	0.61 ± 0.12^{A}	0.19 ± 0.03^{a}	0.03 ± 0.01^{aA}
	F	0.57 ± 0.13^{A}	0.18 ± 0.10^{aA}	0.03 ± 0.01^{aA}
Tr_2	M	1.03 ± 0.16 ^{aA}	0.23 ± 0.01^{a}	0.07 ± 0.01^{A}
	F	1.00 ± 0.09^{A}	0.24 ± 0.01^{b}	0.06 ± 0.01^{a}
Tr_3	M	1.61 ± 0.17 ^{bAB}	0.28 ± 0.02^{a}	0.12 ± 0.02^{b}
	F	1.34 ± 0.15^{B}	0.27 ± 0.06^{B}	0.12 ± 0.02^{b}
Tr_4	M	1.90 ± 0.10^{bB}	0.31 ± 0.02^{a}	0.20 ± 0.04^{aB}
	F	1.71 ± 0.18^{B}	0.30 ± 0.01^{aB}	0.18 ± 0.03^{b}

a-b and A-B: means in the same column and sex of animals scripted with different small or capital letters significantly (P ≤ 0.05 or 0.01, respectively) differ.

Histological alterations due to OA intake were described. Necrosis of the tubular epithelium is often occurs in nephrotoxicity. Some chemicals (minerals) kill the tubular cells by direct action on the cell, since the mineral may be found under or in the pelvic epithelium or more commonly in the tubules at the corticomdullary junction. Interstitial nephritis is somewhat similar to tubular regeneration, it means tubular distortion, basophilic and leukocytes (mainly lymphoid cells) accumulation. Interstitial nephritis is often diffused and of sufficient severity to cause death in some cases (Glaister, 1986).

The association of the oxalate crystals (renal oxalosis) with damaged tubules and giant cells suggests that the oxalate crystals are responsible for the granulomatous interstitial nephritis (Verani *et al*., 1989). Regular receiving of hemodialysis for a renal failure led to primary hyperoxaluria. Calcium oxalate deposits appear in the skin, bone marrow, and both kidneys (Schillinger *et al*., 1990) as well as within sperm granuloma of the epididymis (Coyne *et al*., 1994). Since retention of calcium oxalate crystals within the renal tubules is essential for nephrolithiasis. Crystals appeared to be retained either by attachment to the tubular epithelium or by aggregating with other crystals thus becoming large enough to be retained by their collective size (Khan and Hackett, 1991). It is worth- mentioning that renal epithelial cells are rapidly bound and internalize calcium oxalate (Lieske *et al*., 1994). Oxalate is therefore a cell toxin and can produce cellular degeneration products (Hackett *et al*., 1995).

Moreover, the levels of oxalate during hyperoxaluric state (by receiving banana stem juice) showed remarkable alterations in liver tissue (Kailash and Varalakshmi, 1992). Dhawale and Phatak (1998) reported that the outbreaks of visceral gout may be attributed to organic nephrotoxins such as mycotoxins and phytotoxins. So, it was recommended that the public might be educated about the dangers of eating unknown plants with potentially adverse effects (Sanz and Reig, 1992).

The aforementioned findings and interpretations confirm the obtained data of the present study. All of these refer to the toxicity signs of OA and therefore it is a must to avoid feeding animals (particularly small and mono-gastric animals as well as man) on OA-rich plants.

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تأثير المستويات المدرجة من حمض الأوكساليك فى العليقة على الأداء والاستجابات الفسيولوجية وكذلك التغييرات النسيجية فى أرانب النيوزيلاندى الأبيض0

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استخدم 50 أردب نيوزيلاندى أبيض عمر شهرين (25 ذكر + 25 أنثى) لدراسة تأثير استخدام نسب مدرجة من صفر إلى 30% من حمض الأوكساليك فى العليقة على مظهر النمو وإستهلاك العليقة ومعدل التحويل الغذائى وكذلك بعض التغييرات فى تركيب الدم والأنسجة0 إنخفضت زيادة وزن الجسم بشكل يرتبط بتركيز حمض الأوكساليك فى كلا الجنسين (وكان الإنخفاض معنويا بداية من تركيز 10% حمض أوكساليك فصاعدا) ، وكانت الزيادة فى الذكور أعلى0 انخفض إستهلاك الغذاء بوجه عام بزيادة تركيز حمض الأوكساليك، وكان الإنخفاض معنويا بداية من 10% حمض أوكساليك فصاعدا، وكانت الإناث أقل إستهلاكا للغذاء عن الذكور0 ساء التحويل الغذائى بشكل يرتبط بتركيز حمض الأوكساليك وبشكل معنوى خاصة على أعلى تركيزين0 وكانت الإناث أفضل قليلا فى تحويلها للغذاء عن الذكور0 زاد إستهلاك حمض الأوكساليك بزيادة تركيزة فى الغذاء رغم نفوق المجموعة العالية (30% حمض أوكساليك) فى سادس أسبوع والتى دونها (20% حمض أوكساليك) فى سابع أسبوع، وكانت الفروق بين المعاملات وبين الجنسين معنوية0 زاد وزن الكلى والكبد معنويا بينما قل وزن الذبيحة بالتغذية على حمض الأوكساليك0 أدى حمض الأوكساليك إلى زيادة الترانس أمينات والكوليسترول والكرياتينين وحمض اليوريك وحمض الأوكساليك، وانخفض البروتين الكلى فى الدم، وكانت الفروق معنوية بين المعاملات لكل هذه القياسات0 تراكم حمض الأوكساليك بتركيز تنازلى فى العضلات ثم الكبد فالكلى، وكان هناك إرتباطا بين تركيزة فى هذه الأنسجة وتركيزه فى العليقة، وكان تركيزه فى الذكور أعلى عنه فى الإناث0 أوضح الفحص النسيجى عدم وجود تغييرات إلا فى الحيوانات المغذاة على 30% حمض أوكساليك، فكان الكبد به احتقان فى الوريد البابى، وكانت الكلية بها تحطم فى الأوعية، ورشح كرات الدم البيضاء عديدة الأنوية، والتهاب كلوى بينى، وتراكم لبلورات الأوكسالات0

انخفضت شهية الأرانب من الأسبوع الثالث من التغذية الملوثة خاصة بأعلى التركيزات (30% و20% حمض أوكساليك) مع ظهور أعراض الاضطراب على حيوانات هاتين المجموعتين، وتشتد الأعراض بزيادة فترة التغذية خاصة على التركيز الأعلى من التوكسين، إذ نفقت حيوانات هذه المجموعة كلها فى الأسبوع السادس، بينما نفقت حيوانات المجموعة المغذاة على 20% حمض أوكساليك فى الأسبوع السابع، بينما المجموعة المغذاة على 10% توكسين أظهرت إجهادا أو نقصا فى الوزن فى الأسبوع الثامن0 الصفة التشريحية لحيوانات المجموعة المغذاة على 20% حمض أوكساليك أظهرت التهابا واحتقانا فى القناة الهضمية، وبقع زرقاء على المرئ والمعدة والأمعاء ، وبقع نزفيه على المعدة والأمعاء والكبد والرئة والكلى، وشحوب لون الرئة، وتضخم ودكانة لون الكلى والكبد ، إضافة إلى نقرص المعدة (رواسب بلورية بيضاء)0 مجموعة الحيوانات المغذاة على 30% حمض أوكساليك أظهرت نفس الصفة التشريحية السابقة لكن بصورة أشد، مع نزف الجهاز الهضمى0 باقى الحيوانات فى المجاميع الأخرى كانت طبيعية0

وتشير النتائج المتحصل عليها من هذه الدراسة إلى التأثير السيئ لحمض الأوكساليك، وضرورة تجنب تغذية الحيوانات الصغيرة ووحيدة المعدة على النباتات الغنية بهذا الحمض0