Proceedings 5th World Rabbit Congress, 25-30 July 1992, Corvallis – USA, 1206-1218

HYPERVITAMINOSIS A IN RABBITS. III. REPRODUCTIVE EFFECTS AND INTERACTIONS WITH VITAMINS E AND C AND ETHOXYQUIN

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Summary

Forty New Zealand White does were assigned to five experimental groups which were orally administered vitamins A, C and E and ethoxyquin as follows: no supplementation (group 1), 25,000 IU vitamin A (group 2), 25,000 IU vitamin A + 50 mg vitamin C (group 3), 25,000 IU vitamin A + 50 mg vitamin E (group 4) and 25,000 IU vitamin A +25 mg ethoxyquin (group 5)/animal/day. The animals had been treated for 2 weeks prior to breeding and continued treatment until the 4th week of suckling of the second litter, with a two litter recovery period. There was a significant decrease in litter size in group 2 due to fetal resorption as a result of excess vitamin A compared to the control group, but no significant differences between the other groups. No significant differences in birth or weaning weight were noted between groups. Stillbirths, hydrocephalus and postnatal mortality through the 1st week and suckling period were high in groups 2 and 5, moderate in groups 1 and 4 and low in group 3. Beneficial effects of vitamins C and E on fetal resorption, stillbirths, and postnatal mortality were noted. Ethoxyquin seemed to have a beneficial effect on fetal resorption only. There were significant differences in plasma vitamin A influenced by treatments over time and parities, with high levels noted in groups 2 and 5 at parturition and in the second parity, respectively. Plasma vitamin A seemed to be affected by physiological state of the animal. Throughout the recovery period, the first parity was a transitional parity after discontinued vitamin A administration, during which reproductive performance started to approach normal values. The animals returned to normal reproductive performance by 12 weeks and there were no significant differences between groups through the recovery period.

Introduction

Vitamins are essential for normal health and different physiological functions in different species. Vitamin A is important for growth, cellular differentiation, fertility and maintenance of pregnancy (Cheeke, 1987; Rachman et al., 1987; McDowell, 1989). However, vitamin A is toxic and has a teratogenic effect when given in high doses to

animals (James, 1976). Toxicity signs include reduced growth, bone abnormalities and reproductive failure such as abortions, fetal resorptions, small litters, stillbirths, and high mortality through the first week of life (Cheeke et al., 1984; Moghaddam et al., 1987; Yamini and Stein, 1989; Deeb et al., 1992).

Vitamin E has an important role in fertility and reproduction in addition to its greater function in preventing peroxide damage to tissues and muscular dystrophy in rabbits and guinea pigs. Vitamin E is described as a disease resistance vitamin due to its role in protecting leukocytes and macrophages during phagocytosis and increasing immunity responses (Reddy et al., 1987b). Additional functions of vitamin E have been reported by Scott et al. (1982) in the synthesis of ascorbic acid.

Vitamin C is sufficient in small quantities under ordinary circumstances, but larger quantities may be required to maintain good health during adverse environmental conditions, physiological stress and certain disease conditions (McDowell, 1989).

Ethoxyquin is a synthetic antioxidant which acts to prevent the autoxidation process that causes rancidity of fat, so it is usually added to the diet to maintain vitamin A activity and have beneficial effects of larger litter size and lower mortality (Isenstein, 1970).

It is very important to know the interrelationship between excessive vitamin A and vitamins C and E and ethoxyquin through pregnancy and suckling, and to determine whether vitamins C, E and ethoxyquin help animals overcome the harmful effects of excessive vitamin A or increase the toxicity. Of practical importance is the time required for recovery from the adverse effects of excess vitamin A on reproduction in rabbits. These are the aims of the present study.

Materials and Methods

Forty New Zealand White does about 18 months of age and 3.5 kg average body weight were assigned to five experimental groups, with eight does per treatment. The animals were randomly placed in individual wire cages. A standard OSU diet (Table 1) and water were available ad libitum.

Treatments consisted of orally administered vitamins A (retinol palmitate), vitamin C (L-ascorbic acid), vitamin E as a natural antioxidant and ethoxyquin as a synthetic antioxidant as follows: no supplementation (control), 25,000 IU vitamin A/animal/day (A), 25,000 IU vitamin A + 50 mg vitamin C (A+C), 25,000 IU vitamin A + 50 mg vitamin E (A+E) and 25,000 vitamin A + 25 mg ethoxyquin/animal/day (A + ethoxyquin) for treatments 1, 2, 3, 4 and 5, respectively. Two weeks after starting on the treatments, does were bred to NZW bucks. Oral administration of treatments continued until 4 weeks post-kindling of the second parity.

Table 1. Composition of the standard OSU diet.

Ingredient	% of Mix
Alfalfa	44.2424
Molasses	3.000
Wheat mill run	45.4465
Bentonite	1.25
Vitamin A*	0.6000
Vitamin E**	0.2000
Salt	0.5000
Meat meal	2.4023
Canola oil	2.3588

* Provided 13,200 IU/kg diet.

** Provided 26.4 IU/kg diet.

Blood samples were collected before mating (15 days after treatments began), day 15 of pregnancy, parturition and day 15 of suckling for vitamin A analysis throughout the two parities. Blood was centrifuged and the plasma prepared and frozen until assay. Does were palpated for pregnancy on days 10 and 28 to determine which does resorbed or aborted the fetuses. Data on litter size, birth weight and mortality at birth (stillbirth) were recorded. Post-natal mortality rate and live body weight were recorded weekly until weaning at 4 weeks of age.

For vitamin A analysis of plasma, a high performance liquid chromatography (HPLC) method was used (Bieri et al., 1979; Chow and Omaye, 1983; Omaye and Chow, 1986).

Statistical analysis was conducted by analysis of variance using SAS Package 1990.

After the experimental period of vitamin administration, does were bred again to investigate the depletion period required for does to return to normal reproductive performance. The same parameters were recorded as in the treatment period.

Results and Discussion

Litter Size

Average litter size (± SE)/doe over two parities is shown in Table 2. High levels of vitamin A had a severe effect on litter size by increasing fetal resorption and abortion. This was clearly illustrated by a significant decrease ($P < 0.01$) in litter size in group 2 (A) compared to group 1 (control). No significant differences were noted between groups 3, 4 and 5 or between these groups compared to group 1 or group 2 over two parities. There was no significant difference between the first and second parity. Over the two parities, the number of resorbed litters (palpated pregnant on day 10 and non-pregnant on day 28) were 0, 5, 4, 1, and 4 for treatments 1 through 5, respectively. One abortion occurrred in treatment 2. These results indicate that high vitamin A alone greatly increases fetal resorption, thus reducing litter size, and that vitamins C and E and ethoxyquin have an important role in protecting against the effects of high levels of vitamin A. Litter size increased in groups 3, 4 and 5 to 7.5/doe compared to 4.5/doe in group 2, with no significant differences in comparison to the control, 9.7/doe. The role of vitamin C in reproduction is not well known, but vitamin C has an important role during adverse conditions and physiological stress by increasing immune response (McDowell, 1989), and may have an antagonistic effect against excess vitamin A (Nieman and Obbink, 1954; Ismail et al. 1992b). Excess vitamin A has an antagonistic effect toward vitamin E activity. Thus the infertility, abortions, stillbirths and neonatal deaths due to hypervitaminosis A and hypovitaminosis E can be avoided by supplementation with vitamin E, which reduces the fetal resorption resulting from high levels of vitamin A (Ringler and Abrams, 1970: DiPalma and Ritchie, 1977; Bendich and Langseth, 1989; Yamini and Stein, 1989). Vitamin E also has a role in disease resistance, by increasing immunity responses (Reddy et al., 1987b) and by increasing synthesis of vitamin C (Scott et al., 1982). The mode of action of ethoxyquin seems similar to that of vitamin E in protecting against fetal resorption, increasing litter size and decreasing abortion and physical deformity (Isenstein, 1970).

The present results indicate that vitamins C and E and ethoxyquin may have beneficial effects on rabbit reproduction by protecting against the harmful effects resulting from high levels of vitamin A.

There were numerous cases of fetal deformities, primarily in treatment 2 (high vitamin A). The major deformity was hydrocephalus, while there were several cases of protruding eyes, and one instance of a kit with no eyes.

Table 2. Reproductive data over two parities through the period of treatment administration.

Treatment	Litter Size/Doe	Birth Weight (g)	Weaning Weight (g)	Mean Mortality at Birth	Mortality at Birth (%)	Mean Mortality at 1st Week	Mortality at 1st Week (%)	Total Mortality (%)
1. Control								
	(9)*	(97)	(68)					
First parity	10.77	53.47	509.85		14.43		14.43	29.90
	(8)	(68)	(50)					
Second parity	8.50	54.24	527.34		13.24		8.82	26.47
Overall	9.71 ± 0.91[a]	56.73 ± 2.49	538.16 ± 28.82	1.35 ± 0.39	13.94[b]	1.18 ± 0.79	12.12	28.48
2. Vitamin A								
	(6)	(25)	(15)					
First parity	4.17	67.8	492.13		24.00		16.00	40.00
	(6)	(29)	(0)					
Second parity	4.83	51.83	-		55.17		41.38	100.00
Overall	4.5 ± 0.97[b]	60.76 ± 3.05	491.92 ± 83.36	1.83 ± 0.46	40.74[a]	1.33 ± 0.73	29.63	72.22
3. Vitamins A+C								
	(5)	(46)	(31)					
First parity	9.20	50.83	538.42		8.70		23.91	32.61
	(9)	(59)	(43)					
Second parity	6.560	55.24	495.09		5.80		20.34	27.12
Overall	7.5 ± 1.07[ab]	59.62 ± 3.02	493.72 ± 25.67	0.5 ± 0.17	6.67[b]	1.64 ± 0.57	21.9	29.52
4. Vitamins A+E								
	(8)	(64)	(32)					
First parity	8.00	55.98	487.59		12.50		35.94	50.00
	(6)	(35)	(19)					
Second parity	5.83	60.40	571.53		31.43		8.57	45.71
Overall	7.1 ± 0.86[ab]	59.28 ± 2.89	537.53 ± 27.79	1.36 ± 0.39	19.19[ab]	1.86 ± 0.75	26.26	48.48
5. Vitamin A + ethoxyquin								
	(6)	(39)	(14)					
First parity	6.5	53.38	543.64		51.28		12.82	64.10
	(4)	(32)	(5)					
Second parity	8.00	53.00	400.80		15.63		59.38	84.38
Overall	7.1 ± 1.26[ab]	56.79 ± 2.85	516.78 ± 50.78	2.5 ± 1.02	35.21[ab]	2.4 ± 0.91	33.8	73.24

* Figures in parentheses represent number of animals.

** Within each column, any two means having at least one similar letter are not significantly different.

Birth Weight and Weaning Weight

Average birth weight and weaning weight (± SE) are presented in Table 2. There were no significant differences in birth weight or weaning weight between all the groups or between the two parities. The most important factor affecting litter weight at birth was litter size. There was a negative correlation between birth weight and litter size ($r = -0.365 \pm 0.037$) and no appreciable difference in birth weight between litters of 5, 6 and 7 (Afifi et al., 1977; Khalil et al., 1987; Ismail, 1988).

A decrease was noted in litter size in group 2 (A) due to higher embryonic mortality. Therefore, birth weight in this group would be expected to increase as compared to average birth weight of larger litter sized groups (groups 1, 3, 4 and 5). The high level of vitamin A in group 2 masked this expected increase in birth weight, indicating the harmful effect of excess vitamin A on birth weight. This result tended to agree with Cheeke et al. (1984) and Elmarimi et al. (1989).

Statistically, no significant differences were observed in weaning weight in spite of the decreased number of young per doe in vitamin A group (2), where total kits surviving to weaning through two parities were 15 for 12 does, versus 104 for 17 does in the control group (1). Therefore, average body weight at weaning should increase as number of kits at weaning decrease. This result is in agreement with Afifi et al. (1977, Khalil et al. (1987) and Ismail (1988).

In general, the results show that high vitamin A may have a harmful effect on growth and weaning weight, in agreement with results of Kormann and Schlachter (1984), Brief and Chew (1985), Elmarimi et al. (1989) and Ismail et al. (1992a,b). Although the effects of vitamin C and E and ethoxyquin on birth, weaning weight and growth are unknown, these agents seem to protect against the harmful effects of excess vitamin A and to increase immune response towards stress or adverse environmental conditions. These observations are in agreement with Ismail et al. (1992b).

Postnatal Mortality Rate

Average postnatal mortality (± SE) per doe and mortality rates (%) at birth, week 1, and total mortality rates from birth until weaning (4 weeks) are shown in Table 2. There were significant ($P<0.01$; $P<0.05$) differences in mortality at birth due to treatments and parities, respectively. Group 3 showed the lowest number and rate (6.67%), in comparison to groups 2 and 5 where mortality rates were higher (40.74 and 35.21%, respectively) as a result of the harmful effect of high vitamin A (stillbirths). The beneficial effects of vitamins C and E were clear in this study, especially with regard to stillbirths. This may have been due to increased immune response and protection against the harmful effects of excess vitamin A. Mortality at birth was due to stillbirths and also to changing maternal behavior. Some does left kits inside the placental sac where they subsequently died by asphyxia. Increased mortality was noted with extremely small (10

g) or large (76 g) body size. Mortality rates (%) during the first week of age were high but there was no significant effect due to treatment or parity. This result can be attributed to the high level of vitamin A in the colostrum, in which vitamin A concentration is from 4-25 times that of milk (this concentration declines gradually to normal levels by the third to tenth day [Thompson and McGillivray, 1957; Arthur and Leslie, 1965]), and to chilling and starvation in the nest due to maternal behavior. These results are in agreement with Partridge et al. (1981), Cheeke et al. (1984), Damodar and Jatkar (1985), Roedecha and Chanpongsang (1986), Ismail (1988), Yamini and Stein (1989) and Deeb et al. (1992).

Percentage of mortality during suckling in the control group was higher (28.48%) than normal (17-25%). This may have been due to the high alfalfa (44.24%) in addition to supplemental vitamin A (about 13,200 IU/kg diet) in the control diet. The vitamin A level may have approached toxicity levels, especially in the colostrum. The roles of vitamins C and E on postnatal mortality were indicated by the lowest mortality rates of 29.52 and 48.48%, respectively (in comparison to 72.22 and 73.24 for the vitamin A group (2) and vitamin A + ethoxyquin group (5), respectively), due to increased disease resistance and immunity responses during physiological stress and adverse environmental conditions (Reddy et al., 1987b; McDowell, 1989) as well as antagonistic effects towards the high level of vitamin A.

However, postnatal mortality was generally higher during the first week of age as compared to subsequent weeks during the suckling period. This could be attributed to the low resistance of young during the first week of age to microbial infections, starvation and environmental conditions. Inadequate lactation by does administered vitamin A was observed. Body size of young and litter size were found to have an effect on postnatal mortality. A cumulative effect of vitamin A on mortality in the second parity as compared to the first parity was noted in groups 2 and 5 only. In group A (2) total mortality increased from 40% in the first parity to 100% in the second, and in group 5 it increased from 64.1 to 84.38% (see Table 2).

Average plasma vitamin A through pregnancy, parturition and suckling over two parities are shown in Table 3. There were significant differences in plasma vitamin A ($P<0.01$) and over time ($P<0.01$). Tukey's test revealed a significant increase in plasma vitamin A at the first sampling (15 days) in groups 2 and 5 compared to the other groups. There was no significant difference between the other groups. The same trend was observed at 15 days of pregnancy (first parity). In contrast to previous results, plasma vitamin A at parturition was high in all experimental groups including the control, and there was no significant difference between all groups. There was a significant increase in plasma vitamin A at parturition as compared to other periods (pregnancy, suckling, etc.), which may be attributed to an accumulation of vitamin A in the tissues during the latter stages of pregnancy. Near parturition, body stores of vitamin A are released into the blood to meet the high demands required for colostrum. Thus plasma vitamin A rises rapidly three or four days prepartum, then decreases about three days to 1

Table 3. Means (± SE) for plasma vitamin A over two parities for different physiological situations.

Group	Day 15*	15th Day of Pregnancy 1.	Parturition 1.	15th Day of Suckling 1.	15th Day of Pregnancy 2.	Parturition 2.	15th Day of Suckling 2.
Control (1)	3.55 ± 0.19^{b}	4.40 ± 0.21^{b}	6.57 ± 0.68	4.04 ± 0.54^{b}	4.1 ± 0.18^{b}	6.51 ± 0.27^{b}	5.09 ± 0.44^{b}
A (2)	4.88 ± 0.62^{a}	6.34 ± 0.65^{a}	7.29 ± 0.16	6.05 ± 0.4^{a}	7.23 ± 0.96^{a}	9.08 ± 0.49^{a}	7.1 ± 0.1^{ab}
A+C (3)	3.65 ± 0.41^{b}	5.41 ± 0.62^{b}	6.78 ± 0.35	5.59 ± 0.41^{ab}	6.67 ± 0.51^{ab}	7.92 ± 0.41^{ab}	6.15 ± 0.30^{ab}
A+E (4)	3.83 ± 0.41^{b}	4.69 ± 0.29^{b}	7.33 ± 0.49	5.32 ± 0.75^{ab}	5.71 ± 0.73^{ab}	7.37 ± 0.75^{ab}	7.08 ± 0.83^{ab}
A + ethoxyquin (5)	5.53 ± 0.06^{a}	5.68 ± 0.17^{ab}	7.45 ± 0.22	6.69 ± 0.36^{a}	5.73 ± 0.39^{ab}	7.6 ± 0.33^{ab}	7.96 ± 0.17^{a}

Within each column only two means having at least one similar letter are not significantly different.

* Day 15 after treatments began, immediately before the first mating.

week following parturition. At the 15th day of suckling in the first parity, there were significant differences in the experimental groups as compared to the control group. No significant differences were noted between treatment groups 2, 3, 4 and 5, but it was high in groups 2 and 5 compared to groups 3 and 4, perhaps due to the important role of ethoxyquin in preserving vitamin A activity compared to vitamins C and E. The same manner was observed through the second parity as in the first parity, but plasma vitamin A levels in the second parity were higher than in the first parity as a result of continuous vitamin A administration and accumulation of the vitamin. The results indicate that plasma vitamin A is affected by physiological state of the animal (pregnancy, parturition, suckling). Plasma vitamin A in group 2 was higher than in groups 3, 4 and 5 throughout pregnancy, which may be explained by the high fetal resorption and low litter size in group 2 compared to groups 3, 4 and 5 and also the beneficial effects of vitamins C and E and ethoxyquin on the harmful effects of high levels of vitamin A. These antioxidants may have direct protective effects on the fetus through the early stages of pregnancy. Present results are in agreement with Arthur and Leslie (1965), Bondi and Sklan (1984), Cheeke et al. (1984), Moghaddam et al. (1987), Elmarimi et al. (1989), Deeb et al. (1992) and Ismail et al. (1992a,b).

Average litter size (± SE)/doe in the recovery period is presented in Table 4. The harmful effect of high vitamin A levels on fetal resorption, and subsequently on litter size, decreased gradually after discontinuation of oral administration of vitamin A and disappeared completely over three months. Average litter size in group 2 (A) in the first and second parity was 5.8 and 9.2/doe, respectively (Table 4). Similar trends were observed in the other groups. Litter size/doe began to increase from parity to parity, approaching the control value. There was no significant difference between groups throughout the recovery period (Table 4). The first parity in the recovery period seemed to be a transitional parity between continuation and discontinuation of oral administration of vitamin A and also it can be compared to the second parity which indicated that the animal returned to normal status, due to rapidly decreased liver vitamin A content after discontinuation of the supply of vitamin A. These results are in agreement with Nieman and Obbink (1954) and Elmarimi et al. (1989), who reported that about 98% of liver vitamin A disappeared within 12 weeks and that this period is sufficient for depletion of excess vitamin A.

Birth and weaning weights over the two parities and average birth and weaning weights (± SE) are shown in Table 4. There were no significant differences in birth weight between groups. This result was expected due to nonsignificant differences in litter size through the recovery period (Table 4). Group 2 (A) recorded the lowest number, 5.8/doe, in the first parity (Table 4). Average birth weight was equal to larger litter size groups; thus vitamin A may still have had a slight effect on birth weight in the first parity. The harmful effect of excess vitamin A decreased or stopped after parturition and post-natal growth rate and weaning weights were normal. Group 2 (A) recorded the highest value (603.22 ± 38.17) (Table 4) and weaning weight in the first parity in group 2 (A) was very high (693.76) (Table 4). These results are in agreement with Afifi et al.

Table 4. Reproductive data over two parities through the recovery period and plasma vitamin A at the end of the recovery period.

Group	Litter Size	Birth Weight	Weaning Weight	% Mortality at Birth	% Mortality at 1st Week	Total Mortality (%)	Plasma Vitamin A (IU/ml)
1. Control							
	(5)	(46)	(37)				
First parity	9.2	60.7	527.35	15.22	0	19.57	
	(5)	(44)	(38)				
Second parity	8.8	58.86	483.16	4.55	6.82	13.64	
Overall	9 ± 0.47	60.3 ± 1.27	519.39 ± 31.73^{ab}	10	3.33	16.67	4.6 ± 0.16^{b}
2. Vitamin A							
	(5)	(29)	(17)				
First parity	5.8	56.31	693.76	37.93	3.45	41.38	
	(5)	(46	(37)				
Second parity	9.2	58.7	530.08	3.7	4.35	19.57	
Overall	7.5 ± 1.04	62.99 ± 5.44	603.22 ± 38.17^{a}	20	4	28	4.83 ± 0.31^{ab}
3. Vitamins A+C							
	(8)	(56)	(43)				
First parity	7.00	57.27	496.7	10.71	7.14	23.21	
	(9)	(77)	(62)				
Second parity	8.56	60.10	473.32	5.19	9.09	19.48	
Overall	7.8 ± 0.86	62.1 ± 2.55	498.3 ± 18.79^{ab}	7.52	8.27	21.05	5.06 ± .30^{ab}
4. Vitamins A+E							
	(7)	(53)	(35)				
First parity	7.57	54.89	463.66	22.64	9.43	33.96	
	(6)	(57)	(47)				
Second parity	9.5	53.83	473.57	12.28	5.28	17.54	
Overall	8.467 ± 0.9	56.1 ± 2.43	523.86 ± 36.34^{ab}	17.27	7.27	25.45	4.77 ± 0.20^{ab}
5. Vitamin A + ethoxyquin							
	(6)	(49)	(26)				
First parity	8.17	51.41	478.43	34.69	12.24	46.94	
	(6)	(62)	(48)				
Second parity	10.33	54.37	436.1	11.29	9.68	22.58	
Overall	9.25 ± 0.98	53.35 ± 0.79	461.57 ± 13.77^{b}	21.62	10.82	33.33	5.81 ± 0.15^{a}

* Figures in parentheses represent number of animals.

** Within each column, any two means having at least one similar letter are not significantly different.

(1977), Khalil et al. (1987) and Ismail (1988), who reported that body weight at weaning should increase as number of kits at weaning decrease. Thus the present study clearly indicated that the harmful effect of excess vitamin A which masked this increase before disappeared and the animals returned to normal status. The second parity confirmed this conclusion. Does in group 2 (A) had a high litter size at birth and weaning and high weaning weight (Table 4). Present results indicate that growth is less sensitive to high levels of vitamin A compared to reproduction, and that, to detect harmful effects of vitamin A on growth, levels should be high (Ismail et al., 1992a,b).

Average postnatal mortality rate (%) over two parities through the recovery period and the overall means of postnatal mortality % during the recovery period are shown in Table 4. Postnatal mortality rate % at birth was higher in groups 2 (37.93) and 5 (34.69) than the normal range (17-25%) or when compared to other groups through the first parity. The high mortality rate in this parity at birth can be attributed to maternal behavior more than to stillbirths. Some does in groups 2 and 5 did not take care of the kits or clean them from the placental sac, and the kits died by asphyxia, chilling and starvation. On the other hand, the mortality rate through the 1st week in this parity was within normal range in all experimental groups, indicating that the vitamin A level in the colostrum which may result in high mortality in the 1st week may approach normal level after discontinuation of vitamin A administration. Results in the second parity confirm the previous result, where mortality at birth, the 1st week and all the suckling period were within normal range for all experimental groups (see Table 4). However, postnatal mortality rates % during the entire recovery period were within normal range (except for group 5 which was slightly higher) and in the same trend as in the administration period where the control group recorded the lowest value, then the A+C, A+E, A and A + ethoxyquin groups (Table 4). These results confirm the role of vitamins C and E in alleviating effects of excess levels of vitamin A, and increasing disease resistance and immunity responses during physiological stress and adverse environmental conditions.

The means ($\pm$ SE) for plasma vitamin A through the recovery period are shown in Table 4. By the end of the recovery period (about 12 weeks), plasma vitamin A had returned to normal level and there were no significant differences between groups compared to the control group except in group 5 in which plasma vitamin A was slightly higher than the control group and group 4, with differences significant ($P<0.01$). This result may have been due to the high ethoxyquin effective as a synthetic antioxidant in preserving vitamin A activity (Isenstein, 1970), or may be attributed to the different physiological state of the animal by the end of the recovery period. This result tends to agree with Nieman and Obbink (1954) and Elmarimi et al., (1989), who reported that about 98% of the vitamin disappeared within twelve weeks after discontinuing the supply of vitamin A.

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