BIOCHEMICAL RELATIONSHIP BETWEEN VITAMIN A CONTENT IN LIVER AND NUTRITION STATE

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A B S T R A C T

The aim of the present study was to investigate the biochemical changes in serum and liver retinol, serum nitric oxide (NO), total protein, serum protein electrophoresis, albumin, blood hemoglobin, glucose -6- phosphate dehydrogenises (G6PD), and antioxidant enzymes activities: glutathione peroxidase activity (GSH-PX), glutathione reductase (GR ase), activity reduced glutathione (GSH), superoxide dismutase activity (t-SOD) and catalase (CAT) in experimental under the effect of administration of ordinary, double, toxic doses of vitamin A in rats. In order to achieve this aim 80 male Sprague-Dawely rat 3-6 weeks old weighting 120-250 grams were used in the experimental investigation of this study. The animals were divided into 4 groups each 20 rats that were orally supplemented with retinol palmitate (2500, 5000, 10000 IU/Kg/day) and the fourth group served as control. The result of the present study showed a significant association between vitamin A supplementation and low level of liver and serum retinol, low nitric oxide level, high G6PD level, high catalase activity, low super oxide dismutase activity, low glutathione reductase and peroxidase activity, low reduced glutathione level. These parameters may all be regarded as risk factors for exposure to high doses of vitamin A. Vitamin A can potentially promote liver damage. When you consume large amounts of vitamin A, your body stores the excess vitamin within your liver. After a very high dose or long-term consumption of moderately high doses vitamin A can form toxic accumulations in your liver, leading to liver swelling and damage. In addition, the toxicity can cause skin peeling, kidney damage.

KEY WORDS: antioxidants, free radical, G6PD, NO, oxidative stress, protein electrophoresis, retinol palmitate, and vitamin A.

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1- I N T R O D U C T I O N

Vitamin A (retinol) is an essential nutrient needed in small amounts by humans for the normal functioning of the visual system; growth, development, maintenance of epithelial cellular integrity, immune function, and reproduction. These dietary needs for vitamin A are normally provided as preformed retinol (mainly as retinyl ester) and pro-vitamin A carotenoids [1].

Vitamin deficiencies are especially common in patients with cirrhosis and result both from reduced intake with the diet and, at least for some vitamins, from reduced absorption of those vitamins that are ingested. One important example is the vitamin A deficiency frequently found in patients with cirrhosis. Vitamin A (retinol) is essentially obtained directly from the diet or can be produced in the body from a precursor compound called beta–carotene [2].

Vitamin A deficiency can impair the ability of the eye to adjust to dark conditions (i.e., causing night blindness) and can result in other eye disorders. In the liver, reduced vitamin A levels can change the structures of components of cells, and these changes

may be exacerbated by the consumption of alcohol [3].

On the other hand, excess vitamin A also has harmful effects. For example, in the liver, increased vitamin A levels can promote the formation of scar tissue (i.e., fibrosis) which also is worsened by concurrent alcohol [4].

The aim of the present study was designed to investigate the biochemical changes in serum and liver retinol, serum nitric oxide (NO), total protein, serum protein electrophoresis, albumin, blood hemoglobin, glucose -6- phosphate dehydrogenises (G6PD), and activities of antioxidant enzymes under the effect of administration of ordinary, double, toxic doses of vitamin A in rats.

2. MATERIAL AND METHODS:

This study was conducted on 80 male Sprague-Dawely rat 3-6weeks old weighting 120-250 grams. The animals were divided into 4 groups' each group containing 20 rats were orally supplemented with retinol palmitate

Group I: control group.

Group II: a dose of 2500 IU/kg/day for 60 days (Ordinary doses).

Group III: a dose of 5000 IU/kg/day for 60 days (Double doses).

Group IV: a dose of 10000 IU/kg/day for 60 days (Toxic doses).

2.1. Sampling:

Blood is collected every two weeks for 8 weeks from median canthus by capillary tube. Blood samples divided in to two portions the first one pured in tubes contain 5% ethylenediaminetetra-acetic acid (EDTA) as anti coagulant/1 ml blood used for preparation of haemolysate after washing erythrocytes by physiological saline, this haemolysate used for estimation of Erythrocytes total super oxide Dismutase (t.SOD) according to Misra and Fridovich [5], reduced glutathione (GSH) according to Bergmayer [6], glucose 6 phosphate dehydrogenase (G6PD) according to Makarem,[7], glutathione reductase (GR ase) according to Bergmayer [6], catalase (CAT) according to Sinha [8], glutathione peroxidise (GSH-PX) according to Chiu et al.[9], haemoglobin (HB) according to Wray et al.[10].

The second portion collected in centrifuge tubes and centrifuged for isolation of the serum which used freshly for determination of serum nitric oxide (NO) according to Bories and Bories [11], protein electrophoresis according to Ritzmann, and Daniels, [12] total protein according to Henry, [13], Albumin according to Peters et al., [14], serum and liver retinol according to Periquet et al. [15].

2.2. Preparation of liver sample:

Extraction and analysis of vitamin A from serum and liver was performed according to Periquet et al. [15]. Briefly, liver was homogenized with a Potter-Elvehjem homogenizer, in 9 volumes of buffer (0.25 M sucrose; 0.05 M Tris-HC1, pH 7.6; 0.025 M KC1; 0.005 M MgC12). Serum or liver homogenate was mixed with one volume (v/v) of ethanol solution containing 10 mg. l-' retinyl acetate, used as an internal standard. Samples were extracted with 5 volumes of n-hexane. After centrifugation, 500 p1 of the upper phase was evaporated under a nitrogen streani and subdued light, dissolved in methanol, and injected into TLC system.

2.3. Statistical analysis:

All values were expressed as mean ± standard error (SE). All statistical analyses were performed using SPSS (Version 19). Statistical differences among the experimental groups were assessed by ANOVA. Duncan's test was used as a follow-up test and significance was defined at $P<0.05$.

3. RESULTS:

The obtained data in table 1 demonstrated that oral administration of vitamin A at doses level of 2500, 5000 and 10000 IU/kg/day in male rats for 60 days showed a significant decrease ($P< 0.05$). in liver and serum retinol in the animal group in comparison with the control group,

The obtained data in Table (2) demonstrated that oral administration of vitamin A at doses level of 2500, 5000 and 10000 IU/kg/day in male rats for 60 days showed a significant increase ($P< 0.05$).in erythrocytes catalase activity and G6PD in the animal group administrated toxic dose in comparison with the control group and there is induced significant fluctuations in blood hemoglobin concentration with either decrease or increase during the experimental periods in all animal groups in comparison with the control group.

The obtained data in Tables (3) demonstrated that oral administration of vitamin A at doses level of 2500, 5000 and 10000 IU/kg/day in male rats for 60 days showed a significant decrease($P< 0.05$). In erythrocytes GSH-PX, reductase (GR), reduced GSH, superoxide dismutase activity (t-sod) and NO in the animal group in double dose and toxic dose in comparison with the control group.

The obtained data in Tables (4) demonstrated that oral administration of vitamin A at doses level of 2500, 5000 and 10000 IU/kg/day in male rats for 60 days showed a significant increase ($P< 0.05$) in Serum total protein, and serum alpha1 globulin fraction, Serum alpha2 globulin fraction, Serum beta globulin fraction, Serum gama globulin fraction and Serum albumin in the animal group in comparison with the control group.

4. DISCUSSION:

The liver is quantitatively the most important storage site for retinoid in the body and it is quantitatively the most important tissue site of postprandial retinoid uptake in the body forming and secretion of retinol binding protein (RBP) accounting for 70–80% of all RBP that is normally present in the circulation [16].

Vitamin A can potentially promote liver damage. After consumption of large amounts of vitamin A, the body stores the excess vitamin within liver. After a very high dose or long-term consumption of moderately high doses vitamin A can form toxic accumulations in the liver, leading to liver swelling and damage. In addition, the toxicity can cause skin peeling, kidney damage and an accumulation of fluid within your skull that can cause brain damage [17].

The obtained data presented in Tables (1) demonstrated that, oral administration of vitamin A at doses level of 2500, 5000 and 10000 IU/kg/day in male rats for 60 days caused significant decrease in the value of liver and serum retinol concentrations in all experimental animal groups in comparison with the control group.

In addition the recorded data come in agreement with the results of [18] who demonstrated that, serum retinol levels was lower in patients with chronic liver disease and this decrease is directly related to the liver disease. Also, [19] demonstrated that, a progressive reduction of serum retinol levels has been noted for patients diagnosed with liver cirrhosis compared to healthy subjects and those patients with both cirrhosis and hepatic stellate cells (HSC) had significantly lower levels than patients with cirrhosis alone. Who added that, nutritional deficits often occur in patients

with chronic liver diseases moreover, [20] reported that, a significant decrease of hepatic retinoid levels occurs in patients with alcohol-induced fatty livers, and patients with alcoholic hepatitis and cirrhosis have much lower hepatic total retinol levels, approximately 10% and 5%, respectively than of control subjects.

The obtained data in Table (2) demonstrated that oral administration of vitamin A at doses level of 2500, 5000 and 10000 IU/kg/day in male rats for 60 days showed a significant increase ($P< 0.05$).in erythrocytes catalase and G6PD in the animal group in toxic group in comparison with the control group and there is induced significant fluctuations in blood hemoglobin concentration with either decrease or increase during the experimental periods in all animal groups in comparison with the control group.

These results provide support to those obtained previously by [21] who recorded that, catalase activity was increased with vitamin A administration and the obtained results are nearly similar to those reported by [22] who demonstrated that, G6PD activity significantly increases in liver with macronodular cirrhosis induced by high doses of vitamin A administration.

While these recorded data was come in accordance with the results of [23] who demonstrate that, hemoglobin concentration was significantly increased with supplementation of vitamin A.

The obtained data in Tables (3) demonstrated that oral administration of vitamin A at doses level of 2500, 5000 and 10000 IU/kg/day in male rats for 60 days showed a significant decrease($P< 0.05$). in erythrocytes GSH-PX, reductase (GR), reduced GSH, superoxide dismutase activity (t-sod) and NO in the animal group in double group and toxic group in comparison with the control group.

The obtained results came in agreement with the reported data by [24] who found that, a significant decreased in NO with significantly low values of plasma vitamins A (retinol) were observed in patients compared to controls.

Many studies have demonstrated that antioxidant enzymes such as SOD, CAT, and GPx represent one protection against oxidative tissue damage [25] SOD is an effective defense enzyme that converts the dismutation of superoxide anions into hydrogen peroxide (H2O2) [26]

The obtained data in Tables (4) demonstrated that oral administration of vitamin A at doses level of 2500, 5000 and 10000 IU/kg/day in male rats for 60 days showed a significant increase ($P< 0.05$). in Serum total protein, and Serum alpha1 globulin fraction, Serum alpha2 globulin fraction, Serum beta globulin fraction, Serum gama globulin fraction and Serum albumin in the animal group in comparison with the control group.

These results are nearly similar to those obtained previously by [27] who demonstrated that, increased in serum protein fractions: albumin and globulin was observed with vitamin A administration orally; at a dose of 10000 IU/kg/day for 60 days. Also, [28] reported that, gamma globulins are increased with vitamin A administration.

Table (1): The mean values ± S.E. of liver and serum retinol levels and (nmol/g)

Para-meter	Animal groups	Period (week)				Mean
		Two	Four	Six	Eight	
Liver retinol	Control	23.58±1.52c	22.05±1.75c	23.87±1.62c	21.57±1.95c	22.77±0.82c
	Ordinary	11.83±0.86a	5.75±0.62a	8.27±1.23a	5.29±0.49a	7.78±0.71a
	Double	11.86±0.78a	6.60±1.07a	9.36±1.31a	5.63±0.84a	8.36±0.73a
	Toxic	16.73±3.40b	11.72±4.54b	18.22±1.69b	10.68±4.17b	14.34±1.82b
	Mean	16.00±1.42**B**	11.53±1.88A	14.93±1.63B	10.79±1.86A	
Serum retinol	Control	83.26±4.99c	79.87±4.35c	85.12±3.40c	79.76±4.14c	82.00±2.02c
	Ordinary	40.90±1.86a	43.77±2.36a	49.92±4.06a	44.96±2.60a	44.89±1.50a
	Double	41.03±2.38a	47.39±2.44a	55.12±2.55a	45.76±2.11a	47.33±1.59a
	Toxic	53.77±9.97b	58.33±9.51b	71.67±3.63b	56.92±8.27b	60.17±4.09b
	Mean	54.74±4.77a	57.34±4.1A	65.46±3.56b	56.85±3.93a	

Data are presented as (Mean ± S.E). S.E = Standard error.
a, b & c: There is no significant difference (P> 0.05) between any two means, within the same column within the same parameter and the same group.
A, B & C: There is no significant difference (P> 0.05) between any two means, within the same raw within the same parameter and the same group.

Table (2): Mean values ± S.E of G6PD (U/gHb), CAT (U/ml), Hb (g/dl).

Para-meter	Animal groups	Period (week)				Mean
		Two	Four	Six	Eight	
G6PD	Control	8.96±0.61a	7.64±0.18a	7.79±0.35a	8.74±0.35a	8.28±0.23a
	Ordinary	11.19±0.18b	10.55±0.49b	10.50±0.57b	10.31±0.41a	10.64±0.21b
	Double	15.62±1.30c	13.40±0.31c	14.81±0.86c	17.44±0.75b	15.32±0.52c
	Toxic	24.37±1.97d	25.34±2.30d	24.87±1.81d	43.02±0.96c	29.4±1.99d
	Mean	15.04±1.47A	14.23±1.64A	14.50±1.57A	19.88±3.17B	
Catalase	Control	40.80±1.13b	39.60±1.05b	42.64±3.23b	38.58±0.49a	40.41±0.90a
	Ordinary	46.68±2.06c	41.97±1.15b	40.93±1.23ab	39.64±0.85a	42.31±0.88a
	Double	36.16±1.20a	39.26±3.02a	38.94±0.71a	46.13±1.53b	40.12±1.19a
	Toxic	65.67±1.75d	75.93±1.62c	82.00±3.39c	94.80±2.29c	79.60±2.65b
	Mean	47.33±2.68A	49.19±3.65AB	51.13±4.25B	54.79±5.38C	
HB	Control	14.50±0.28c	10.12±2.19a	12.04±0.29a	12.64±0.26a	12.33±0.63a
	Ordinary	13.38±0.30b	13.30±0.71c	12.56±0.25ab	12.74±0.28a	13.00±0.21a
	Double	12.42±0.54a	13.48±0.33c	13.22±0.37b	13.84±0.27b	13.24±0.22a
	Toxic	13.06±0.60a	12.68±0.25b	12.80±0.53ab	12.72±0.32a	12.82±0.21a
	Mean	13.34±0.27A	12.40±0.62A	12.66±0.20A	12.99±0.17A	

Data are presented as (Mean ± S.E). S.E = Standard error.
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Table (3): Plasma NO (µmol/l) SOD (U/ml)) GPX (U/L), GR (U/L), GSH (mmol/L).

Para-meter	Animal groups	Period (week)				Mean
		Two	Four	Six	Eight	
NO	Control	62.06±1.66c	65.02±1.42d	70.69±2.32c	65.3±2.27c	65.77±1.15d
	Ordinary	63.90±1.92c	58.76±0.54c	61.63±3.22b	57.66±0.30b	60.49±1.04c
	Double	56.01±1.59b	51.57±0.87b	61.03±1.46b	54.30±4.65b	55.73±1.43b
	Toxic	25.52±3.49a	31.92±3.17a	25.22±3.07a	16.45±2.10a	24.78±1.87a
	Mean	51.87±3.71AB	51.82±2.97AB	54.64±4.17B	48.43±4.52A	
SOD	Control	14.98±0.26b	14.45±0.20c	14.30±0.91c	14.70±0.39d	14.61±0.25c
	Ordinary	14.66±0.37b	12.88±0.35b	13.17±0.47b	13.33±0.48c	13.51±0.25b
	Double	14.36±0.56b	13.44±0.25b	13.76±0.92bc	12.21±0.22b	13.44±0.31b
	Toxic	8.61±0.69a	7.43±0.24a	8.05±0.30a	6.50±0.42a	7.65±0.27a
	Mean	13.16±0.65B	12.05±0.64A	12.32±0.66A	11.68±0.74A	
GSH-PX	Control	5.14±0.37b	5.23±0.49c	4.77±0.24c	5.28±0.30d	5.11±0.17c
	Ordinary	5.07±0.27b	4.96±0.29c	4.73±0.26c	4.81±0.28c	4.89±0.13b
	Double	4.98±0.66b	4.16±0.08b	3.98±0.24b	3.92±0.07b	4.26±0.19a
	Toxic	2.02±0.26a	2.52±0.20a	1.90±0.27a	2.35±0.16a	2.20±0.12a
	Mean	4.30±0.36AB	4.22±0.28AB	3.85±0.29A	4.09±0.28AB	
Reductase	Control	9.89±0.14c	9.06±0.42b	10.75±0.40b	9.26±0.47b	9.74±0.23b
	Ordinary	9.52±0.28bc	9.04±0.37b	10.07±0.47b	9.68±0.79b	9.58±0.25b
	Double	8.94±0.35b	9.44±0.56b	10.61±1.76b	9.07±0.33b	9.52±0.46b
	Toxic	3.85±0.09a	3.84±0.35a	3.21±0.32a	2.95±0.05a	3.46±0.14a
	Mean	8.05±0.57AB	7.85±0.57AB	8.66±0.84B	7.74±0.67A	
GSH	Control	12.95±1.21d	13.16±0.72b	13.81±0.23bc	15.1±0.95c	13.75±0.44c
	Ordinary	9.96±0.51b	14.40±0.24c	13.25±0.35b	12.78±0.32b	12.60±0.41b
	Double	11.64±0.79c	13.15±0.15b	14.14±0.62c	13.05±0.22b	12.99±0.31bc
	Toxic	6.63±0.21a	6.46±0.61a	6.70±0.34a	8.74±0.18a	7.13±0.27a
	Mean	10.29±0.65A	11.79±0.75B	11.97±0.73B	12.42±0.58B	

Data are presented as (Mean ± S.E)..
S.E = Standard error.
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A, B & C: There is no significant difference (P> 0.05) between any two means, within the same raw within the same parameter and the same group.

Table (4): The mean values ± S.E. of serum total protein and albumin levels (g/dl) alpha1, alpha2, beta and Gamma globulin fraction

Para-meter	Animal groups	Period (week)				Mean
		Two	Four	Six	Eight	
Total protein	Control	6.08±0.09a	5.48±0.34a	6.25±0.30a	5.94±0.24a	5.94±0.14a
	Ordinary	7.65±0.19c	7.75±0.62c	7.75±0.62c	6.27±0.44a	7.35±0.27c
	Double	6.72±0.13b	6.53±0.22b	6.84±0.11b	7.44±0.21c	6.88±0.11b
	Toxic	6.84±0.10b	6.93±0.14b	6.94±0.19b	6.91±0.13b	6.9±0.07b
	Mean	6.82±0.14A	6.67±0.25A	6.94±0.21A	6.64±0.18A	
Albumin	Control	3.19±0.09a	2.73±0.19a	2.83±0.13a	2.59±0.14b	2.84±0.08a
	Ordinary	3.91±0.07c	3.74±0.28c	3.14±0.22bc	2.22±0.24a	3.25±0.18b
	Double	3.42±0.09b	3.15±0.14b	3.27±0.08c	3.57±0.12c	3.35±0.06b
	Toxic	3.22±0.10a	3.05±0.10b	3.01±0.03ab	2.78±0.04b	3.02±0.05a
	Mean	3.44±0.08C	3.17±0.12B	3.06±0.07B	2.79±0.13A	
Alpha1	Control	0.26±0.01a	0.39±0.03c	0.32±0.02a	0.26±0.02a	0.31±0.02a
	Ordinary	0.42±0.01c	0.26±0.02a	0.39±0.03b	0.38±0.03b	0.36±0.02b
	Double	0.30±0.01b	0.32±0.02b	0.35±0.01a	0.42±0.02c	0.35±0.01b
	Toxic	0.33±0.02b	0.39±0.02c	0.34±0.00a	0.39±0.01b	0.36±0.01b
	Mean	0.33±0.01A	0.34±0.02AB	0.35±0.01AB	0.36±0.02B	
Alpha2	Control	0.48±0.02a	0.35±0.03a	0.51±0.02b	0.50±0.04a	0.46±0.02a
	Ordinary	0.67±0.01c	0.57±0.05c	0.46±0.04a	0.59±0.06b	0.57±0.03c
	Double	0.57±0.02b	0.43±0.02b	0.47±0.02a	0.56±0.03b	0.51±0.02b
	Toxic	0.58±0.02b	0.62±0.02d	0.54±0.01b	0.64±0.03c	0.59±0.01c
	Mean	0.57±0.02B	0.49±0.03A	0.49±0.01A	0.57±0.02B	
Beta	Control	1.04±0.06a	0.95±0.07a	1.01±0.05a	1.23±0.08a	1.06±0.04a
	Ordinary	1.28±0.03bc	1.39±0.11c	1.14±0.10b	1.49±0.17b	1.32±0.06b
	Double	1.18±0.05b	1.25±0.05b	1.33±0.02c	1.33±0.05a	1.27±0.02b
	Toxic	1.32±0.02c	1.42±0.03c	1.64±0.05d	1.47±0.04b	1.47±0.03c
	Mean	1.21±0.03A	1.25±0.05A	1.28±0.06A	1.38±0.05B	
Gama	Control	0.58±0.03a	0.77±0.06a	1.03±0.05b	0.72±0.05a	0.77±0.04a
	Ordinary	0.96±0.02c	1.21±0.09c	1.28±0.09c	0.80±0.09b	1.06±0.06c
	Double	0.86±0.03b	0.93±0.04b	1.00±0.03b	1.01±0.04c	0.95±0.02b
	Toxic	0.79±0.02b	0.77±0.03a	0.77±0.01a	1.01±0.01c	0.84±0.03a
	Mean	0.80±0.03A	0.92±0.05B	1.02±0.05C	0.88±0.04B	

Data are presented as (Mean ± S.E)

S.E = Standard error.

a, b & c: There is no significant difference (P> 0.05) between any two means, within the same column within the same parameter and the same group.

A, B & C: There is no significant difference (P> 0.05) between any two means, within the same raw within the same parameter and the same group.

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العلاقة الكيميائية الحيوية بين محتوي فيتامين أ في الكبد والحالة الغذائية

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الملخص العربي

تم اجراء هذا البحث لدراسة العلاقة الكيميائية الحيوية بين محتوي فيتامين أ في الكبد والحالة الغذائية في الفئران وقد اجريت الدراسة الحالية علي 80 من ذكور الفئران البالغة وتتراوح عمرها من 21 – 40 يوم تم رعايتهم خلال التجربة في غرفة الحيوانات المعملية الملحقة بمعمل قسم الكيمياء الحيوية بكلية الطب البيطري بمشتهر تم تقسيمها الي اربع مجموعات متساوية كل مجموعة تحتوي علي 20 فأر. كالاتي: المجموعة الاولي: غير معالجة (ضابطة). المجموعة الثانية: (الجرعة العادية) تم تجريعها فيتامين أ عن طريق الفم بجرعة 2500 وحدة دولية\كجم\يوم لمدة 60 يوم متوالية .المجموعة الثالثة: (الجرعة المضاعفة) تم تجريعها فيتامين أ عن طريق الفم بجرعة 5000 وحدة دولية\كجم\يوم لمدة 60 يوم متوالية .المجموعة الرابعة: (الجرعة السامة) تم تجريعها فيتامين أ عن طريق الفم بجرعة 10000 وحدة دولية\كجم\يوم لمدة 60 يوم متوالية .هذا وقد استخدم مصل الدم لقياس الريتينول واكسيد النيتريك والبروتين الكلي والفصل الكهربائي للبروتين والزلال .كما استخدمت خلايا الدم الحمراء لقياس الجلوتاثيون بيروكسيديز والجلوتاثيون ريدكتيز والجلوتاثيون المختزل والسوبر اكسيد ديسميوتيز الكلي والكتاليز وايضا الهيموجلوبين والجلوكوز 6 فوسفات ديهيدروجينيز. تم ذبح الفئران واستخراج الكبد لفحص ريتنول الكبد . هذا وقد اسفرت الدراسة عن وجود تغيرات كيميائية حيوية واضحة تمثلت في نقص معنوي في مستويات كل من الريتينول في المصل والكبد واكسيد النيتريك ونشاط انزيم سوبر اوكسيد ديسميوتاز وجلوتاثيون ريدكتاز و وجلوتاثيون بيرواكسيداز وتركيز الجلوتاثيون المختزل. كما اسفرت عن وجود زيادة معنوية في الجلوكوز 6 فوسفات ديهيدروجينيز وانزيم الكتاليزوالزلال والبروتين الكلي وهيموجلبين الدم .ولقد بينت الدراسة ان المجموعات المعالجة بجرعات مختلفة من فيتامين ا لفترة طويلة تؤدي الي امراض الكبد وخلل في الانزيمات المضادة للأكسدة مقارنة بالمجموعة الضابطة. لذا تنصح الدراسة بالابتعاد عن الجرعات السامة من فيتامين ا واستخدام الجرعات العالية لفترات قصيرة او جرعات منخفضة لفترة طويلة.

(مجلة بنها للعلوم الطبية البيطرية: عدد 25(1):173–182, سبتمبر 2013)