BIOCHEMICAL STUDIES ON THIOACETAMIDE TOXICITY IN MALE ALBINO RATS AND THE ROLE OF TOMATO JUICE AS AN ANTIOXIDANT

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ABSTRACT

Lycopene is a fat-soluble hydrocarbon carotenoid pigment that gives tomatoes their red color with a high capacity for scavenging free radicals. Thioacetamide (TAA) is one of several agents that produce structural and functional changes, not only in liver, but also in other tissues as kidneys, thymus, spleen, intestine and lungs. The present study was carried out on male albino rats to investigate the effects of intraperitoneally (i.p.) injection of thioacetamide, as a single dose of 150 mg/kg b.wt. in adult male albino rats and the possible prophylactic action of tomato juice. Thioacetamide toxicity were evidenced by an increase in thiobarbituric acid reactive substance (TBARS) which is an indicator for lipid peroxidation concomitant with decline in the iducenes of antioxidant capacity inducing, reduced glutathione (GSH), glutathione reductase activity (GSH-Rx) superoxide dismutase (SOD), glucose-6-phosphate dehydrogenase (G6PD) and catalase (CAT) the kidney. Treatment with tomato juice (7.9 ml/kg b.wt.) daily for 2 weeks before TAA injection, significantly reduced kidneys TBARS concentration, at the same time, ameliorated the TAA-induced inhibition of GSH content as well as , GSH-Rx, SOD,G6PD and CAT activities. Thioacetamide caused an inhibition in the Na^+/K^+ adenosine triphosphatase activity of the kidneys , elevation of sodium ions and water content paralleled with a decrease in potassium content. At the same time an increase in serum K and urine Na levels concomitant with a decrease in serum Na and urine K levels were observed. The results revealed an increase in the kidney, serum and urine activities of alkaline phosphatase accompanied with an elevation in urea and creatinine in serum and urine. Administration of tomato-juice before TAA ameliorated most of these parameters. It is concluded that, ingestion of tomatoes, may provide natural protection against nephrotoxicity damage caused by thioacetamide.

Key words: *Thioacetamide - Tomato juice as antioxidants - Albino rats .*

INTRODUCTION

Lycopene the carotenoid pigment responsible for the red color is the most distinctive compound present in tomatoes and it has an exceptionally high capacity for scavenging free radicals (Riso and Porrini, 2001). In this regard, lycopene may be biologically active by contributing the antioxidative defense system of the organism (Franceschi et al., 1994). Lycopene which is a cyclic carotenoid has attracted attention because of its biological antioxidant properties (Stahl et al., 1992). Antioxidants of lycopene may counteract the adverse effects of oxidative stress and lead to improved immune functions, reduced risk of infectious diseases and therby, diminish tissue damage in vivo (Ribaya-Mercado et al., 1995). Epidemiological studies show that supplementation of lycopene reversely connects with the risk of many chronic diseases (Giovannucci, 1999).

Thioacetamide (TAA) is an organosulfer compound, it is one of the several agents that produce centrilobular necrosis of the liver. The effects of TAA are not limited to the liver, but also extend to other tissues by where it produces many structural and functional changes as in the thymus (Barker and smuckler 1973), kidneys (Barker and smuckler 1974), intestine (Ortega et al., 1997) ,spleen (Al-Bader et al., 2000) and lungs (Latho., 2003). TAA is an experimental hepatotoxin that can be classified under the subclass indirect intrinsic (Kaplowitz et al., 1986). The direct subclass of intrinsic hepatotoxins are know to exert their action via hepatocyte membrane peroxidation by free radicals, whereas indirect hepatotoxins are suggested to act through their metabolites which react with intracellular molecules or the cellular membrane to disrupt cellular integrity. TAA-induced cirrhosis has been widely studied in rats and other animal species (Shakoori and Drakhshan, 1975), using different times, doses and routes of administration. Many of observing histologial and biochemical changes were the same as those observed in TAA-induced liver cirrhosis (Zimmerman et al., 1987). The present study aims to investigate the role of tomato-juice as a protective agent against thioacetamide oxidative effect in male albino rats.

MATERIAL AND METHODS

(A) Material:

1- Experimental animals:

Adult male rats (Rattus norvegicus) weighing 120 - 150 g were used in this study. They were placed in separate cages and allowed food and water ad libitum. They were kept under suitable air flow and temperature during the whole period of experimentation.

2- TAA and route of administration:

Thioacetamide (TAA) obtained from Sigma Co., USA. It was administered at a single dose of 150 mg/kg body weight inteperitoneally (i.p.) according to Mangipudy et al. (1996).The animals received tomato juice daily (7.9 ml/kg b. wt.)through an orogastric tube for 2 weeks prior to the administration of TAA according to Paetau et al. (1998).

(B) Methods:

1- Animal grouping:

Animals were randomly divided into six groups of 5 rats each as follows:

Group 1: Animals served as control receiving no treatment.

Group 2: Animals received daily tomato-juice(7.9 ml/kg b. wt.) for 2 weeks.

Group 3: Animals were injected i.p. with a single dose of TAA 150 mg/kg b.wt.

Group 4: Animals received tomato-juice for 2 weeks then injected i.p. with a single dose of TAA 150 mg/kg b. wt.

Group 5: Animals were injected i.p. with a single dose of TAA 150 mg/kg b.wt. then scarificed after 72 hours.

Group 6: Animals received tomato-juice for 2 weeks and injected i.p. with one dose of TAA 150 mg/kg then sacrificed after 72 hours.

At the end of the experimental period, animals were housed in metabolic cages for 24 hours. Urine samples were collected, centrifuged and stored at - 20°C for future analysis.

Animals were sacrificed and dissected at the designated times, blood were collected and sera were separated for biochemical measurements. Kidneys were stored deep frozen for biochemical studies.

2- Biochemical analysis:

Estimation of total lipids according to the method of Zoliner and Kirsch (1962), alkaline phosphatase was estimated according to Belfield and Goldberg (1971). Total protein was determined according to the method of Bradford (1976).

Na^+/K^+ ATPase was determined as described by Bonting (1970). Sodium and potassium concentration were determined by the method of Zettner and Seligson (1964) using the flame photometer (Jenway PEP7).

Lipid peroxidation was estimated by measuring the formation of thiobarbituric acid reactive substances (TBARS) according to Ohkawa et al. (1979). Reduced glutathione (GSH) content was estimated by the method of Nishikimi et al. (1972). Glutathione reductase (GSH-Rx) was determined as described by Beutler (1975). Catalase (CAT) activity was determined according to Bock et al. (1980) and glucose-6-phosphate dehydrogenase (G6PD) was determined as described by Chan et al. (1965).

Creatinine was measured according to Henry (1974) and urea according to Patton and Grouch (1977).

Statistical analysis:

The data was subjected to one-way analysis of variance (ANOVA) to detect significant effects of treatments followed by Tukey test to compare between means of different groups.

RESULTS

Tables (1,2 and 3) revealed that, the administration of tomato-juice (7.9 ml/kg) daily for 2 weeks did not induce significant changes in the tested parameters as compared with those of control.

Table (1) shows that , animals that received a single injection of TAA, especially those tested after 72hrs had higher levels of TBARS when compared with the control values. While a decrease in the kidney content of GSH and the activities of GSH-Rx, G6PD, SOD and CAT were recorded.

Table (2) shows that, a single dose of TAA induced a decrease in Na^+/K^+-ATPase activity in the kidney especially after 72 hrs of treatment. A decrease in serum total protein content after 24 and 72hrs concomitant with an elevation in serum total lipids content is recorded. In addition a decrease in serum sodium content along with an increase in its content in both kidney and urine. But an increase in serum potassium content and a decrease in that of kidney and urine. The treatment with tomato-juice prior to TAA injection lead to amelioration in most of these parameters.

Table (3), shows an elevation in urea, creatinine and alkaline phosphatase in kidney, serum and urine for TAA treated-groups 24 and 72 hrs . On the other hand, tomato-juice treatment for 2 weeks before TAA injection caused slight amelioration in some of the studied parameters.

DISCUSSION

The present results have clearly demonstrated the ability of TAA to induce oxidative stress in rat kidney as was evidenced by the significant rise of lipid peroxidation end product (TBARS), and the significant decline of the endogenous components of antioxidants defense system GSH, SOD and CAT. These findings are in agreement with other reports (Akbay et al., 1999 and Abul et al., 2002). Also, a significant decrease in both GSH-Rx and G6PD activities were reported in this study, these observations are in agreement with those of Akbay et al. (1999). These results may be attributed to the effect of TAA which is known to induce hepatocyte damage and renal damage following its metabolism to thioacetamide sulphene and sulphone, via a critical pathway involving cytochrome P450-mediated biotransformation (Okuyama et al., 2003). These metabolites are highly reactive and thus lead to the denaturation of cellular biomolecules such as lipids, resulting in lipid peroxidation which was indicated by increased TBARS concentration (Cheng-Haung et al., 2004).

The mechanisms that contribute to the occurrence of lipid peroxidation do not only include oxygen free radical generation, but also include alterations in the cellular antioxidant defense system with a decline in the intracellular free radical scavengers (Abul et al., 2002).

The decrease in the activities of SOD, CAT and GSH level may indicate an increased chance of free radical accumulation and subsequent cellular damage.

The reduced glutathione GSH level might be attributed to the inhibition of its regenerating enzyme GSH-Rx by TAA-treatment (Akbay et al., 1999). GSH is regenerated from oxidized glutathione (GSSG) and NADPH in a reaction catalyzed by GSH-Rx. NADPH, inturn, is generated via the hexose monophosphate shunt by a reaction catalyzed by G6PD (Ammon et al., 1980). The deficiency of GSH may be attributed, in part, to a deficiency in G6PD which is considered a housekeeping enzyme that catalyses the first-step in the pentose phosphate pathway. It produces NADPH, which is necessary for reduction of GSSG by GSH-Rx to GSH (Frederiks et al., 2003).

The present study also revealed an inhibition of Na^+/K^+ ATPase activity in the kidney of TAA-treated rats, these data are in agreement with Die Fernandez et al. (1996). The inhibition of Na^+/K^{+-} ATPase activity may be attributed to the generation of free radicals which may initiate toxic reactions with unsaturated fatty acids present in bilayer core and with membrane proteins containing oxidizable amino acids leading to changes in hydrophobic interactions between adjacent proteins and phospholipids.This would lead to altered membrane fluidity and perturbated activities of all membrane associated enzymes including Na/K ATPase.

Treatment of rats by tomato-juice (7.4 ml/kg), daily for two weeks before TAA-treatment resulted in a marked protection against lipid peroxidation as well as amelioration of the inhibition of SOD, CAT and GSH. These observations may be attributed to the antioxidant properties of tomato juice which contains a large amount of lycopene (Hartal and Danzing, 2003).

These results are in agreement with Kattab et al. (2003) who recorded that lycopene resulted in a markedly reduced nephro-toxicity of gentamicin. This effect might be explained by the work of Mortensen et al. (1997) who reported that, lycopene was an extremely effective singlet oxygen quencher and direct reaction between lycopene and radicals of nitrogen dioxide (NO_2), thiol and sulfonyl (RSO_2) have been proven. Moreover, lycopene has been reported to be effective in prevention of oxidative damage to lymphocytes (Collins et al., 1998) and to cell membrane (Bohm et al., 1995). Lycopene is considered as excellent free radical quencher and has the capacity to prevent radical damage of cells caused by reactive oxygen species. It is a potent antioxidant in vitro and in human studies, reducing the susceptibility of cell components to oxidative damage (Di Mascio et al., 1989).

El-Missiry et al. (2001) reported that free radicals enhance calcium release from the sarcoplasmic reticulum and also inhibit sarcolemmal Na^+/K^+ ATPase that possibly causing the activation of Na^+/Ca^{++} exchange mechanism in the myocardium. In addition, the disserved enzyme reduction may explain the elevation of Na^+ and decline in K^+ levels of the kidney tissues. These findings suggest that cellular Na^+ and K^+ transport which is mostly dependent on Na^+/K^+ ATPase activity seemed to be disturbed by TAA and this distribution is associated with slow movement of water inside the cells. Matels et al. (1999) showed that lipid peroxidation products can cause DNA damage and directly inhibit protein synthesis including Na^+/K^+ ATPase. These observations go in parallel with a decrease in Na^+ and an increase in K^+ levels in the serum of TAA-treated rats (Keller, 1986), but in urine there was a highly significant increase in Na^+ content with a highly significant decrease in K^+ content a result which is in agreement with Kattab et al. (2003) and Farag et al. (1996) who found that the injection of gentamicin (100 mg/kg) for 5 days resulted in a significant decrease in serum Na^+ associated with significant decrease in serum K^+ levels. In addition, Takamoto et al. (2003) reported that aminoglycosides induced a significantly decline in serum Na^+ content with gentamicin treated mice. The importance of serum ionic Na^+ and K^+ is correlated with their involvement in many vital activities of cells and tissues where they are actively transported through cell membranes, beside their role in muscle contraction and nerve impulse conduction.

Kattab et al. (2003) correlated these changes in Na^+ and K^+ contents with cell membrane damage which lead to disturbance in Na^+ and K^+ pumping and disorders in membrane permeability.

In contrast, the administration of tomato juice daily for 2 weeks might have improved the stability of the cell mechanism as it contain a large amount of lycopne acts as a scavenging of free radical and so protects the cell against the oxidative stress.

It was previously reported that, lycopene can reduce markedly the nephrotoxicity (Kattab et al. , 2003). This obtained amelioration may be attributed to the chemical nature of lycopene which contains polyene chain consisting of 11 conjugated double bonds. This polyene chain represents an important radical-scavenging structure of this compound (Halliwell and Gutteride, 1999).

Intoxication by TAA resulted in a decrease in total protein content and an increase in lipids content in serum. This result is in agreement with that of Fontana et al. (1998) A result which may be due to destruction of hepatic protein synthesizing subcellular structures following oral thioacetamide administration .

The results of the present study also indicated that pretreatment with tomato juice prior to TAA administration caused a marked elevation in the level of serum total proteins and a reduction in the lipid content compared to that get TAA only, this reduction may be due to inhibiting the enzyme -3-hydroxy-3-methyl glutaryl coenzyme A (HMG-CoA) reductase (the key enzyme in cholesterol synthesis) and by enhancing LDL degradation (Sesso et al., 2003).

TAA intoxication resulted in a significant increase in serum alkaline phosphatase activity.This observation is in agreement with Giffen et al. (2002) and may be attributed to the production of free radicals after intoxication which could have affected the cellular permeability leading to elevation in circulating level of this enzyme (Amer and Areida, 2004).

The current study elicited TAA-induced an increase in kidney, serum and urine levels of urea and creatinine. Rats treated with tomato-juice for 2 weeks prior to TAA administration exhibited significantly improvement in these parameters. This result agrees with Sener et al. (2002) and Ali, (2003). Moreover, Abd El-Naim et al. (1999) found that gentamicin induced nephrotoxicity was evidenced by marked elevation in serum urea and creatinine levels, and the prior treatment with antioxidatents pretreatment significantly lowered the elevated serum urea and creatinine. Naidu et al. (2000) reported that ,serum urea and creatinine were significantly increased with gentamicin compared with control, these changes were significantly prevented by pretreatment with antioxidant.

Rao and Agarwal (1998) observed that, dietary supplementation of lycopene from traditional tomato products increased lycopene concentration in plasma and reduced oxidative damage to lipids and proteins. The importance of lycopene may be mainly attributed to its effective antioxidant capability against hydroxyl radical. Wenli et al. (2001) concluded that, lycopene is effective in scavenging reactive oxygen species (ROS) as superoxide anion, hydroxyl radical, singlet oxygen and lipid free radicals.

In conclusion, the present data indicated that ,thioacetamide-induced nephrotoxicity might be related to oxidative damage. Tomato juice has been proven effective in counter activity and ameliorating some of the biomarkers indicative of toxicity.

Table (1) : Effects of Tomato juice administration and thioacetamide treatment on the contents of TBARS, GSH and activities of GSH-Rx, G6PD, SOD and CAT Lipid peroxidation product and antioxidant enzymes in kidneys of male rats.

Groups / Parameters	Control	TJ	TAA 24h	TJ+TAA 24h	TAA 72h	TJ+TAA 72h	ANOVA F	ANOVA P
TBARS (n mol/g wet t.)	59.52 ± 2.12	57.90 ± 2.39	88.94 a ± 3.3	85.88 a ± 3.2	89.32 a ± 4.6	68.56 c ± 2.9	48.80	< 0.05*
GSH (mg/g wet t.)	2.98 ± 0.086	2.96 ± 0.03	2.64 ± 0.11	2.94 ± 0.08	2.22 a ± 0.05	2.68 ± 0.1	5.55	< 0.05*
GSH-Rx (U/g wet t.)	44.52 ± 0.62	45.00 ± 0.38	41.84 ± 0.45	45.44 b ± 0.48	40.84 a ± 0.81	43.20 ± 0.26	8.64	< 0.05*
G-6-P-D (U /g wet t.)	29.06 ± 1.68	28.90 ± 1.52	24.24 ± 0.35	28.20 ± 1.78	18.62 a ± 1.88	22.72 ± 0.96	6.86	< 0.05*
SOD (U /g wet t.)	28.22 ± 2.57	28.12 ± 2.32	24.40 ± 0.98	26.42 ± 0.65	19.46 ± 1.75	22.52 ± 2.13	2.90	< 0.05*
CAT (k U/mg wet t.)	0.21 ± 0.004	0.21 ± 0.003	0.20 ± 0.002	0.20 a ± 0.004	0.17 a ± 0.002	0.20 ac ± 0.002	27.71	< 0.05*

Data are expressed as means ± S. E. of 5 animals.
TJ: Tomato Juice.
TAA: Thioacetamide.

ANOVA:
F = F tabulated
P = Probability

Tukey test:
a = significant difference as compared to control.
b = significant difference as compared to TAA for 24 h post-treatment.
c = significant difference as compared to TAA for 72 h post-treatment
* = significant (P<0.05)

Table (2) : Effects of tomato juice administration and thioacetamide treatment on some biochemical parameters in kidney, serum and urine of male rats .

Groups / Parameters		Control	TJ	TAA 24h	TJ+TAA 24h	TAA 72h	TJ+TAA 72h	ANOVA	
								F	P
Kidney	Na^+/K^+ ATPase (_mole/Pi/g/min)	2.24 ± 0.109	2.45 ± 0.07	1.98 ± 0.058	2.22 ± 0.287	1.69 ± 0.08	2.24 ± 0.16	24.01	< 0.05*
	Na^+ content (mg/g dry free lipid tissue)	4.50 ± 0.174	4.38 ± 0.097	5.30 ± 0.198	4.47 ± 0.201	5.79 a ± 0.087	4.99 ± 0.123	7.80 ± 0.162	< 0.05*
	K^+ content (mg/g dry free lipid tissue)	15.16 ± 0.125	15.14 ± 0.09	14.91 ± 0.16	14.82 ± 0.14	14.66 ± 0.11	15.06 ± 0.09	0.10	>0.05
	Water content (mg/g wet tissue)	680.26 ± 26.36	676.62 ± 22.09	716.97 ± 9.04	745.46 ± 9.09	796.02 a ± 5.2	779.70a ± 10.47	0.0001	<0.05*
Serum	Na^+ content (mg/100 ml)	431.90 ± 0.56	430.10 ± 0.26	418.33 a ± 2.56	427.16 ± 3.87	414.88 a ± 2.21	426.34 ± 2.27	6.15	<0.05*
	K^+ content (mg/100 ml)	34.15 ± 0.09	34.15 ± 0.07	34.13 ± 0.05	34.46 ab ± 0.09	34.79 a ± 0.05	34.37 c ±0.04	13.63	<0.05*
	Total protein (g/100 ml)	9.3 ± 0.1	9.33 ± 0.08	8.93 ± 0.16	9.00 ± 0.05	8.73 a ± 0.07	8.96 ± 0.05	3.80	<0.05*
	Total lipids (mg/100ml)	987.38 ± 14.4	1000.60 ± 19.62	1098.60 a ± 23.41	1028.40 ± 25.85	1185.50a ± 5.56	1119.70 ± 22.87	13.31	<0.05*
Urine	Na^+ content (mg/100ml)	0.10 ± 0.005	0.10 ± 0.004	0.52 a ± 0.02	0.28 b ± 0.01	1.30 a ± 0.08	0.91 ac ± 0.07	122.21	<0.05*
	K^+ content (mg/100ml)	0.42 ± 0.02	0.44 ± 0.01	0.31 a ± 0.004	0.47 b ± 0.005	0.19 a ± 0.003	0.33 ac ± 0.004	96.37	<0.05*

Data are expressed as means ± S. E. of 5 animals.
TJ: Tomato Juice.
TAA: Thioacetamide.

ANOVA:
F = F tabulated
P = probability

Tukey test:
a = significant difference as compared to control.
b = significant difference as compared to TAA for 24 h post-treatment.
c = significant difference as compared to TAA for 72 h post-treatment
* = significant ($P<0.05$)

Table (3) : Effects of tomato juice administration and thioacetamide treatment on the Urea, and creatinine levels as well as alkaline phosphatase activity in kidney, serum and urine of male rats.

	Parameters \ Groups	Control	TJ	TAA 24h	TJ+TAA 24h	TAA 72h	TJ+TAA 72h	ANOVA	
								F	P
Kidney	Urea (mg/100g wt T)	9.64 ± 1.55	9.44 ± .32	11.90 ± 0.67	10.98 ± 0.22	14.28 ± 0.2	11.96 ± 0.8	0.89	> 0.05
	Creatinine (mg/100g wt T)	13.52 ± 0.44	13.76 ± 1.75	15.80 a ± 0.58	12.12 ab ± 0.36	15.80 a ± 0.9	13.20 a ± 0.4	99.17	<0.05*
	Alkaline phosphatase (K.Arm. μ/100g)	2.46 ± 0.1	2.50 ± 0.049	2.94 ± 0.15	2.30 ± 0.12	2.74 ± 0.21	2.06 ± 0.17	3.68	<0.05*
Serum	Urea (mg/dl)	44.64 ± 0.49	44.50 ± 0.33	56.76 a ± 1.49	52.72 ± 3.31	68.44 a ± 3.54	47.08 c ± 2.42	12.7	<0.05*
	Creatinine (mg/dl)	1.98 ± 0.2	1.85 ± 0.24	2.38 a ± 0.19	1.76 ± 0.13	2.88 a ± 0.13	2.16 c ± 0.1	6.18	<0.05*
	Alkaline phosphatase (K.Arm. μ/100 ml)	89.32 ± 2.3	89.24 ± 3.86	100.04 a ± 9.23	88.242 b ± 11.7	99.60 a ± 5.92	97.14 ± 0.46	6.29	<0.05*
Urine	Urea (mg/dl)	9.44 ± 0.16	9.28 ± 0.05	11.00 ± 0.73	9.22 ± 0.05	12.60 ± 0.72	9.10 ± 0.11	2.52	>0.05
	Creatinine (mg/dl)	10.76 ± 0.79	10.75 ± .076	12.70 a ± .073	10.82 a ± 0.82	13.50 a ± 0.32	13.40 a ± .043	3.8	<0.05*
	Alkaline phosphatase (K. Au./100ml)	42.54 ± 0.65	42.88 ± 0.5	45.00 ± 2.3	42.56 ± 4.53	47.48 ± 0.87	47.94 ± 0.77	1.07	>0.05

Data are expressed as means ± S. E. of 5 animals.
TJ: Tomato Juice.
TAA: Thioacetamide.

ANOVA:
F = F tabulated
P = probability

Tukey test:
a = significant difference as compared to control.
b = significant difference as compared to TAA for 24 h post-treatment.
c = significant difference as compared to TAA for 72 h post-treatment
* = significant

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دراسات بيوكيميائية على سمية مركب الثيوأسيتاميد فى ذكور الجرذان ودور عصير الطماطم كمضاد للأكسدة

المشتركون فى البحث

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يهدف البحث إلى دراسة تأثير عصير الطماطم كعامل وقائى ضد سمية الثيوأسيتاميد فى أنسجة الجرذان وقد تم ذلك من خلال إعطاء الحيوانات عصير الطماطم يومياً بجرعة تساوى (7.9سم3/كجم من وزن الجسم) عن طريق الفم لمدة إسبوعين ثم أعقب ذلك حقن الحيوانات بجرعة واحدة من الثيوأسيتاميد عن طريق الحقن فى الجدار البريتونى بجرعة تساوى 150مجم/كجم بعد المعالجة تم تقسيم الحيوانات إلى مجموعتين ثم تم ذبح الأولى بعد 24 ساعة من حقنها بالثيوأسيتاميد والثانية بعد 72 ساعة من الحقن.

وقد أسفرت هذه الدراسة عن النتائج التالية :

١- أحدث الحقن بالثيوأسيتاميد زيادة ملحوظة فى مستوى الأكسدة الفوقية للدهون والتى تمثلت فى إرتفاع مستوى (TBARS) ونقص فى مستوى الجلوتاثيون (GSH) كما حدث نقص أيضاً فى مستوى كل من إنزيم جلوكوز -6- فوسفات ديهيدروچنيز (G6P.D) وكذلك إنزيم (CAT).

٢- سجلت الدراسة زيادة ملحوظة فى إنزيم الفوسفاتيز القاعدى (ALP).

٣- ظهرت أيضاً زيادة فى محتوى الماء فى أنسجة الكلية وكانت هذه الزيادة مصحوبة بزيادة فى محتوى الصوديوم ونقص فى محتوى البوتاسيوم إضافة لنقص واضح فى نشاط إنزيم (Na^+/K^+-ATPase) وعلى الجانب الآخر كان هناك نقص فى محتوى الصوديوم فى المصل مع إرتفاع محتوى البوتاسيوم.

٤- أوضحت الدراسة زيادة فى محتوى الدهون الكلية فى المصل مع نقص فى محتواه البروتينى.

٥- لوحظ أيضاً زيادة فى مستوى الصوديوم فى البول مع نقص فى مستوى البوتاسيوم وكذلك زيادة ملحوظة فى مستوى الكرياتينين والبولينا.

٦- ولقد أوضحت الدراسة أن المعالجة بعصير الطماطم قبل الحقن بالثيوأسيتاميد كان له دور وقائى ضد سمية المركب وقد ظهر ذلك واضحاً من خلال عدم حدوث الخلل فى معظم المعايير السابق ذكرها.