THE PROTECTIVE EFFECT OF SOME ANTIOXIDANTS AGAINST HEPATOTOXICITY

Fatma E. G., Sawsan M. E., Hosny A. F. I.,

Nagah E. E. and Nanise S. E. A.

Animal health research institute,

Zagazig -Vetrinary college Zagazig University, Egypt

ABSTRACT

Thirty male mature albino rat were used in this study .They were of about 250gm body weight The rats were randomly divided into six equal groups each of (5) .The first group was given normal saline 0.2ml/200gm .b.wt.I.P for fourteen successive days (control group)..while the second group I.P injected with normal saline 0.2ml/200gm . b.wt. for fourteen successive days followed by a single I.P .does of diluted CCL_4 . 0.4ml/100gm .b.wt. on the 15thday.The third group was I.P. injected with ascorbic acid (vitamin C)100mg/kg.b.wt. for fourteen successive days followed by a single I.P. does of CCL_4 0.4ml/100gm b. wt. on the 15^{th} day. The obtained results showed that, there was a significant increase in the levels of albumin whereas a significant decrease was observed in AST activity total bilirubin ,direct bilirubin and glucose levels when compared with CCL_4 treated rats. The fourth group was given corn oil 0.2ml/ 200gm .b.wt.IP. for fourteen successive days. The fifth group of rats were given repeated I.P. does of @-tocopherol 100mg/kg b wt.dissolved in corn oil for fourteen successive days followed by a single I.P. does of diluted $CCl_4$0.04ml/100gm b.wt.on the 15^{th}day, there was a significant increase in the levels of total proteions and albumin while the glucose level was significantly decreased when compared with those of control rats ..There was a significant decrease in AST activity total bilirubin ,direct bilirubin as well as glucose levels ,while a significant increase was recorded in total proteins and albumin when compared with those of CCL_4 treated rats .The six group of rats given repeated I.P does of ascorbic acid (vitamin C) 100mg/ kg b. wt.and @-tocopherol (vitamin E) 100mg/kg b wt. dissolved in corn oil for fourteen successive days followed by a single I.P. does of diluted CCL_4 0.4ml /100gm on the 15^{th},there was a significant increase in total proteins while glucose level was significantly decreased when compared with those of the control rats. There was a significant decrease in AST activity

and glucose level whereas a significant increase was recorded in the total proteins compared with those of CCL_4 treared rats ..The activities of ALT, ALP and albumin level as well as total and direct bilirubin levels when compared with those of CCL_4 treated rats. This study was carried out to evaluate the protective effect of antioxidant vitamin C(ascorbic acid), vitamin E (@-tocopherol) and their combination against hepatotoxicity induced by CCL_4.

INTRODUCTION

The antioxidant drugs are widely used in both prophylaxis and treatment of various diseases .Antioxidant drugs are non enzymatic defense against reactive oxygen species and free radicals , it constitutes the second line of defense in the living cell, it consists of substances that eliminates the free radicals from the body **(Gupta et al 1997); and Skrzydlew and Farbizewski (1998)**.

Murray et al.,(1993).reported that the toxic effect of free radicals has been extensively studied for induction of liver necrosis by halogenated methanes such as the solvents chloroform ($CHCL_3$) and carbon tetrachloride (CCL_4).The formation of trichl-oromethyl radical appears to be responsible for the damage of the lipid membranes, it is thought that a secondary metabolite causes cell death.

Di Mascio et al.,(1991). recorded that the aerobic metabolism entails the generation of oxygen species are capable of damaging DNA, proteins, carbohydrates, and lipids. In the pattern of antioxidant defense, some biological compounds like carotenoids, vitamin E and C and thiol play a prominent role.

Vitamin C, vitamin E and B-carotene are known to be particularly important, and their role in maintaining health and preventing diseases has been received much attention. **(Slater and Block, 1991and Frei, 1994)**.

Gey (1993). reported that vitamins have considerable interest in recent years in the potential amelioration of oxidative damage of tissues by dietary supplementation of antioxidants such as vitamin C, vitamin E and B-carotene.

Vitamin C has also be shown in animal,s studies to block the endogenous formation of N-nitrose compounds. **(Hong et al., 1986)**.

Boeing, (1991). Said that vitamin C is a potent antioxidant against superoxide anion radical formation in cytosol. Morcover vitamin C reduces potential carcinogens of some chemicals .it was a water soluble vitamin. Ascorbic acid reacts quiet rapidly with the superoxide anion radi-

cals, and with the hydrogen peroxide but even faster with hydroxyl radicals. Further more it can eliminate the singlet oxygen.

Vitamin E is a major antioxidant .It may play a role in the chemoprevention of cancer. Its function as antioxidant, interrupting the cascades of oxidative free radicals damage initiated by activated metabolites of several polycyclic hydrocarbons and aromatic amines **Gould et al., (1991) and Nagah et al (1991).**

Pascoe and Reed (1987).and Guehenberger et al.,(1988). referred that vitamin E content of membranes often determines the susceptibility of microsomal membrane ,low density lipoproteins ,hepatocytes ,all organs to damage by peroxidizing agents .

Vitamin E is a potent membrane protecting phospholipids of cell membrane, endoplasmic reticulum membrane and mitochondrial membrane from per oxidation damage by reacting with free radicals or reactive oxygen species **(Murray et al., 1993) and Niesink et al.,1995.** Reported that the fatty acid chain reaction in the biological membranes is mostly unsaturated .They are sensitive to oxidation by singlet oxygen or hydroxyl radicals .The oxidation cause serious membrane damage and may lead to cell death .Membrane content of antioxidant bloek the reaction, like vitamin E which react with the lipid radicals yield @-toeopherol and harmless fatty acid.

MATERIAL AND METHODS

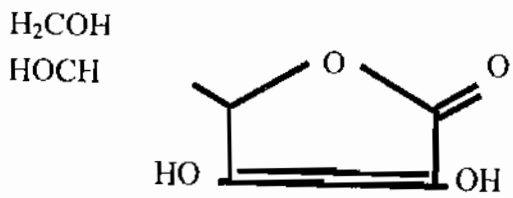
Drugs used

a- Ascorbic acid (Cevarol^{R}) (Vitamin C):

It was prepared by Memphis Co. for Pharm. & Chemical Ind. Cairo - Egypt.

This product was supplied as ampoules (each ampoule contains 5 ml & each ml contains 1000 mg ascorbic acid).

Structural formula:



Mol. Wt = 176.1

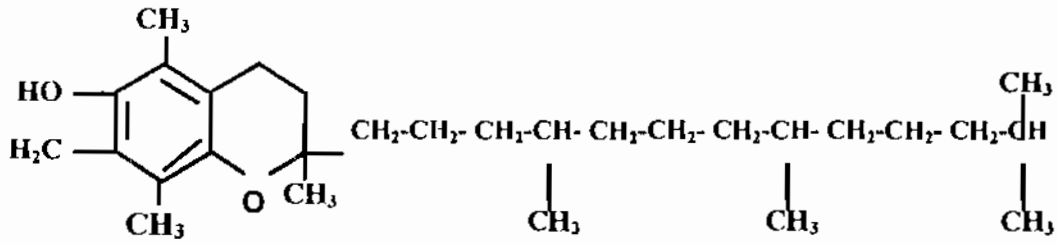
α - Tocopherol

(Richard, 1995)

b- α Tocopherol:

It was produced by PHARCO pharmaceutical Co. Alex., Egypt. The pure vit E is oily solution. Each ml of solution contains 1421mg α- tocopherol.

Structural fromula:



Mol. Wt = 430.7

Ascorbic acid

(Richard, 1995)

Experimental animals:

This study was carried out on thirty mature male albino rats of average body weight (250-300gm) and of the same age. They were obtained from laboratory animal farm, faculty of veterinary medicine, zagazig university, Egypt.. They were fed on balaneed pellet ration and watered ad-libitum. They were put under observation and, acclimatization for one week before starting the experiment.

Chemical used.

Carbon tetraehloride(CCL4) induced hepatotoxicity:

A single I/P injection of 0.2 ml/100gm b. wt CCL4to induce acute hepatic desfuction **(Jayathilaka et al., 1989)**.

CCL4 was diluted in corn oil (1:1 v/v)and used in this study as 0.4ml/100gm b.wt according to **Abdo et al., (1986)**.

Experimental design

Blood sampling: At the end of the experiment ,all rats were saerificed 24 hour after injection of CCL4, and blood samples were collected from carotid artery, according to ***Lin, et al. (1994).*** Serum was collected from each sample for biochemical analysis. (liver function tests).

Determination of serum aminotransferase activity. (AST& ALT) was carried out according to **REITMAN and fRANKEL, (1957)**. Alkaline phosphatase,activity was determined according to **Bessey et al., (1946).** Determination of serum total proteins and albumin;was carried out according to **Gassbaro et al., (1972)**. Determination of serum bilirubin (total and direct bilirubin) was carried out according to **Jendrassik and Grof (1938)**. Determination of glucose was carried out according to **Trinder (1969) and Siest et al.,(1981)**. Statistical analysis was according to **Snedecor, (1969)**.

RESULTS AND DISCUSSION

1- Effect of ascorbic acid on some serum biochemical parameters in male rats post treated with CCL4 :

I.P injection with ascorbic acid (100mg/kg b. wt) for fourteen successive days prior to CCL4-treatment (2ml/kg b.wt) improved the activities of AST and ALT as well as total bilirubin level which reverted to normal levels of control rats. Non significant changes were recorded in total proteins, albumin and direct bilirubin as well as glucose levels when compared with those of control rats (table1)

There was a significant increase in the levels of albumin ($P<0.001$) whereas a significant decrease was observed in AST activity ($P<0.001$),total bilirubin ($P<0.05$), direct bilirubin ($P<0.01$) and glucose levels ($P<0.05$) in the group received ascorbic acid (14 days) and post treated with CCL4 when compared with CCL4 -treated rats .ALT,and ALP activities as well as total proteins level of this group when showed non -significant changes compared with CCL4 -treated rats (tab 1).

The results demonstrated in this study were agreed with those recorded by **Hallm et al., (1997)** as they found that oral supplementation of vitamin C (50mg/kg b.wt) in CCL4 treated rats (200µ l/100mg b. wt) twice a week modulated the liver function to normal level .

Our results were also confirmed by the results of **Ademuyiwa et al., (1994).** They reported that vitamin C (2mg/kg b. wt) prevented the liver damage induced by CCL4 (8ml/kg b. wt) in mal albino rats

The remarkable protective effect of vitamin C against liver damage attributed to the fact that vitamin C is a major water soluble antioxidant and acts as the first defense against free radicals in the whole blood **(Niki et al .,1988)** and plasma **(Frei et al .,1989)**.

The protective effect of vitamin C may be due to its antioxidant effect as it could trap the free radicals generated from carbon tetrachloride metabolism **(Packer et al., 1980)** thus a prevent-

ing them from binding with protein molecules **(Hinson, 1980)**. Vitamin C could also prevent radicals from being formed. Moreover, vitamin C may interact with membrane phospholipids and thus protect them from the per oxidative action of carbon tetrachloride **(Neumann and zannoni, 1990)**.

2- Effect of @-tocopherol on some serum biochemicals parameters in mal rats post treated with CCL4:

The I.P administration of CCL4 (2mg/kg b. wt)in male rats produced a significant increase in AST activity (P<0.001) , ALT activity (P<0.05),ALP activity (p<0.01), total bilirubin (P<0.05) and direct bilirubin (P<0.05). Non significant changes were recorded in total proteins, albumin and glucose levels when compared with those of the control group (table 2).

The I.P administration of @-tocopherol (100mg/kg b.wt) for fourteen successive days prior to CCL4 -treatment (2ml/kg b. wt) produced non significant changes in AST, ALT and ALP as well as total and direct bilirubin levels which nearly regained to their normal levels of control rats .On other hand there were a significant increase in the levels of total proteins (P<0.01) and albumin (P<0.05) while the glucose level was significantly decreased (P<0.001)when compared with those of control rats. (table 2).

There a significant decrease in AST activity (P<0.001) total bilirubin (P,0.05),direct bilirubin (P<0.05) as well as glucose levels (P<0.001) while a significant increase was recorded in total proteins (P<0.05) and albumin (P0.05) in the group administered @-tocopherol (14days) and CCL4 -post treated rats when compared with those of CCL4 -treated rats (table 2)

The recorded results were similar to those obtained by **Vinogradovaet al .,(1989)** as they concluded that antioxidant vitamin E, sodium selenite and their combination blocked lipid per oxidation, reduced the activity of ALT and AST in the blood serum considerably and caused a protective effect on the structure Of rat liver against damage by carbon tetrachloride .

Our obtained results coincide with those reported by **Naziroglu, et al., (1999)**. They found that intraperitoneal administration of vitamin E had protective effect against carbon tetrachloride -induced chronic liver damage and cirrhosis as evidenced by biochemical data .

Our data coordinated with recorded by **Tirmenstein et al., (1997)**, they reported that only d-@-tocopherol hemisuccinate (TS) provided a significant protection against carbon tetrachloride induced liver damage in rats . They suggested that the ability of TS to protect against carbon tetrachloride induced hepatic damage relates to its enhanced hepatic accumulation and subsequent hydrolysis of @-tocopherol .

Our obtained results added further support to those previously reported by **Halim et al.,**

(1997) who found that oral supplementation of vitamin E 200 IU/kg b.wt into carbon tetrachloride treated rats (200µL/100kg b.wt) twice a week modulated the liver function to the normal liver.

On the other hand , our obtained results are in disagreement with those recorded by **Campo et al., (2001)** as they found that acute treatment with vitamin E failed to exert any protective effect against carbon tetrachloride induced hepatic damage.

3-Effect of treatment with combination of ascorbic acid and @-tocopherol on some serum biochemical parameters in male rats post-treated with CCL4:

The I.P administration of CCL4 (2ml/kg b.wt) to mal rats produced a significant increase in the activities of AST (P<0.001), ALT (P<0.05), ALP(0.01) as well as total bilirubin (P<0.05), and direct bilirubin (P<0.05). Non significant changes were observed in total proteins, albumin and glucose levels when compared with those of the control group (table 3).

Treatment of male rats with combination of ascorbic acid (100 mg/kg b. wt) and @-tocopherol (100mg/kg b. wt) for fourteen successive days prior to CCL4 —treatment displayed non significant changes in the activities of AST,ALT, ALP as well as total, and direct bilirubin and albumin levels which nearly returned back to normal levels when compared with control rats .Also, there was a significant increase in total proteins (P<0.05) while glucose level was significantly decreased (P<0.001) when compared with those of the control rats (table 3).

There was a significant decrease in AST activity (P<0.001) glucose level (P<0.001) whereas significant increase was recorded in total proteins (P<0.05) in the group received combination of ascorbic acid & @-tocopherol and CCL4 -post - treated rats when compared with those of CCL4 —treated rats .Non significant changes were recorded in the activities of AST, ALP and albumin level as well as total and direct bilirubin levels when compared with those of CCL4-treated rats (table 3).

The obtained results are in accordance with those recorded by **Etsuo et al., (1995)**. The previous authors reported that ascorbic acid and @-tocopherol act as potent antioxidant and is probably the most important hydrophilic and lipophilic antioxidant respectively.

Doba et al., (1985) and Sato et al., (1990) recorded that @-tocopherol and ascorbic acid act synergistically to inhibit the oxidation of liposomal membrane and LDL. They further added that ascorbic acid scavenges aqueous radicals and also act as synergist to regenerate @-tocopherol by reducing @-tocopherol radical formed from @-tocopherol when it react with a radical .

In the glow of the previous notion, one could view the obvious protective effect of ascorbic acid and @-tocopherol combination against CCL4 induced hepatic des-function, as straight forward sequel to the synergistic effect between the two vitamins.

Table (1) : Effect of I.P. injection of ascorbic acid (100mg/kgb.wt) for fourteen successive days on some serum biochemical parameters in male rats post-treated with CCl_4 (Mean ± SE) (n=5).

Parameter / Group	AST U/l	ALT U/l	ALP U/l	T.Proteins gm/dl	Albumin gm/dl	T.bilirubin mg/dl	D.bilirubin mg/dl	Glucose mg/dl
Control rats (Saline 14 d)	40.8 ± 2.6	19.8 ± 1.934	41.89 ± 2.355	6.938 ± 0.080	4.520 ± 0.293	0.440 ± 0.017	0.132 ± 0.018	115.0 ± 2.829
CCl_4-treated rats	123.8 ± 4.903***	25.8 ± 1.594*	45.724 ± 2.792**	6.546 ± 0.359	4.018 ± 0.064	0.558 ± 0.041*	0.168 ± 0.018	122.6 ± 1.965
ascorbic acid (14d) and CCl_4 post-treated rats	41.6 ± 2.3+++	21.6 ± 3.544	43.798 ± 0.169	7.550 ± 0.271	4.682 ± 0.050+++	0.428 ± 0.008+	0.102 ± 0.004++	113.2 ± 2.538*

* P<0.05 *** P<0.01 *** P<0.001

\+ P<0.05 ++ P<0.01 +++ P<0.001

* Compared with control rats.

\+ Compared with CCl_4-treated rats.

Table (2) : Effect of I.P. injection of @-tocopherol (100mg/kgb.wt) for fourteen successive days on some serum biochemical parameters in male rats post-treated with CCl_4 (Mean±SE) (n=5).

Parameter / Group	AST U/l	ALT U/l	ALP U/l	T.Proteins gm/dl	Albumin gm/dl	T.bilirubin mg/dl	D.bilirubin mg/dl	Glucose mg/dl
Control rats (oil for 14 d)	41.6 ± 2.064	21.0 ± 0.707	35.5 ± 0.225	6.992 ± 0.036	3.666 ± 0.188	0.426 ± 0.002	0.114 ± 0.002	122.0 ± 1.414
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@tocopherol(14) and CCl_4 post-treated rats	48.6 ± 6.638+++	22.4 ± 2.315	36.718 ± 1.258	7.73 ± 0.144+ **	4.22 ± 0.003+ *	0.428 ± 0.004+	0.112 ± 0.004+	106.0 ± 2.168+++ ***

* P<0.05 *** P<0.01 *** P<0.001
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* Compared with control rats.
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Table (3) : Effect of I.P. injection of combination of ascorbic acid (100mg/kgb.wt) &@-tocopherol(100mg/kg b wt) for fourteen successive days on some serum biochemical parameters in male rats post-treated with CCl_4 (Mean ± SE) (n=5).

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ascorbic acid &@tocopherol(14d) and CCl_4 post-treated rats	54.0 ± 8.911 +++	23.4 ± 2.853	41.9 ± 5.020	7.792 ± 0.0.291 + *	4.054 ± 0.041	0.492 ± 0.033	0.13 ± 0.007	103.6 ± 3.187 +++ ***

* P<0.05 *** P<0.01 *** P<0.001

\+ P<0.05 ++ P<0.01 +++ P<0.001

* Compared with control rat.

● + Compared with CCl_4-treated rats.

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REFERENCES

Abdo, K. M.; RAO, G. and Montgonery C. A. (1986) : Thirteen week toxicity study of d-@tocopherol aectate in fisher344 Rat. Fd. Chem. Toxic. 24(1011): 1043-1050.

Ademuyiwa , O.: Aesanya, O. and Ajuwon, O. R. (1994) : Vitamin C in CCL4 hepatotox-icity- a preliminary report. Hum Exp. Toxicol. Feb; 13 (2): 107-109.

Bessey, O. A.; Lowry, O. H. and Brock, M. J. (1946) : Kinetic colorimetric method for measurement of alkaline phosphatase Activity in serum. J. B. Chem., 164:321.

Boeing, H. (1991) : Epidemiological research in stomach cancer :progress over the last ten years.J. Cancer Res. Clin. Oncol. 117: 133-143.

Campo, G. M.; Squadrito, F.; Ceccarelli, S; Calo, M.; Avenoso,A . ;Campo, S.;Spuadrito, G. and Altavilla, D. (2001) : Reduetion of carbon tetrachloride —induced rat liver injury by IRFI 042, a novel du-al vitamin E - like antioxidant. Free Radic Res.,34(4)379-393.

Di Mascio, P.; Murphy, M. E. and Sies, H. (1991) : Antioxidant defense systems: the role of carotenoids, tocopherols, and thiols. Am. J. Clin. Nutr.; 53(Suppl) :194S-200S.

Doba. T.; Burton, G. W. and Ingold, K. U. (1985) : Antioxidant and c0- antioxidant activity of vitamin C. The effect of vitamin C, cit -Her alone or in the presence of vitamin E or a water — soluble vitamin E analogue, upon the peroxidation of aqueous multil-amellar phospholipid liposomes. Biochim. Biophys Acta ; 835:298-303.

Etsuo, N.; Noriko, N.; Hideyasu, T. and Naohiro G. (1995) : Interaction among vitamin C, Vitamin E and B-carotene. Am. J. Clin. Nutr; 62(Suppl):1322 S-1326 S.

Frei , B.; England, L. and Ames, B. N. (1989) : Ascorbate us an outstanding antioxidant in human blood plasma. Proc. Natl. acad.Sci. USA; 86; 6377-81.

Frei, B. (1994) : Natural antioxidants in human health and disease. San Diago: Academic press. Snedecor, G. W. (1969) Statisical Methods. 4th ED., Iowa State College Press, Ames, Iowa..

Gassbaro, L.; Bendinelli, R. and Tomassini, G. (1972) : Colourmetrical determination of total proteins and albumin. Clin. Chem. Acta, 36-255.

Gey, K. F. (1993) : Prospects for the prevention of free radical disease, regarding cancer and cardiovascular disease. Britisb Med. Bulletin 49:679-699.

Gould, M. N.; Haag, J. D.; Kennan, W. S.; Tanner, M. A. and Elson, C. E. (1991) : Acomparison of tocopherol and tocotrienol for the chemoprevention of chemically induced rat mammary tumors. Am . J. Clin. Nutr. 53:1068S-1070S.

Gupta, M.; Dobashi, K.; Green, E. L.; orak, J. K. and Singh, I. (1997) : Studies on hepatic injury and antioxidant enzyme aetivities in rat subcellular organelles following in vivo ischemia .Mol. Ceil. Biochem. 176(1-2)337-347.

Halim, A. B; EL-Ahmady, O. Hassab-Allah, S.; Abdel-Galil, F.; Hafez,Y. and Darwish, A . (1997) : Biochemical effect of antioxidants on lipids and liver function in experimentally -- Induced liver damage . Ann. clin Biochem., 34 (6): 656-663.

Hinson J. (1980) : Biochemical toxicology of acetaminophen. Reviews in biochemical toxicology; 2: 103-29.

Hong, W. K.; Endicott, J. and Itri, L. H. (1986) :13-cis retinoic acid in the treatment of oral leukoplakia N. Engl. J. Med. 315·1501.1505

Jayathilaka, KA. P. W.; Thabre, M. I.; Pathirana, C.; De Slive, D. G. H. and Berra, D.L.B.; (1989) : An evaluation of the potency of osbeckia octandra and Melothria Madera spontana as anti-hepatotoxic agents. Planta Med., 55: 137-139.

Jendrassik, L. and Grof. P. (1938) : A colorimetric method for the quantitative determination of total and direct bilirubin .Biochem. Z. 297-81.

Lin, C. C.; Lin, W. C.; Yang, S. R. and Enshieh, D. (1994) : Anti-Inflammatory and hepatoprotective effects of solanum salatum. American J. Chinese Med., xxIII (1) :pp. 65-69.

Murray, R. K.; Granncry, D. K.; Mayes, P. A. and Rodwell , V. W. (1993) : Harper, s Biochemistry. Twenty-third edition, Middle. East Edition, Appleton and Lange Libratric du Liban., Beirut, California.

Nagh, V. Z. W.; Jarlen, Z.; San, M. M.; Marzuki, A.; Top, G. M.; Shamaan, N. A. and Kadir, K. A. (1991) : Effect of tocotrienols on hepatocarcinogensis induced by 2- acetelamino fluorene in rats . Am J. Clin. Nutr. 53: 1076S-1081S.

Naziroglu, M.; Cay, M.; Ustundag, B.; Aksakal, M.; and Yekeler, H. (1999) : Protective effects of vitamin E on carbon tetrachloride induced liver damage in rats. Cell Biochem Funct.; 17 (4) :253-259.

Neumann, C. M. and Zannoni, V. G. (1990) : Ascorbic acid deficiency and hepatic UDP- glucuronyltransferase. Qualitative and Quantitative differences Biochemical pharmacology ; 39:1085-1093.

Niesink , R, J. H.; De Vries, J. and Hollinger, M. A. (1995) : Toxicology. Principles and Applications. Published by CRC press, INC. and Open University of Nether Lands.

Niki E. (1993) : Antioxidant defenses in eukaryotic cells In : Poli G. Alban DianzaniMU, eds. Free Radicals: From Basic Science to Medicine. Basel, Switzerland: Birkhauser Verlag. 365-73.

Niki, E.; Yamamoto, Y. and Takahashi, M. (1988) : Free - radical mediated damage of blood and its inhibition by antioxidan J. Nutr .Sci. Vitaminal (Tokyo); 34 :507-512.

Packer, J. E.; Slater T. F. and Wilson R. K. (1980) : Direct observation of a free radical interaction between vitamin E and vitamin C. Nature: 278:737-738.

Pascoe, G. A. and Reed, D. J. (1987) : Vitamin E protection against chemical — induced cell injury . II. Evidence for a threshold effect of cellular @-tocopherol in prevention of adriamycin toxicity. Arch. Biochem. Biophys :256:159-166.

Quehenberger, O.; Jurgens, G.; Zadravec, S. and Esterbauer, H. (1988) : Oxidation of human low density lipoprotein initiated by copper (II) chloride. In T-aylor K, Ward. J., Van Somtag C. Oxygen Radicals in Biology and Medicine. Basic life sciences. New York: Plenum Press, 49:387-390.

Reitman, S. and Frankel, S. (1957) : Acolorimetric method for the determination of serum oxalacetic and glutamic pyruvic transaminases. Am. J. Clin. Pathol., 28:56-63.

Richard, A. H. (1995) : Veterinary Pharmacology and Therapeutics. 7th Edition. Iowa State University Press. Ames.

Sato, K.; Niki, E. and Shimasaki, H. (1990) : Free radical -mediated chain oxidation of low density lipoprotein and its synergistic inhibition by vitamin E and vitamin C. Arch Biochem. Biophys; 279: 402-405.

Siest, G.; Henny, F. and Seliele), F. (1981) : Enzymatic determination of glucose .interpret Examens Lab., Kargered, 206-223.

Slater, T. F. and Block, G. (1991) : Antioxidant vitamins and B —carotene in disease prevention Am. J. Clin. Nutr. 53(suppl): 189S-396S.

Skrzydlewska, E. and Farbizewski, R. (1998) : Lipid Peroxidation and antioxidant status in liver, erythrocytes and serum of rats after methanol intoxication. J. Toxicol. Environ. Health 53 (8): 637-649.

Snedecor, G. W. (1969) : Statistical Methods. 4th Ed., Iowa State College Press, Ames, Iowa.

Tirmenstein, M. A.; Leraas, T. I. and Fariss, M. W. (1997) : Alpha-tocopherol hemisuccinate administration. Increase rat liver subcellular. Alpha-tocopherol levels and protect against carbon tetrachloride -Induced hepatot oxicity. Toxicol Lett 16;(1):67-77.

Trinder, P. (1969) : Enzymatic determination of glucouse. Ann. Clin. Biochem., 6 , 24-27.

Vinogradova, L. F. and Mirzoian, Zh. A.; Kharlitskaia, E. V. and Beketova, T. P. (1989) : Experimental antioxidant therapy in toxic liver damage from CCL4 and chloxyl. Patol Fiziol Eksp .Ter.(4):52-56.

الملخص العربى

التأثير الواقى لبعض مضادات الأكسدة ضد التسمم الكبدى

المشتركون فى البحث

فاطمه السيد جابـــر سوسن محمد الشيخ حسنى عبدالفضيل إبراهيم

نجاح السيد إدريس نانيس سالم السيد أحمد

معهد بحوث صحة الحيوان - الزقازيق وكلية الطب البيطرى - جامعة الزقازيق

إستهدفت هذه الدراســة كشف النقــاب عن الــدور الوقائى لبعض مضــادات الأكسدة A-ntioxidant مثل فيتامين ج Ascorbic acid وفيتامين هـ a-tocopherol وخليط منهما على التسمم الكبدّ التجريبى (الفشل الكبدى) فى الجرذان الناتج عن الحقن البريتونى لرابع كلوريد الكربون earbon tetrachloride

١- تأثير إعطاء ڤيتامين ج على بعض القياسات البيوكيميائية فى ذكور الجرذان :-

أدى إعطاء رابع كلوريد الكربون (٢ ملليتر/كجم من وزن الجسم) بالحقن البريتونى فى ذكور الجرذان البيضاء إلى حدوث زيادة معنوية فى إنزيم الأسبرتيت أمينو ترانسفيريز ومستوى إنزيم الالانين أمينو ترانسفيريز وصفة الصفراء الكلية.

وقد أدى الاستخدام الوقائى لفيتامين ج (١٠٠ مج / كجم من وزن الجسم) لمدة أربعة عشر يوماً متتالية قبل الحقن البريتونى لرابع كلوريد الكربون (٢ ملليتر/كجم من وزن الجسم) إلى تحسن معنوى فى نشاط إنزيم الاسبرتيت أمينو ترانسفيريز والآلانين أمينو ترانسفيريز وصفة الصفراء الكلية حيث عادو للمستوى الطبيعى، ولم تحدث تغيرات معنوية فى البروتين الكلى والزلال وصفة الصفراء المباشرة وسكر الدم.

٢- تأثير إعطاء ڤيتامين هـ على بعض القياسات البيوكيميائية فى ذكور الجرذان :

لقد أدى الحقن البريتونى لرابع كلوريد الكربون (٢ ملليتر / كجم من وزن الجسم) فى ذكور الجرذان إلى حدوث زيادة معنوية فى خميرة الأسبرتيت أمينو ترانسفير وخميرة الآلانين أمينو ترانسفيريز وخميرة الفوسفاتيز القاعدى وصفة الصفراء الكلية والمباشرة بينما لم يحدث تغير معنوى فى البروتين الكلى والزلال ونسبة سكر الدم.

ولقد اتضح من هذه الدراسة أن إعطاء ڤيتامين هـ بالحقن البريتونى (١٠٠مجم/كجم من وزن الجسم لمدة أربعة عشر يوماً متتالية قبل الحقن البريتونى لرابع كلوريد الكربون فى اليوم الخامس عشر أدى إلى حدوث تحسن فى نشاط خميرة الأسبرتيت أمينو ترانسفيريز والآلانين أمينو ترانسفيريز والفوسفاتيز القاعدى وصفة الصفراء الكلية والمباشرة للمستوى الطبيعى بينما زاد البروتين الكلى والزلال زيادة معنوية ولقد تبين أيضاً حدوث انخفاض فى مستوى سكر الدم.

٣- تأثير إعطاء خليط من ڤيتامين ج وڤيتامين هـ على بعض القياسات البيوكيميائية فى ذكور الجرذان البيضاء :

أظهرت هذه الدراسة أن الحقن البريتونى لرابع كلوريد الكربون فى ذكور الجرذان أدى إلى حدوث زيادة معنوية فى خميرة الأسبرتيت أمينو ترانسفيريز والآلانين أمينو ترانسفيريز والفوسفاتيز القاعدى وصفة الصفراء الكلية والمباشرة كما لم تشاهد تغيرات معنوية فى مستوى الذكور لبروتين الكلى وسكر الدم.

واتضح من هذه الدراسة أيضاً أن إعطاء خليط من فيتامين ج (١٠٠مجم/كجم من وزن الجسم) وفيتامين هـ (١٠٠ مجم/كجم من وزن الجسم) لذكور الجرذان لمدة أربعة عشر يوماً متتالية قبل الحقن البريتونى رابع كلوريد الكربون أدى إلى حدوث تحسن فى نشاط خميرة الأسترتيت أمينو ترانسفيريز والألانين أمينو ترانسفيريز والفوسفاتيز القاعدى وصفة الصفراء الكلية والمباشرة إلى المستوى الطبيعى كما حدث نقص معنوى فى مستوى سكر الدم بينما حدثت زيادة معنوية فى البروتين الكلى.

يستخلص من هذه الدراسة أن مضادات الأكسدة مثل فيتامين ج وفيتامين هـ لهما تأثير وقائى ملحوظ على التسمم الكبدى التجريبى (الفشل الكبدى فى الجرذان) حيث تبين أن إعطاء هذه الڤيتامينات أدى إلى حدوث تحسن ملحوظ لأغلب الآثار الجانبية الناتجة عن إعطاء رابع كلوريد الكربون، ومن ناحية أخرى تبين أن إعطاء ڤيتامين ج وهـ معاً أدى إلى حدوث نفس التأثير الوقائى الملحوظ على التسمم الكبدى التجريبى (الفشل الكبدى).