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THE EFFECTIVENESS OF SPECIFIC DIET REGIMEN AGAINST DIMETHOATE HEPATOTOXICITY: EFFECT OF HIGH-LIPID DIET.

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Key words; Dimethoate, Diet regimen & Mucopolysaccharides.

ABSTRACT

In the present study, the changes in hepatic mucopolysaccarides (MPS) and their serum metabolites were investigated in male albino rats fed high-lipid diet along with oral administration of dimethoate insecticide (1\10 LD50, 21 mg/kg body weight / day) for 15, 30, 45, and 60 days.

The amount of liver MPS fractions (non-, mono-, and highly sulfated) recorded a gradual significant elevation in the insecticide treated groups compared with their normal control. Serum MPS metabolites (uronic acid, hexosamine, fucose, and N-acetylneuraminic acid) exhibited similar significant elevations under the forementioned experimental conditions.

Feeding on high-lipid diet along with dimethoate produced slight additive elevations in both liver and serum MPS levels throughout the feeding period (60 days).

The metabolic disturbances of MPS may reflect the combined effects of dimethoate intoxication and/or high-lipid diet. However, the recorded higher elevations in MPS and its metabolites may be attributed to the enhanced rates of both its synthesis and/or degradation.

Thus, it is reasonable to speculate that high-lipid diet showed fallacy in protection against dimethoate hepatotoxicity.

INTRODUCTION

Mucopolysaccarides (MPS) components consists of hexosamine and either hexuronic acid or galactose units that are arranged in alternating unbranched sequence and carry sulfate substituents in various positions (Richardson et al., 1991).

Liver MPS include non-sulfated hyaluronic acid and chondroitin, mono-sulfated chondroitin and dermatan sulfate and the more heavily sulfated fractions, keratan and heparan sulfate (Meir and Wood, 1969; Gressner and Koster-Eiserfunke, 1983). MPS in tissues are essential for maintaining the structural integrity of connective tissues (Hook, 1984; Hassel et al., 1986 and Lohmander, 1988).

Liver MPS components vary according to the experimentally induced pathological state as well as from species to species (Koizumi et al., 1967; Gregoire et al., 1972). An excessive accumulation of MPS in liver cirrhosis (Murata and Qnuma, 1983; Murata et al., 1985) and sever liver fibrosis (Murata et al., 1985; Abdel Ghaffar, 1994) was recorded.

Serum glycoproteins simply represent proteins which have carbohydrate covalently attached to their peptide portion (Spiro, 1970). The carbohydrate chain linked to the protein is made up of hexoses (galactose or mannose), hexosamine (glucosamine or galactosamine), methyl pentose (fucose), and sialic acid (N-acetylneuraminic acid) of which there are several related forms (Cantraw, 1975).

The members of serum MPS are used, particularly, as indicator of pathological process in some diseases such as uronic acid in renal failure (Bower et al., 1992); hexosamine in bilharziasis and acute hepatitis (Khafagy et al., 1972; Nishizono, 1985); hexose in patient with colorectal carcinoma (Putzki et al., 1992); sialic acid in cancer and inflammatory diseases (Shamberger, 1984; Tautu et al., 1988), and finally serum fucose in gastric ulcers and cirrhosis of liver (Sakal et al., 1990) and patients of carcinoma cirvex (Bandlish et al., 1991).

Dimethoate is an effective organophosphate against a wide range of insects and has a moderate mammalian toxicity (Khoury and AbdulWali,1980;Fattaleh,1984;El-Elaimy et al., 1988;Abdel-Ghaffar et al.,1998; Bayomy et al., 1998. Sanderson and Edson (1964) reported that the metabolism of dimethoate in mammals, takes place mainly in the liver and consists of not only hydrolysis to harmless ionic products, but also of oxidation to the thiolate analogue, and to three other toxic metabolites Hassan et al. (1994) speculated that the catabolic disturbance conditions of the dimethoate treated rats may result in the shortage of fat, or the lyposis including ?-oxidation. This may explain the remarkable decrease in the body and liver weights in the dimethoate treated animals (Hassan, 1997).

Reddy et al. (1992) reported that high concentration of dimethoate treatment produced an elevation in the activity of β-glucouronidase, -N-acetylglucosamindase and cathepsin D, in serum, skin, liver, kidney and spleen tissues

It was reported that nutritional factors affect body structure and function and subsequent pathophysiological changes as well as the rate of metabolic detoxification of foreign compounds, which ultimately influence the toxic effect of insecticides (Goodhart and Shils, 1980; Hathcock, 1982; Mortimor and Poso, 1987; Iwasaki et al., 1988) Fat represents an important constituent in the diet which offers, high caloric value, essential fatty acids, and is considered as a good factor for fat-soluble vitamins

Vijayakumar and Kurup (1975) reported that atherogenic, high-fat cholesterol, diet produced disturbances in biosynthesis and biodegradative enzymes of the MPS rats.Meanwhile,the activity of butyrylcholinesterase (B.Ch.E)increased in rats with increasing the intakes of corn oil(Van Lith et al.,1991).Accordingly,the present study concerns the toxic effects produced by dimethoate under the condition of high-lipid diet in male albino rats.

MATERIAL AND METHODS

Insecticide used:

The insecticide dimethoate(CH3O)22P(S)S CH2 C(O)NHCH2 was used as a commercial solution(40%;Rogor-L40.,Isagro-Milanio-Italy). It was emulsified in distilled water and orally administered daily at a dose level of 1/10 LD50 (21 mg /kg weight, El-Elaimy et al., 1988) during the course of the present study and at the different periods of treatment.
Diets used:

1- The standard diet consisted of 16% protein, 3.2% fats, 3.5% fibers, 70% carbohydrates and balanced with vitamins and mineral salts mixture.

2- High-lipid diet: This diet was prepared by addition of 10% (in weight of the diet) cotton seed oil to standard diet irrespective to its original fat content.

Animal groups:

A number of 120 male Wister albino rats with an average weight of 100-150 gm. were used and were grouped as follows:

Group 1: 30 normal healthy rats were fed the standard control diet. They were served as normal control group.

Group 2: 30 normal healthy rats were fed the standard control diet (16% protein) along with oral administration of 1/10 LD50 dimethoate (21 mg /kg. Body weight daily). They were served as dimethoate treated group.

Group 3: 30 normal healthy rats were fed the high-lipid diet.

Group 4: 30 normal healthy rats were fed the high-lipid diet along with oral administration of (21 mg./kg. Body weight daily). They were served as high-lipid dimethoate treated group.

5 animals from each group (1, 2, 3, and 4) were decapitated and dissected at intervals 15, 30, 45, and 60 days post the first day of the experiment.

Blood and tissue samples:

The animals under investigation were anaesthetized by inhalation of diethyl ether and blood samples were withdrown from hepatic portal vein. Blood was collected in as non-oxalated clean centrifuge tube and was then allowed to coagulate. The tubes were centrifuged in a cooling centrifuge at 3.000 rpm. (Heraeus Christ) for 15 min. to separate blood serum. The separated sera were sampled into clean tube and kept at -40 oC for subsequent analysis. The animals were dissected, their liver were excised and blotted using filter paper, placed in plastic containers and kept in deep-freezer at -40 oC till biochemical analysis.

Biochemical analysis:

Liver mucopolysaccarides (MPS) non-, mono-, and highly sulfated assays were performed according to Mier and Wood (1969).

Serum mucopolysaccarides metabolites were performed according the following methods; serum uronic acid (Seibert and Atno, 1946), serum hexose (Wiemer and Moshine, 1953), serum hexosamine (Winzler, 1955), serum fucose (Dische, 1949) and N-acetylneuraminic acid (Hess et al., 1957).

RESULTS

The liver mucopolysaccharides (MPS) and their serum metabolites exhibited a gradual mild increases with the development of hepatotoxicity induced by administration of 1/10 LD50 dimethoate. The higher levels of recorded MPS were depended on the insecticide feeding period.

The three fractions of liver MPS (non-, mono-, and highly sulfated mucopolysacchrides) displayed significant elevations that reached their highest values with percentage of 56.77%, 50.54% and 38.60% respectively, after 60 days of dimethoate administration (Figs. 1, 2 & 3).

High-lipid diet ingestion induced slight gradual elevated levels that amounted to 21.49% , 20.12 % and 29.70 % in liver non - sulfated ,mono sulfated and highly sulfated MPS, respectively, after 60 days of ingestion

compared with the control (Figs. 1, 2 and 3). Moreover, feeding on the same diet along with dimethoate produced slight additive effects.

Serum MPS metabolites, uronic acid, hexosamine, hexose, fucose and N-acetylneuraminic acid levels increased significantly with the development of dimethoate hepatotoxicity. The maximum increases recorded after 60 days treatment were, 44.24%, 39.39%, 31.20%, 46.51% and 28.09% respectively, compared with the normal control (Figs. 4, 5, 6, 7 & 8).

Ingestion of high-lipid diet only produced slight additive increases in uronic acid, fucose and N-acetylneuraminic acid (15.90%,19.43% &16.03%) while hexosamine and hexose displayed mild significant increases (20.77% & 24.11%) after 60 days of feeding when compared with their normal levels.

Furthermore feeding on high-lipid diet along with dimethoate induced slight additive elevation in serum MPS, uronic acid, hexosamine, hexose, fucose and N-acetylneuraminic acid (56.80%, 48.80%, 44.34%, 50.26% and 35.82%) at the end of feeding period compared with their control levels.

DISCUSSION

The present data showed that, the dimethoate administration produced a mild significant increases in both liver and serum MPS. These elevations may be attributed to the activation of MPS synthesis and/or degradative enzymes.

The ability of the liver to hydrolyze dimethoate to harmless products (Sandrson and Edson, 1964; Fattaleh, 1984; Khoury and Abdul Wali, 1980;). explaned the mild elevations in the levels of MPS and its metabolites recorded herein. In a similar investigation, the elevation in MPS level were attributed to higher activity in some of their degradative enzymes such as β- glucuronidase, N-acetyl-glucosaminidase, cathepsin B and cathepsin D, in serum, skin, liver, kidney and spleen under the effect of dimethoate treatment (Reddy et al 1992).

The diet composition was considered to be among the factors which can affect the rates of the metabolic detoxification of foreign compounds such as organophosphorus insecticides (Hathcock, 1982; Iwasaki et al., 1988). This fact was principally considered in the explanation of the different effects of dimethoate in rats reared on diets with different composition (Abdel-Gaffar et al., 1998 ; Bayomy et al., 1998).

The influence of high-lipid diet on different metabolic pathways was heavily investigated, thus, high-fat diet induced abnormal glucose tolerance

(Bue et al., 1989), high activity of plasma butyrylcholinesterase in rats (Van-Lith et al., 1991),an impaired clearence and metabolism of pyruvate in the liver (Nagase et al., 1996), and an inhibition of the hepatic very low density lipo-protein secretion of obese and lean-zusker rat by altering hepatocyte metabolic state (Oussadou et al., 1996). Moreover, Vijayakumar and Kurup (1975) studied some important enzymes concerned with biosynthesis, of the mucopolysaccarides precursor, degradation, and biological sulfation in rats fed on atherogenic, high-fat cholesterol diet. The authors found that L-glutamine-D-fructose-6-phosphate aminotransferase, glucosamine-6-phosphate-N-acetylase, UDPG-dehydrogenase and UDPG-pyrophosphorylase were decreased in the liver of rats. While liver enzymes concerned with degradation of MPS, hyaluronidase, β- glucuronidase, N-acetyl hexosaminidase, cathepsins and arylsulphatase were increased.

Finally it can be concluded that the rate of synthesis and degradation of MPS was increased under the effect of dimethoate toxicity leading to an elevation in their levels in both liver and serum. To some extend, it seems also that high-lipid diet potentiates such effect.

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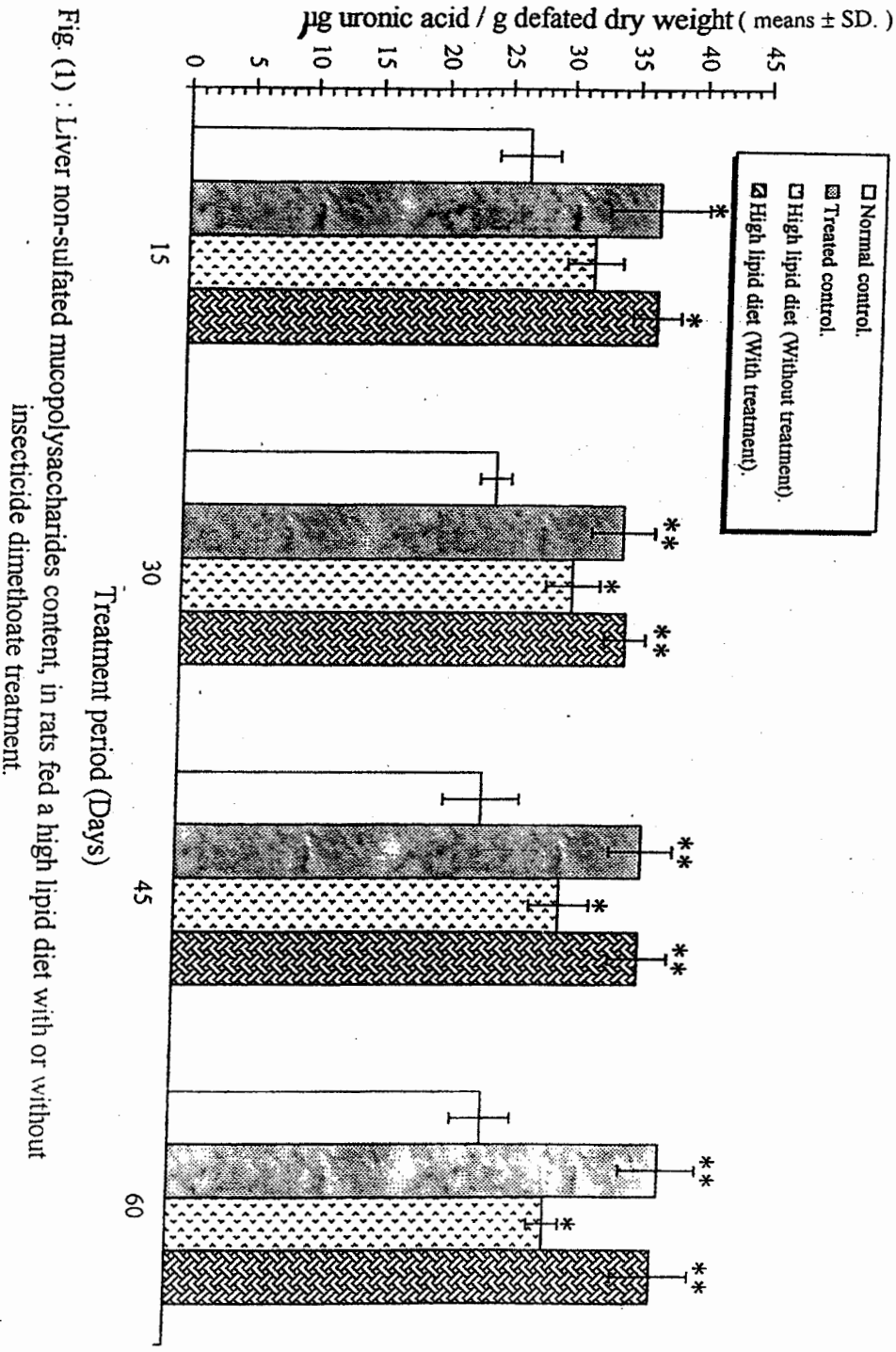

Fig. (1) : Liver non-sulfated mucopolysaccharides content, in rats fed a high lipid diet with or without insecticide dimethoate treatment.

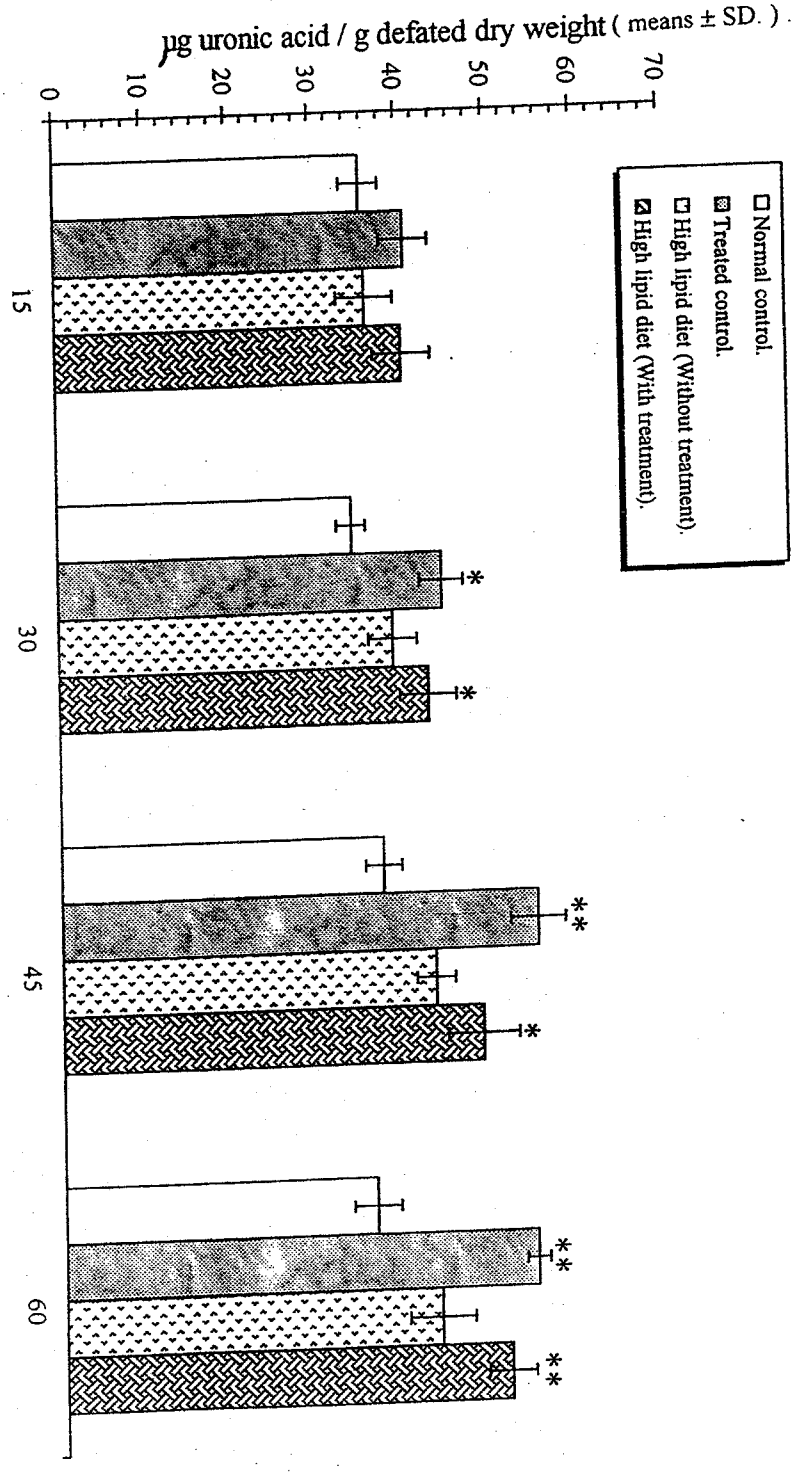

Fig. (2) : Liver mono-sulfated mucopolysaccharides content, in rats fed a high lipid diet with or without insecticide dimethoate treatment.

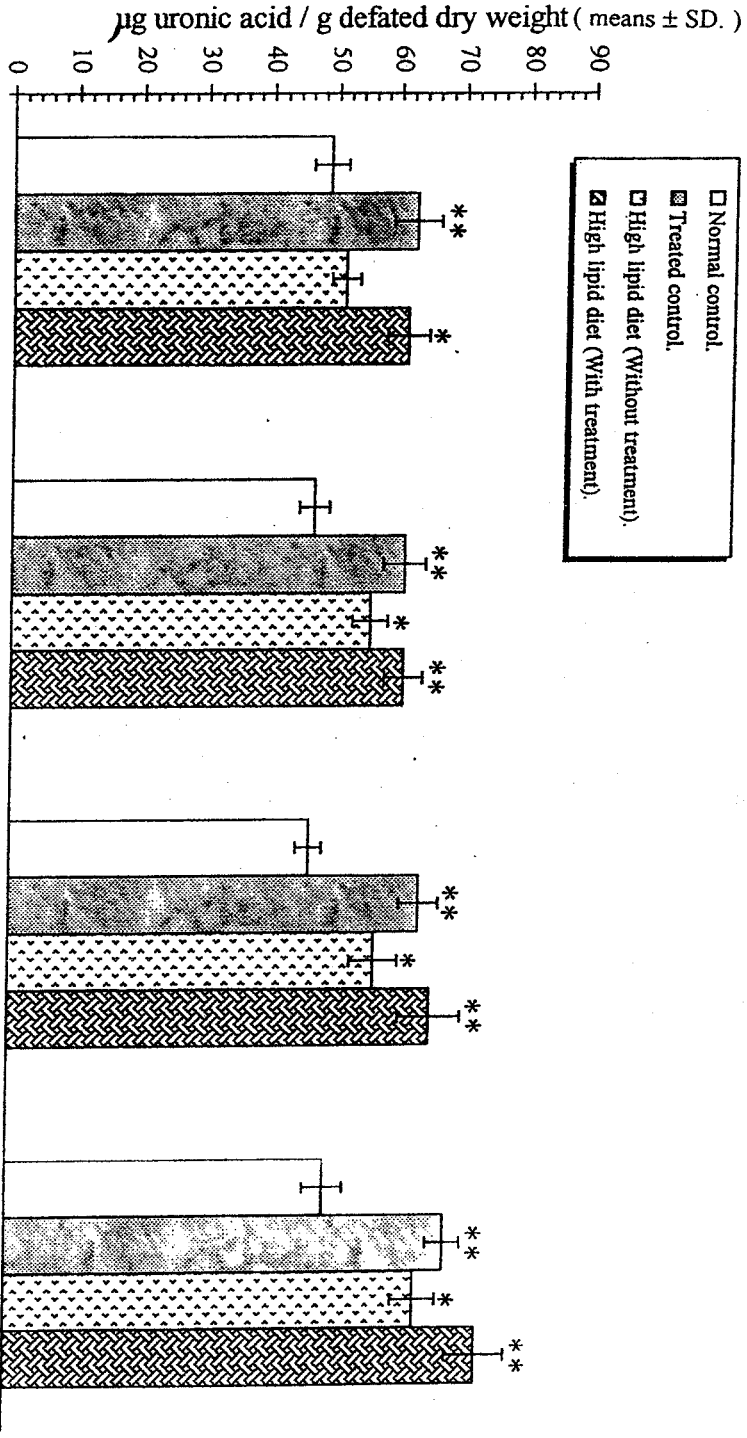

Fig. (3) : Liver highly-sulfated mucopolysaccharides content, in rats fed a high lipid diet with or without insecticide dimethoate treatment.

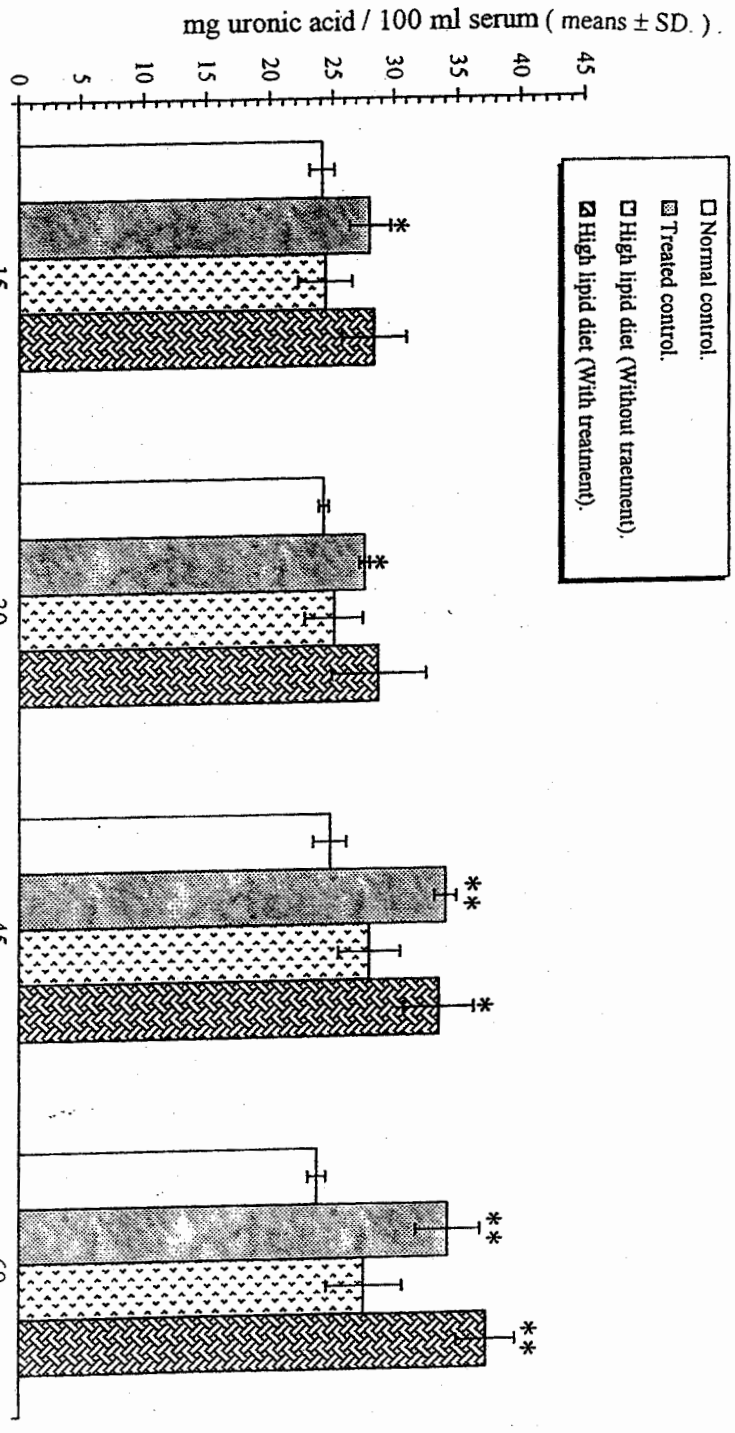

Fig. (4) : Serum uronic acid content, in rats fed a high lipid diet with or without insecticide dimethoate treatment.

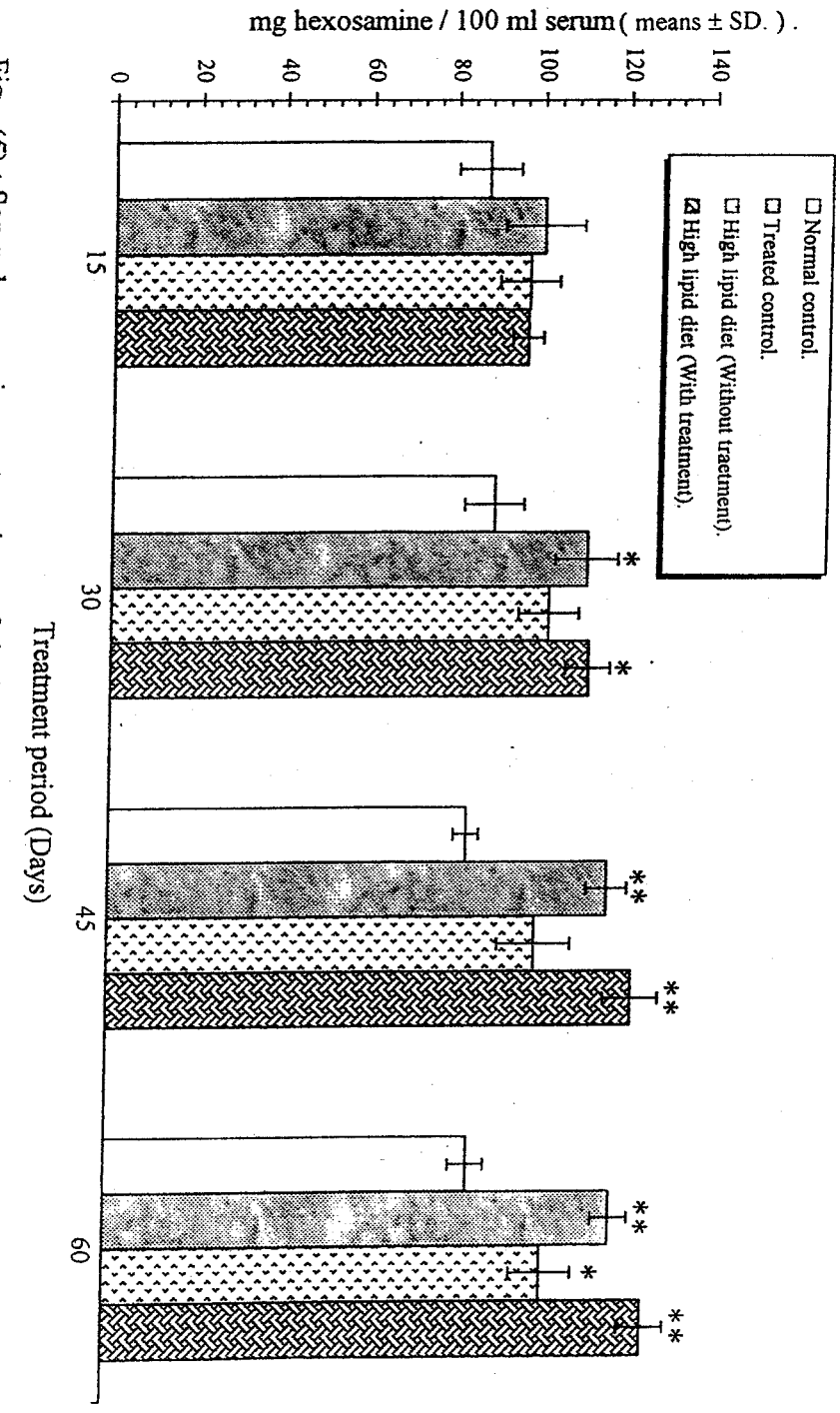

Fig. (5) : Serum hexosamine content, in rats fed a high lipid diet with or without insecticide dimethoate treatment.

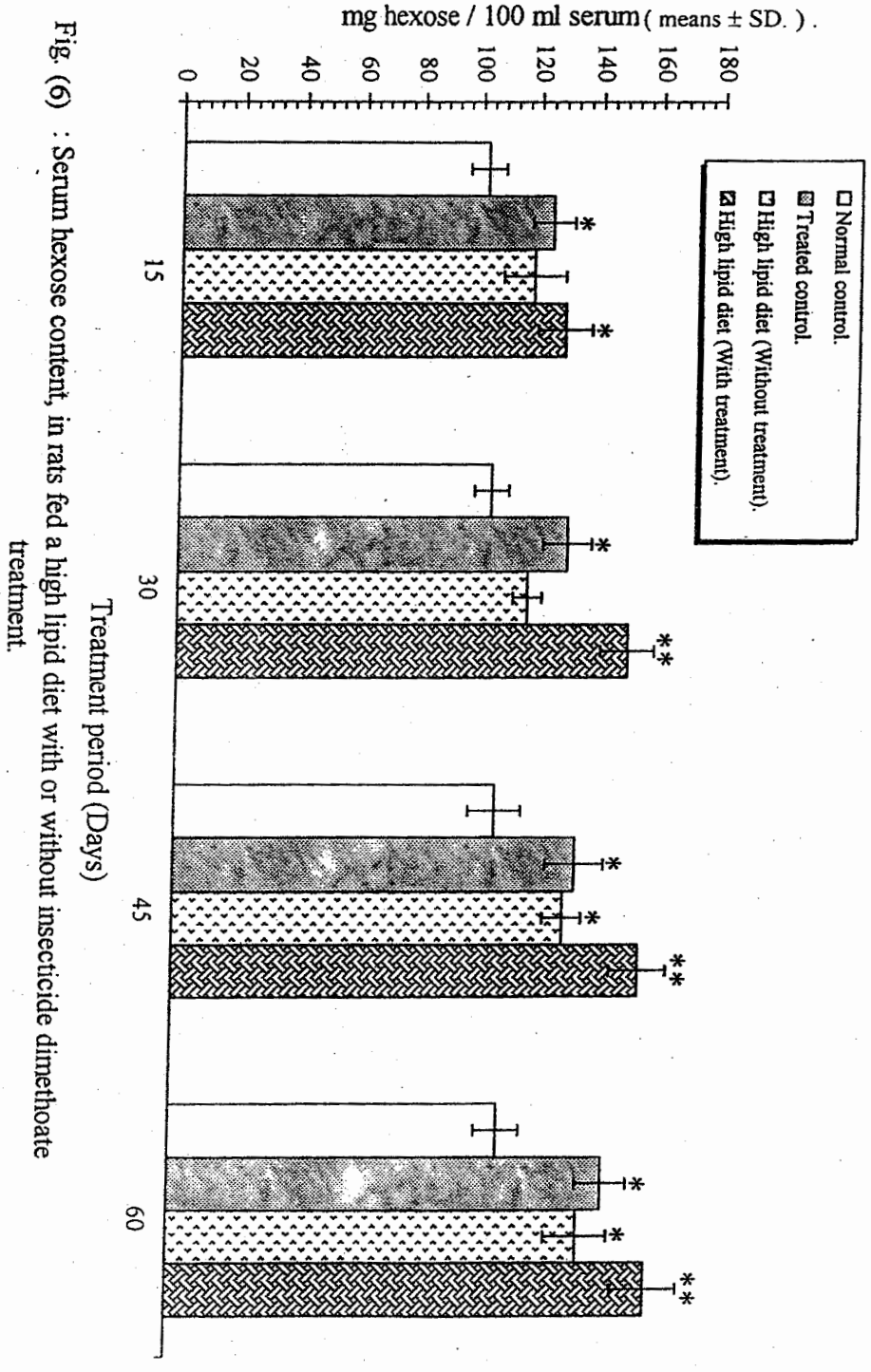

Fig. (6) : Serum hexose content, in rats fed a high lipid diet with or without insecticide dimethoate treatment.

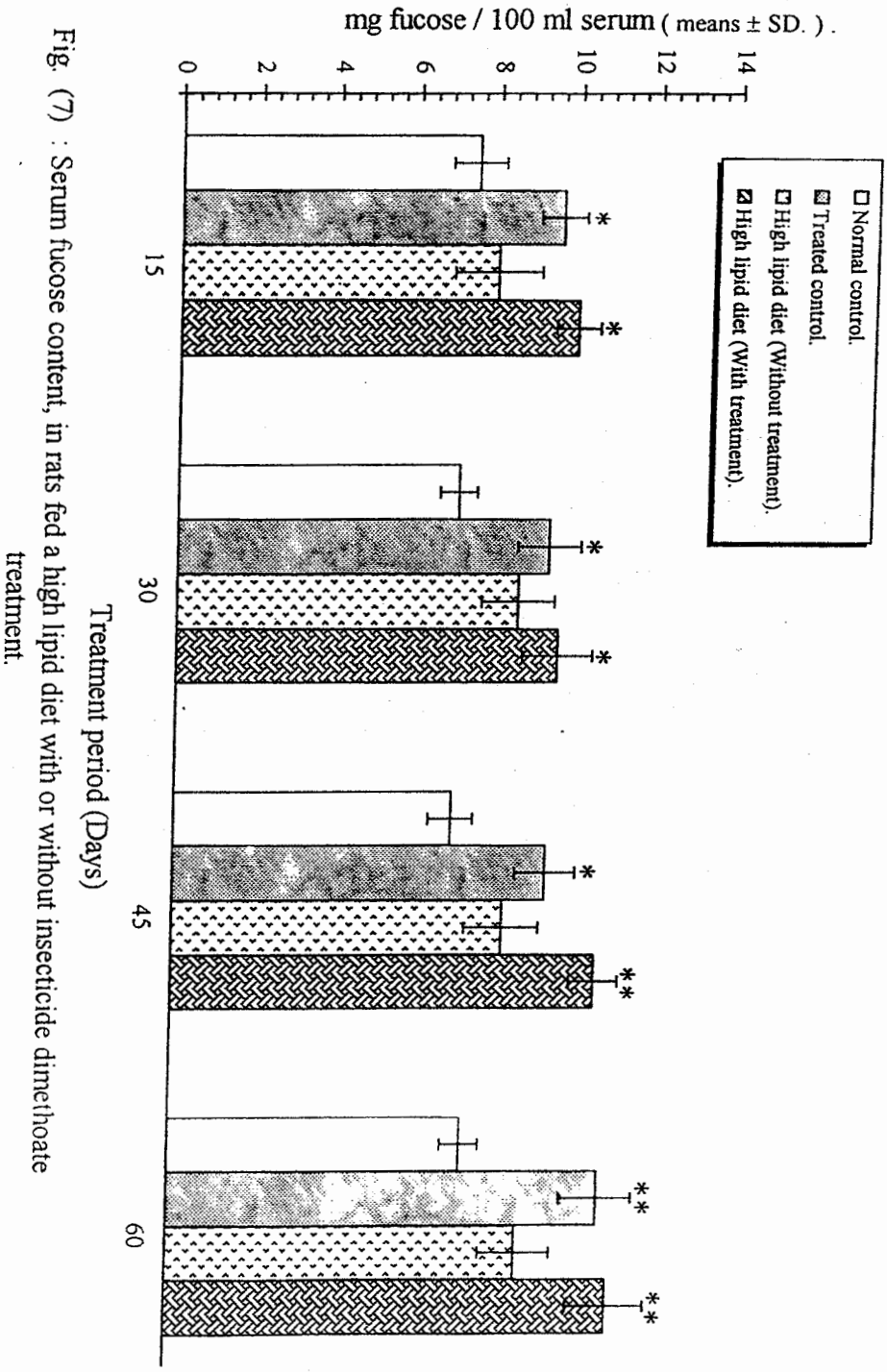

Fig. (7) : Serum fucose content, in rats fed a high lipid diet with or without insecticide dimethoate treatment.

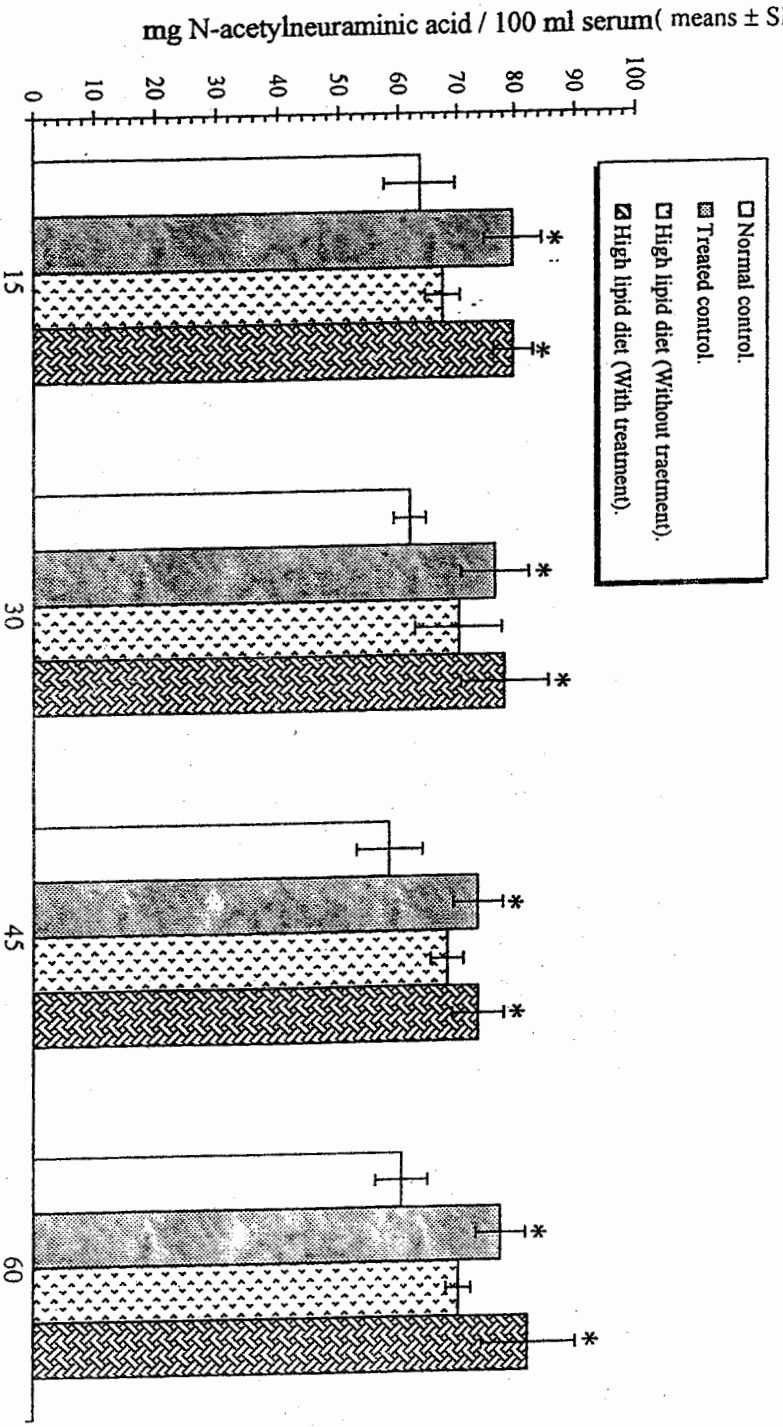

Fig. (8) : Serum N-acetylneuraminic acid content, in rats fed a high lipid diet with or without insecticide dimethoate treatment.

فاعلية نظام غذائي معين ضد التسمم الكبدي بمبيد الدايمثويت
تأثير وجبة غذائية ذات محتوى دهني عالي

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أظهرت الدراسة مدى التغير فى المركبات عديدة التسكر الميوسينية ومركبات أيضها في كبد ومصل ذكور الجرذان البيضاء المغذاة بوجبة عالية المحتوى الدهني مع المعالجة بالمبيد الحشري الدايمثويت(0.1 من الجرعة المميتة للنصف تساوى 21مجم/كجم يوميا(عن طريق الفم و لمدة 15-30-45-60 يوما.

سجلت عديدات التسكر الميوسينية في الكبد (عديمة الكبريت، ذات المحتوى الجيد من الكبريت وذات المحتوى العالي من الكبريت) ارتفاعا تدريجيا في المجموعات المعالجة بالمبيد بالمقارنة بالمجموعات القياسية . أما المركبات الأيضية لعديدات التسكر الميوسينية في المصل (حامض اليورونيك،الهكسوزأمين،الهكسوز،الفيوكوز و حامض الأسيتيل نيورأمينيك)فقد أظهرت زيادة متشابهة و ذات مغزى وذلك تحت نفس ظروف المعاملة بالمبيد و المذكورة سابقا.

و عند دراسة التأثير المشترك للتغذية بوجبة ذات محتوى عالى من الدهون مع مبيد الدايمثويت في نفس الوقت ظهرت زيادة إضافية بسيطة في مستوى عديدات التسكر الميوسينية في كل من الكبد و المصل و ذلك خلال فترة التغذية (60 يوما) كما أن الاختلال الأيضى لعديدات التسكر الميوسينية ربما يعكس التأثير المشترك للتسمم الكبدي بالدابمثويت و الوجبة عالية المحتوى الدهني أو أحدهما.

على الرغم من ذلك فإن الزيادة الإضافية التي سجلت في عديدات التسكر الميوسينية و مركباتها الأيضية ربما تُعزى إلى تحفيز كل من معدل تخليقها أو معدل تكسيرها أو كلاهما.

و هكذا فإنه من المرجح أن نقترح أن الوجبة عالية المحتوى الدهني قد أظهرت فشلاً في الوقاية من التسمم الكبدي بمبيد الدايمثويت.