

# A Protective Role Of Nigella Sativa Oil Against The Harmful Effect Of CCl<sub>4</sub> On The Liver Cells

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## Citation

K Al-Kubaisy, M Al-Noaemi. *A Protective Role Of Nigella Sativa Oil Against The Harmful Effect Of CCl<sub>4</sub> On The Liver Cells*. The Internet Journal of Nutrition and Wellness. 2006 Volume 3 Number 1.

## Abstract

The effects of the essential oil Nigella sativa was studied for its antihepatotoxic effects in rats against carbon tetrachloride (CCl<sub>4</sub>) which induced hepatocytic damage.

The increased levels of serum enzymes (SGOT, SGPT and SAP) and bilirubin observed in rats treated with CCl<sub>4</sub> were greatly reduced in the animals treated with N.sativa oil and CCl<sub>4</sub>. The decreased levels of proteins and albumin observed in rats after treatment with CCl<sub>4</sub> were found to increase in rats treated with N. sativa oil and CCl<sub>4</sub>. These biochemical observations were supported by histopathological test of liver sections.

## INTRODUCTION

A number of plants used in the traditional medicine were shown to possess antioxidant activity (Kiso et al., 1985; Hikino et al., 1986; Halliwell, 1991; Udem et al., 1997; Aniya et al., 2000 ; Suboh et al., 2004). Nigella sativa, L- a widespread medicinal plant of the Ranunculaceae family has multiple application in many countries, because of its insecticidal action ( Dashpande et al., 1974). It improved the T-cells activity ( El- kadi and Kandil, 1987), prevents the decrease in hemoglobin level and leukocytes counts caused by cisplatin ( Nair et al., 1990). Antimicrobial effect of Nigella sativa have been reported (Hanafy and hatem, 1991; Osfor et al., 1995). It has also been shown to affect smooth muscles of rats and guinea pig (Aqal and shaheen, 1996).

The main constituents of Nigella sativa reported to be present in the oil are thymoquinone, dithymoquinone carvacol and anethole 4-terpinole (Worthen et al., 1998; Bruits and Bucar, 2000).

This study was aimed to produce additional antihepatotoxic information on the effect of N.sativa oil in rats.

## MATERIAL AND METHODS

The Nigella sativa oil was obtained from pharm, Saudia Arabia.

Test animals: Wistar rat of either sex weighing (100-150g)

were used.

The animals were housed at 25C and 60-70% RH, they were given balanced diet and water ad libitum.

The 24 rats were divided in four groups:

1. The first group received single dose of carbon tetrachloride 2 ml / kg i.p. on day 3,4 and 5.
2. The second group was treated with 20ml/ kg i.p. of Nigella sativa oil on all 5 days and carbon tetrachloride 2 ml/ kg on day 2 and day 3 about one hour after the administration of thoil.
3. The third group was treated with 30ml/ kg i.p. of Nigella sativa. oil on all 5 days and carbon tetrachloride 2 ml/kg i.p. on day 2 and 3 about one hour after administration of oil
4. The forth group serving as control and received single daily dose of normal saline every day up to 5 days.

After day five, blood sample were obtained by cardiac puncture. The blood samples were allowed to clot for 30 min. The serum samples obtained by centrifugation at room temperature, were used for biochemical estimation.

Serum levels of glutamate oxaloacetate transaminase (GOT),

glutamate pyruvate transaminase (GPT) and Alkaline phosphatase (AP) were measured by standard method using (Boehringer-mannheim) diagnostic kits. Total protein and albumin determination were carried out using Boehringer diagnostic kits.

The animals were then sacrificed and liver were removed and fixed in 10 % formalin.

The paraffin sections, 6 micron thickness were cut and stained with hematoxylin and eosin (H&E) and observed under the light microscope.

**STATISTICAL ANALYSES**

Results were expressed as mean ± S.E. statistical evaluation was performed using (ANOVA) for comparison between groups.

**RESULTS**

Administration of carbon tetrachloride (CCl4) caused a significant (P<0.001) increase in the serum levels of hepato-specific enzymes as compared to control group (table 1). Serum bilirubin level was also significantly

(P < 0.001) increased by CCl4 treated rats, whereas, total protein and albumin levels were significantly (P < 0.001) decreased by CCl4 treated rats than the control level (table 1).

Treatment of animals with Nigella sativa oil and CCl4 (i.p.) resulted in reduction of (SGPT), (SGOT), (SAP) and T. bilirubin levels as compared to CCl4 treated group. While the levels of total protein and albumin were increased as compared with CCl4 treated group.

Histopathological studies demonstrated that CCL4 induced sever and generalized degeneration necrosis of hepatocytes, postal infiltration and Kupffer cell hyperplasia as compared to normal group. Pretreatment with Nigella sativa oil markedly reduced the extent of necrosis.

**Figure 1**

Table 1: Effect of Nigella Sativa oil on biochemical parameters in rats intoxicated with CCl4 (2ml/ kg), (each value is the mean ± S.E).

Groups parameters	(I) Control	(II) CCl4	(III) CCl4+20 ml oil	(IV) CCl4+ 30ml oil
GOT (u/ml)	76.83±5.50	161.87±12.73	129.49±13.02**	102.15+4.58**
GPT (u/ml)	31.56±5.11	67.04±3.01	40.97±1.53**	36.15+1.72**
AP(u/ml)	43.40±1.83	174.38±4.19	40.98±1.53**	36.15+1.73**
T. bilirubin (mg%)	1.36±0.15	8.55±0.28	2.52±0.16**	2.07+0.20**
T Protein (mg%)	8.45±0.30	5.35±0.24	6.72±0.41**	6.57+0.29**
Albumin (mg%)	3.53± 0.17	0.74±	3.66±0.15**	2.62±0.25**

\*\* The mean difference is significant at the 0.001 level  
Groups (II) and III are compared with group I. P < 0.001  
Groups II and IV are compared with group I. P <0.001

**Figure 2**

Table 2: Histopathological changes in hepatocytes of rats

Microscopic observation	Groups			
	I	II	III	IV
Necrosis:	absent	sever	moderate	moderate
Portal infiltration:	absent	sever	moderate	moderate
Kupffer cell hyperplasia:	absent	sever	moderate	moderate

**DISCUSSION**

Measurement of the enzyme activity in serum is of important value because it helps to assess the state of the liver and other organs. Normally serum GPT, GOT and AP levels are low, but these enzymes are released into circulation after cellular damage and increased because they are cytoplasmic in location.

It is well known that CCl4 is converted into the CCl3 free radicals and this reacts rapidly with oxygen which may contribute to hepatotoxicity and subsequent increase in hepatic enzymes (Cheesmen et al., 1985). Hepatotoxicity action of CCl4 and leakage of liver enzymes into blood were recorded by several investigators (Hikino et al., 1986; Gadgoli and Mishra, 1995; 1999).

In the present study N-sativa oil was used as protector against harmful effect of carbon tetrachloride. When it was given before CCl4 treatment it produced protective effects against CCl4- induced hepatotoxicity. These results were evident from the significant reduction in serum (SGOT), (SGPT) , (SAP) and in total bilirubin. Furthermore, there were an increase in the level of total protein and albumin levels in the treated animals with N. sativa oil. The above results were supported by the histopathological results.

Our observations are consistent with the results of Burits and Bucer (2000) who found that the constituents of the essential oil of N.sativa possessed variable antioxidant activity and

were also found to have an effective free radical scavenging activity, when tested for lipid peroxidation in liposomes.

The anti-protein oxidant activity of N.sativa oil observed in the this study, seems to be due to the richness of this oil with many radical scavenging compounds (Houghton et al., 1995; Ghosheh et al., 1999; Enomoto et al., 2001).

Worthen et al. (1998) reported that thymoquinone and dithymoquinone constituent of N.sativa have an antitumor activity.

Also, Badary et al. (2002) found that thymoquinone has strong antioxidant potential due to the scavenging activity towards free radicals.

Meanwhile, Swamy and Tan (2000) concluded that N.sativa possesses a cytotoxic effect as well as a potent effect on the cellular immune response.

From the results obtained in this study, it is concluded that N.sativa oil may have affinity to repair liver tissue from free radicals and can be used as adjuvant therapy.

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