PROTECTIVE EFFECT OF NIGELLA SATIVA SEED OIL ON LIVER INJURY IN RAT

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KEYWORDS

Protective
Nigella sativa
liver injury
liver marker enzymes
ABSTRACT

*Nigella sativa* seeds have been used as a natural remedy for a number of illness. The objective of the present study was to investigate the potential protective effect of *N. sativa* seed oil on liver injury in albino rat. Alcohol was administered to animals for eight weeks to induce liver injury. Alcohol induced rats were treated with *N. sativa* seed oil at a dose of 10 mL and 20 mL/kg body weight. After eight weeks of treatment, liver function markers, alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT) and albumin level were studied. A significant decrease (p<0.05) in the level of ALT, AST, ALP, GGT were observed in the rats treated with oil as compared to alcohol induced rats. These results suggested the protective effect of *N. Sativa* on alcohol induced liver injury. Thus, *N. sativa* oil can be useful in the treatment of liver damage caused by alcohol.

INTRODUCTION

*Nigella sativa* L. (*N. sativa*), Ranunculaceae family, is an annual herbaceous plant growing in countries bordering the Mediterranean Sea, Pakistan and India. This plant has been used by Asian and far Eastern countries as a spice and food preservative. It is also used in health remedies in traditional folk medicine for the treatment of numerous disorders (Gali-Muhtasib et al., 2004). The seeds of this plant (commonly known as black seed, black caraway, black cumin or *kolanji*) have also been used as a natural remedy for more than 2000 years to promote health and treat diseases, which may be due to the seed’s rich and diverse chemical composition. In recent years, the seeds of *N. sativa* have been extensively investigated both phytochemically and pharmacologically. Some of the reported pharmacological properties of *N. sativa* include hypotensive, anti-nociceptive, uricosuric, choleretic, anti-fertility, anti-diabetic, anti-histaminic, anti-oxidant, anti-inflammatory, anti-microbial, anti-tumor and immuno-modulatory effects (Salem, 2005). Black seed contains 15 amino acids, proteins, carbohydrates, both fixed oils (84% fatty acids, including linolenic and oleic) and volatile oils, alkaloids, saponins, crude fibre, as well as minerals, such as calcium, iron, sodium and potassium. Most properties of the whole seeds are mainly attributed to the quinone constituents present in the volatile oil, of which thymoquinone is the most abundant component (Ali and Blunden, 2003; Gali-Muhtasib et al., 2006). Other pharmacologically active constituents, identified by HPTLC, include dithymoquinone, nigellone and thymol (Ghosheh et al., 1999; Nehar and Rani, 2011).

Chronic alcoholism produces a wide spectrum of liver diseases. The toxicity of alcohol is linked to its metabolism via alcohol dehydrogenase enzyme which convert ethanol to cytotoxic acetaldehyde in liver which is further oxidized to acetate by aldehyde oxidase or xanthine oxidase giving rise to reactive oxygen species (ROS) via cytp 450 (Fridovich, 1989; Nordmann et al., 1992), which causes lipid peroxidation (Sadrzadeh et al., 1994) and membrane damage (Tsukamoto, 2001). This causes lowering of body’s normal defence mechanism, altered enzyme activity, decreased DNA repair which eventually leads to hepatitis, necrosis and liver cirrhosis. In recent years, the popularity of native medicine has increased for various reasons. Since there is no reliable hepato-protective drug available in modern science. Researchers have focussed on developing phyto-therapeutic medicine which can provide many individual drugs to treat alcoholic liver disease. The research conducted on several natural plant products used as hepato-protective agent is well documented (Saravanan et al., 2006).

Therefore, the present study was undertaken to establish the hepato-protective effect of oil of *N. sativa* seed in ethanol induced albino rat.

MATERIALS AND METHODS

*Animals:* Male albino rats (*Rattus norvegicus*) weighing 125-175g and 12-14 weeks old were used for study. They were acclimatized in the laboratory condition at a
constant temperature of 22º ± 3º and 12: 12h. Light: dark for fifteen days. They were provided with pelleted rat feed (M/S Amrut Feed, Pranav Agro Industries Ltd, Sangli, India) and water ad libitum. All the animals receive humane care during the study and the protocol was approved by institutional animal ethics committee.

Dehydrated ethanol was purchased from Meck (India) and Nigella sativa was purchased from Mohammedia Products, Hyderabad, India. All other the chemicals used were of laboratory standard.

Experimental design
Albino rats (40) were divided into four groups each containing ten rats.

Group 1: Normal control, receiving equal amount of vehicle (distilled water) for eight weeks.
Group 2: Alcohol induced, receiving alcohol at a dose of 6g/kg/day for first week and 8 g/kg/day for seven weeks.
Groups 3 and 4: N sativa treated, receiving 10mL and 20mL/kg body weight of N. Sativa oil respectively. Both the group received same amount of ethanol, after one hour administration of N. sativa oil for the same period of time. After eight weeks of experiment, blood samples were collected from the retro-orbital plexus and the serum obtained was stored in eppendrof tube at -20ºC for further analysis.

Biochemical analysis
Estimation of liver marker enzymes
The activities of serum aspartate amino-transferase (AST) and serum alanine aminotransferase (ALT) were analyzed by method by Reitman and Frankel (Rietman and Frakal, 1957). Serum alkaline phosphate (ALP) was estimated using Kind and King’s method (Kind and King, 1954). The serum gamma-glutamyl transferase (GGT) was assayed according to the method of Rosalki and Race (Rosalki and Rau, 1972). Serum albumin was measured with bromocresol green (Doumas et al., 1971)

Statistical analysis
The values obtained were expressed as mean ± SD. Statistical evaluation was done using one way analysis of variance (ANOVA). The level of statistical significance was set as p<0.05.

RESULTS
Table 1 shows that intoxication with alcohol significantly increased (p<0.05) the serum ALT, AST, ALP and GGT as compared to normal rats. However, administration of N. Sativa oil at 10mL and 20mL/kg body weight orally, decreased the activity of these enzymes as compared to alcohol induced rats. The observed changes were found to be more significant (p< 0.05) at 20 mL/kg body weight dose of N. sativa. The level of albumin was decreased in alcohol induced rat which on treatment with N. sativa oil returned back to near normal, however it was more significant (p< 0.05) at 20 mL/kg body weight dose.

DISCUSSION
The present study was undertaken to demonstrate the ameliorating effect of N. sativa seed oil on alcohol induced liver injury in albino rat. The results of the current study showed significant increase in the serum enzyme such as AST and ALT in alcohol intoxicated rat. The elevated level of these enzymes were primarily due to leakage of cellular enzymes in the blood stream leading to their increase in serum (Baldi et al., 1993) which indicate liver injury. Increased level of ALP was also recorded in the alcohol induced group which was similar to the results of Soliman et al., 2006 The increase in ALP was attributed to the damage in lysosomal membrane (Mc Cord 1985). This was in agreement with Salah et al., 1976 who noticed that lysosomal enzymes were activated in conditions characterized by increased tissue catabolism. The increase of cytosolic calcium could contribute to more breakdown and damage of lysosomal and other cellular membrane structure. In our study treatment of alcohol-intoxicated rat with N. Sativa oil alleviated the increased level of ALT, AST and ALP to near normal which could be manifested to reduction in cell membrane disturbances, Serum GGT is a sensitive marker enzyme widely used as a laboratory test for the hepatobillary disease especially alcoholic liver disease and alcohol induced damage (Nakanishi et al., 2006). In our present study we observed that GGT has invariably decreased after N. sativa oil treatment reflecting the reduction in liver damage and hence the ameliorating effect of N. sativa seed oil (Table 1).

Albinin is one of key component of serum protein. As albumin is synthesized in the liver, it can be used as bio-marker to monitor liver function (Friedman et al., 1980). In the present study albumin level was reduced in N. sativa treated rats. This is a clear indication of N. sativa being related to an improvement in the functional status of the liver cells. Thus, this study suggest that N. sativa has ameliorating effect on alcohol induced injury and the mechanism may involve the prevention of cell membrane disturbances and reduction of oxidative stress by radical scavenging and antioxidant activity, this in turn prevents kupffer cell activation and pro-inflammatory mediators and normalization of altered redox
state in addition to hastened elimination of ethanol and acetaldehyde from the blood. Further studies are needed to unravel the precise mechanism of action.

**ACKNOWLEDGEMENT**

The author is grateful to University Grant Commission, New Delhi, for providing financial assistance by granting major research project (No. 37-325/2009 SR).

**REFERENCES**


