Available online at www.ijpcr.com
International Journal of Pharmaceutical and Clinical Research 2015; 7(6): 395-398

ISSN- 0975 1556

Research Article

Evaluation of the Potential Beneficial Effects of Thymoquinone Against Nicotine Induced Toxicity

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Available Online:31st October, 2015

ABSTRACT

Tobacco smoking is a global serious health problem. Approximately one person dies every six seconds due to tobacco smoking, it affects different organs of the body primary the heart and the lungs. Thymoquinone (TQ) is a compound derived from the black seeds of a flower called Nigella Sativa.This plant has been used as a medicinal herb to fight diseases and boost immunity. Science has proven that thymoquinone has anti-inflammatory, antioxidant and anti-cancerous properties. This research attempts to investigate the protective effect of thymoquinone against organ damage induced by nicotine in rats. Thirty rates were involved in this study divided into three groups of ten rats, they treated as: Group (1) Control; Group (2) Nicotine treated (1 mg/kg body weights per day, SC, for 21 days); Group (3) treated with S.C injection of nicotine (1 mg/kg b.w per day) with oral administration of Thymoquinone (5mg/kg b.w) for 21 days. After 21days, the blood was collected from the heart immediately after decapitation prior to further analysis. Lungs,livers are dissected out. The lipid components such as total cholesterol(TC) ,high density lipoprotein cholesterol (HDL-C) and triglyceride(TG) are estimated in plasma using standard kits. Group (2)produced a significant increase in serum total cholesterol (TC) and triglysrol (TG)levels also increase in aspartate aminotransferase (AST) and alanine transaminase (ALT) as compared to group(1)with significant decrease inserum HDL-C and by histological examination of lung and liver tissues showed marked inflammatory damage Regarding group(3)the oral administration of TQ significantly reversed all changes occur in TC,TG and HDL-C due to nicotine administration, also decreased elevated (AST) and (ALT),also have a protective effect on the lung and liver tissues. This study highlights the interest toward using Nigella sativa as a natural medicinal plant for protection against multiple diseases especially nicotine induced organ damage.

Keywords: thymoquinone, Liver toxicity, cardiopulmonary disease, nicotine.

INTRODUCTION

Nicotine exposure via tobacco chewing/cigarette smoking is considered to be a major risk factor involved in the induction and progression of pulmonary and cardiovascular disorders. Nicotine has been reported to induce oxidative stress both in vivo and in vitro. The process of lipid peroxidation plays an important role in the pathogenesis of numerous human diseases. The initiation of lipid peroxidation is carried out in most cases by free radicals such as superoxide, hydroxyl radicals etc. and other reactive oxygen species like H2O2 causing cellular injury. Increased lipid peroxidation levels in tissues of intra-peritoneal nicotine administered rats have been reported[1]. Nicotine is oxidized to its main metabolite cotinine in liver and causes the formation of free radicals in tissues. The formation of these radicals along with reduction in glutathione in tissues causes oxidative damage[2]. The lung is a primary target of cigarette smoke induced oxidative damage, and cigarette smoke exerts its oxidative effects on the rest of entire organs eventually[3]. Cigarette smoke significantly increases oxidative stress in mouse heart, liver and lung tissues[4]. Nicotine administration significantly depleted glutathione contents and increased lipid peroxidation in the liver[5]. Thymoquinone (TQ) is the major component of the volatile oil of Nigella sativa seeds. The antioxidant activity of TQ against experimental oxidative injury is well known. Oral administration of TQ protected several organs against oxidative damage induced by free radical generating agents[6]. TQ possesses strong antioxidant properties through the scavenging ability of different free radicals, its scavenging power being effective against superoxide anions[7].

Aim of the study

This study aims to investigate and gain the insight concerning the histological protective effect of TQ against multiple organs damage induced by nicotine in rats.

MATERIAL & METHODS

Chemicals

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Table 1. Effect of TQ on serum TC, TG, LDL-C and HDL-C levels in nicotine administered rats.

	Control	Nicotine	Nicotine+ TQ
TC (mg/dl)	50.83 ± 2.27	103.33 ± 4.49 ***	73.17 ± 3.25 **###
TG (mg/dl)	112.5 ± 3.19	151.83 ± 2.46***	129.67 ± 3.04 **###
HDL (mg/dl)	85.33± 2.98	61.83± 2.60**	79.16 ±4.99 #
LDL (mg/dl)	29.1 ± 2.69	68.5 ± 3.2***	34.30 ± 2.74###

** P< 0.01, *** P< 0.001 as compared to the control group.
#P< 0.05, ###P< 0.001 as compared to the nicotine group.

Table 2. Effect of TQ on serum transaminases levels in nicotine administered rats.

	Control	Nicotine	Nicotine+ TQ
AST(mg/dl)	31.1 ± 2.1	100.67 ± 3.1 ***	63.3 ± 2.01***###
ALT(mg/dl)	46.36 ± 2.7	93.16 ± 3.3 ***	55.5 ± 2.5 ###

*** P< 0.001 as compared to the control group.
###P< 0.001 as compared to the nicotine group.

Nicotine tartrate (5 gm), TQ (1 gm) from Sigma pharmaceutical company.

Animals and diet

Adult male Wistar albino rats (n=30) of Wistar strain of body weight 120-130 g . They are housed in polypropylenecages and fed standard pellet diet for 1 wk and water. Animals are divided into 3 groups of 10 animals each. Animals are treated as follows:

Group 1- Control group

Group 2- Nicotine treated (1 mg/kg body weights per day, SC, for 21 days)

Group 3- treated with S.C injection of nicotine(1 mg/kg b.w per day) with oral administration of Thymoquinone (5mg/kg b.w) for 21 days [8]

Sample collection

After 21 days, the rats are kept-fasting overnight and sacrificed by decapitation between 9:00 – 11:00 h. Blood are collected from heart immediately after decapitation in heparinized tubes and plasma are separated by centrifugation and stored in vacuum desicatotor at -20 C prior to further analysis. Lungs, livers, aortas and kidneys are dissected out and wiped clear with tissue paper to remove adhering blood and tissue fluid and stored in neutral buffered formaline.

Lipid profile test

The lipid components such as TC, HDL-C and triglyceride are estimated in plasma using standard kits. VLDL-C and LDL-C are calculated from the value of triglyceride, TC and HDLC by Friedwald and Fredickson's formula.

Statistics

The data are expressed as means ± standard errors (S.E.M.). Differences between groups were determined using one way analysis of variance (ANOVA) followed by Tukey-Kramer multiple comparisons test using Instat-3 (GraphPad Software, version 3.05, San Diego, CA, USA). Statistical significance was considered when $P < 0.05$.

RESULTS

Effect on serum lipid profile As shown in table 1, nicotine administration for 21 days produced a significant increase in serum TC and TG levels as compared to control group with significant decrease in serum HDL-C. The oral administration of TQ significantly reversed all changes occur in TC, TG and HDL-C due to nicotine administration. Effect on Liver transaminases As presented in Table 2, nicotine administration produced significant increase in serum ALT and AST as compared to control one. TQ treatment decreased the elevated transaminases levels. Effect on histological examination of the lung and liver tissues As shown in Figure 1, rats of the control group showed normal lung architecture, while rats of the nicotine group showed marked inflammatory damage. These changes included oedema, tissue injury and infiltration of high amount of lymphocytes. TQ treatment markedly attenuated the degree of injuries and the lymphocytic infiltration. In the liver, histological examination showed massive degenerative changes versus the control animals. These changes included oedema, fatty degeneration and lymphocytic infiltration. TQ administration ameliorated the majority of the morphologic changes.

DISCUSSION

The present study investigated the in vivo protective effects of thymoquinone against nicotine induced toxicity showed that Cholesterol level significantly increased in experimental group as compared to the control group and our findings were similar to the previous studies (Annida and Venugopal, 2007) described in their study that the level of free fatty acids, cholesterol and triglycerides increased in plasma of male albino Wistar rats treated with nicotine subcutaneously. The presences of hypercholesterolemia and triglyceridemia in heavy smokers are due to increased activity of 3–. hydroxy–3–methyl–glutaryl CoA reductase and increased incorporation of labeled acetate into cholesterol[9]. Chattopadhyay in 2008[10] also indicated that the administration of nicotine in adult albino rats caused a significant increase of total cholesterol and triglycerides. There was significant increase in triglycerides (mg/dl) level in experimental group as compared to control group. Our results were according to the previous studies that reported increased cholesterol and triglyceride levels and decreased levels of HDL cholesterol[10]. Higher level of triglycerides occurred due to the presence of nicotine that decrease the activity of lipoprotein lipases and these

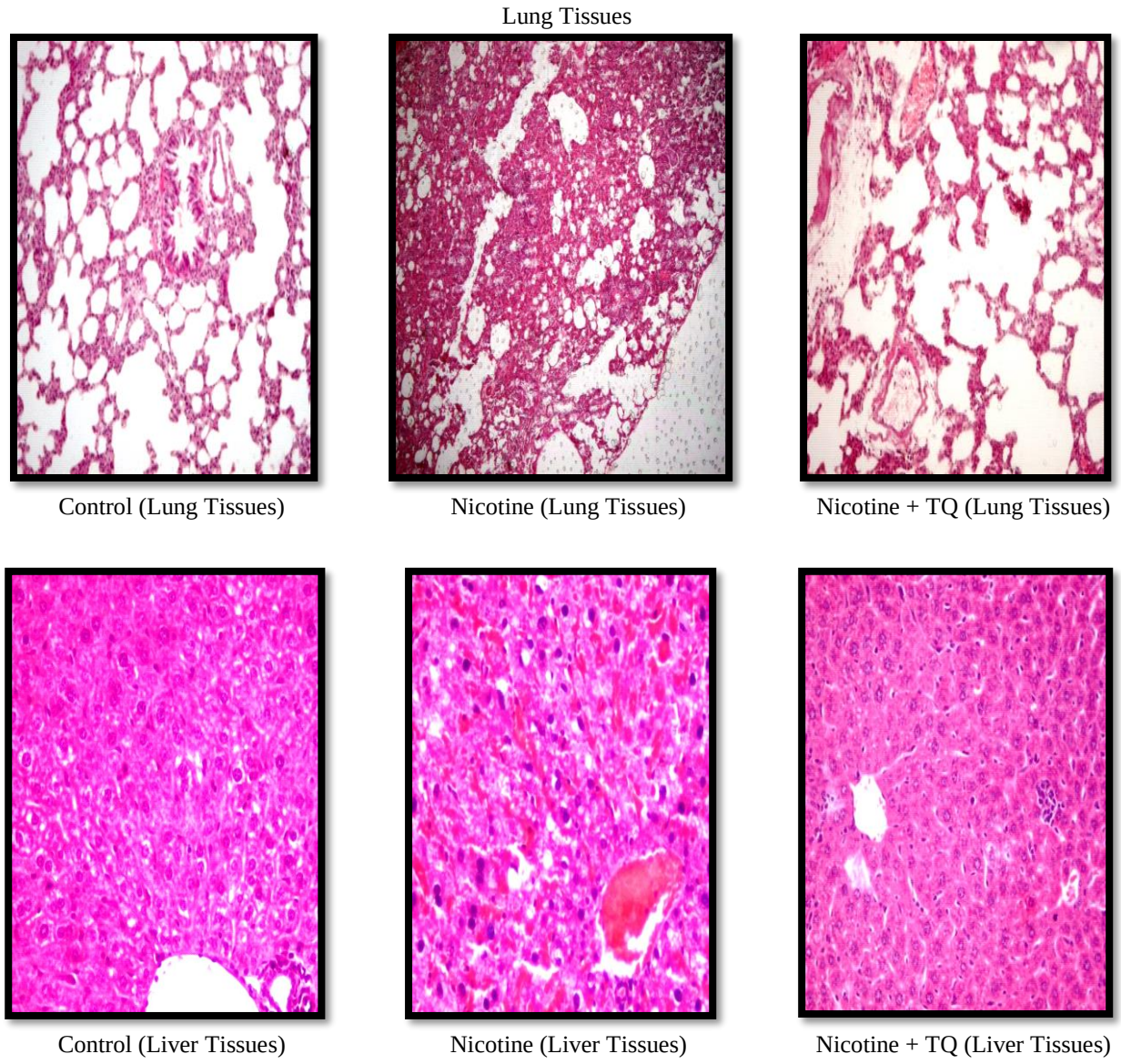

Figure 1. Effects of TQ on lung and liver histopathological examination in nicotine-treated rats. Hematoxylin–eosin staining (×100): Control: no signs of inflammation; Nicotine: marked inflammatory changes; Nicotine+TQ: reduced inflammatory reaction.

enzymes involved in the uptake of circulating triglycerides rich lipoprotein and VLDL by the extra hepatic tissue[11]. It was observed that administration of nicotine decreases the total proteins, albumin and bilirubin but increased ALT, AST and ALP levels[12]. Similar results were also reported by (Jang et al., 2012)[13]. In the present study, the oral administration of TQ significantly reversed all changes occur in TC, TG and HDL-C due to nicotine administration.with some hepatic enzyme also decreased the elevated transaminases levels[13]. Previously, (El-Mahmoudy et al 2002) found that N. sativa fixed oil suppressed the nitric oxide production. In this regard, the anti-inflammatory potentials of thymoquinone and nigellone, components of N. sativa essential oil, are of considerable importance as they act immune boosters[14]. Overall, results of present study further supported the traditional use of N. sativa and its derived products as a protective for many diseases. Moreover, N. sativa fixed and essential oils significantly ameliorate free radicals and improve antioxidant capacity thus reducing the risk of multiple organ damage induced by nicotine. The beneficial effects of TQ with its antioxidant/anti-inflammatory effects were observed. Injection of rats with CP markedly affected the liver functions and histopathological changes[15].Nigella sativa and its constituents may be proved as good therapeutic options in the prevention of cancer. Earlier studies have shown that N. sativa and its constituent thymoquinone (TQ) have important roles in the prevention and treatment of cancer by modulating cell signaling pathways. In this review, we summarize the role of N. sativa and its constituents TQ in the prevention of cancer through the activation or inactivation of molecular cell signaling pathways[16].

CONCLUSION

The present study has shown that TQ has a significant protective effect against multiple organs damage induced by nicotine.

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