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BENEFICIAL ROLE OF *EMBLICA OFFICINALIS* ON NICOTINE INDUCED TOXICITY IN RATS (RATTUS NORVEGICUS)

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ABSTRACT

Emblica officinalis (Amla) is widely used in the Indian system of medicine and is believed to increase defense mechanism against diseases. It is one of the oriental traditional medicine used for hepatic disorders from time immemorial. Nicotine is the most abundant component in cigarette smoke and it is first metabolized in the liver. The present study was carried out to investigate the role of *Emblica officinalis* on nicotine induced toxicity in rats. Animals were divided in to four groups of which each group containing six rats. Male wistar rats (Group - II, Group - III and Group - IV) were treated with oral nicotine diluted with drinking water for 32 days, while (Group - I) control was administrated with drinking water simultaneously. After 32 days, Group - III and Group - IV were administered with two different concentrations of *Emblica officinalis* (250 mg/kg, 500 mg/kg body weight) for 7 days. Group - II served as a toxicity group (5 mg/kg body weight of nicotine). Rats were sacrificed 24 hours after last day of administration (40^{th} day), the blood was analyzed for lipid profile.

Nicotine toxicity on rats showed an increase in the levels of Total Cholesterol (TC), Triglycerides (TG), Low Density Lipoprotein (LDL) & Very Low Density Lipoprotein (VLDL) and decrease in High Density Lipoprotein (HDL) level when compared with the control animals. On treatment with *Emblica officinalis* in 500 mg/kg body weight doses to rats the changes showed a marked decrease in TC, TG, LDL, VLDL levels whereas a significance increase in HDL level. On treatment with *Emblica officinalis* in 250 mg/kg body weight doses to rats, the slight changes showed a lipid profile when compared with the Nicotine treated animals.

Key words: Nicotine, *Emblica officinalis*, Total Cholesterol, Triglycerides, Low Density Lipoprotein, Very Low Density Lipoprotein and High Density Lipoprotein.

INTRODUCTION

Cigarette addiction, the most common form of tobacco product, continues to be one of the world's most serious public health problems and it is responsible for large number of deaths. Cigarette smoke has enormous negative health consequences worldwide, and the use of tobacco is still rising globally (CDC, 2000). Although approximately 4000 components occur in the cigarette, nicotine is the alkaloid most active in the tobacco. Nicotine is an amine composed of pyridine and pyrrolidine rings (Trushin and Hecht, 1999). The actions of nicotine have been extensively investigated in human, in animal, and in a variety of cell

systems (Cooke and Bitterman; Valenca *et al.,* 2004). Nicotine is responsible for a high toxicity effect (Elli Slaughter *et al.,* 2012). The predominant effects of nicotine in the whole intact animal or human consist of an increase in pulse rate, blood pressure, plasma free fatty acids and lung injury (Benowitz *et al.,* 2002; Liu *et al.,* 2001). It has been reported long back that it induces oxidative stress in both in vitro and in vivo (Church and Pryor, 1958).

Emblica officinalis (Phyllanthus Emblica L.) is a euphorbiaceous plant widely distributed in subtropical and tropical areas of India, China, Indonesia, and Malaysia. It has abundant amounts of Vitamin C and superoxide dismutase (Saniet *et al.,* 2008; Verma and Gupta, 2004) and is used in many traditional systems of medicine. Many other countries add this as important dietary sources in addition to their use in traditional medicine for wound healing, inflammation and stomach acidity. *Emblica* fruit is reported to have hypoglycemic activity (Abesundara *et al.,* 2004).

Several investigators have determined the efficacy of amla as an anti- atherosclerotic (Thakur *et al.,* 1988), antidiabetic (Tripathi *et al.,* 1979), antimutagenic (Sharma *et al.,* 2000) and anticancer agents (Zhang *et al.,* 2004). It is also used as antimicrobial agent (Rani and Khullar, 2004) and anti-inflammatory agent (Perianayagam *et al.,* 2004), antibacterial agent **(**Saeed and Tariq 2007**)**. It was reported that *Emblica* has a strong antioxidant activity (Islam *et al.,* 2008; Bafna and Balaraman, 2004), which may be partially due to the existence of flavonoids and several gallic acid derivatives including epigallocatachin gallate (Anila and Vijayalakshmi, 2002; Sabu and Kuttan, 2002). And also contain Vitamin C, minerals and amino acids. (Zhang et al. 2000)

MATERIALS AND METHODS

Animals

Male albino rats (Rattus Norvegicus) ranging in body weight from 175-200 gms were obtained from the King Institute, Guindy, Chennai and maintained according to the guidelines of CPCSEA (No: 324), under the supervision of Animal Ethical Committee were used for the experiment. They were acclimatized to laboratory conditions prior to use and fed with pelleted chow (supplied by Poultry Research Station, Chennai) and water provided ad libitum.

Chemicals

Nicotine ((-) - nicotine ([-]-1methyl-2-[3-pyridyl]- pyrrolidine), was purchased from Sigma Fine chemicals, Chennai, India. Nicotine solution was prepared daily. (Separate drinking bottles were used to avoid nicotine solution exposition to light).

Plant material

Emblica officinalis was procured from local market and fruit of Emblica officinalis was separated, shade dried, grounded with mortar and pestle and sieved to get fine powder.

Experimental design

The rats were randomly distributed into four different groups of six animals each under identical conditions and were grouped as follows:

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Group -I Served as control animals and was given drinking water.

Group- II Animals received nicotine (5 mg/kg bwt) in drinking water for 32 days.

Group -III Animals received Emblica officinalis (250 mg/ kg bwt) in drinking water for 7 days (after 32 days of nicotine administration).

Group -IV Animals received Emblica officinalis (500 mg/ kg bwt) in drinking water for 7 days (after 32 days of nicotine administration).

At the end of the experimental period (40th day) all the animals were anaesthetized and sacrificed by cervical dislocation after an overnight fast. Blood was collected and the serum and organs were separated for further studies.

The plasma cholesterol was estimated as per Allain et al., 1974. Triglycerides were estimated by Foster and Dunn (1973); Tietz (1987), HDL by Burstein et al., 1970 and LDL, VLDL by Friedewald et al., 1972.

Statistical analysis

The data were analyzed using Analysis of Variance (ANOVA) and the group means were compared by Duncan's Multiple Range Test (DMRT). The difference was considered to be significant at $p<0.05$ level.

RESULTS

Table 1. Changes in Lipid Profiles in rats (*Rattus norvegicus)* treated with Nicotine and *Emblica officinalis*

Parameters	**TC** (mg/dl)	**TG** (mg/dl)	**HDL** (mg/dl)	**LDL** (mg/dl)	**VLDL** (mg/dl)
Control	78.42 ± 4.58 [a]	70.24 ± 4.26 [a]	28.10 ± 1.5 [a]	11.2 ± 1.1[a]	39.4 ± 2.6 [a]
Nicotine (5 mg/kg)	148.28 ± 5.72[b]	94.32 ± 4.46 [b]	18.26 ± 1.2 [b]	26.5 ± 1.5 [b]	44.6 ± 2.7 [b]
N+EO (250 mg/kg)	96.32 ± 4.72[c]	81.67 ± 4.28[c]	24.32 ± 1.6 [c]	14.6 ± 1.4[c]	38.3 ± 2.6 [c]
N+EO (500 mg/kg)	80.14 ± 4.44 [d]	71.28 ± 3.56[d]	29.12 ± 1.8 [d]	11.4 ± 1.2[d]	40.2 ± 2.8 [d]

N-Nicotine; EO-Emblica officinalis; TC-total Cholesterol; TG-Triglycerides; HDL-high density lipoprotein; LDL-low density lipoprotein; VLDL- very low density lipoprotein
Values represent mean± SD of six animals
Values not sharing a common superscript letter (a,b,c and d) differ significantly at $P<0.05$ (Ducans Multiple Range Test)
Group comparison: Group 1 with all; Group 3 & 4 with 2

The effect of Nicotine toxicity for 32 days followed by treatment of *Emblica officinalis* on lipid profile in rats (*Rattus norvegicus*) are shown in table1.

Nicotine toxicity on rats showed a increase in the levels of TC, TG, LDL & VLDL and this increase was statistically significant at $P<0.05$ level and decrease in HDL level which is statistically significant at $P<0.05$ level when compared with the control animals.

On treatment with *Emblica officinalis with* 250 and 500 mg/kg body weight doses to rats the changes showed a decrease in TC, TG, LDL, VLDL levels and this decrease was statistically significant at P<0.05 level whereas a significant increase in HDL level and this increase was statistically significant at P<0.05 level and it was dose dependent when compared with the Nicotine treated animals.

DISCUSSION

In the present study the cholesterol level was elevated in the nicotine treated animals. The prevalence of hypercholesterolemia and triglyceridemia has been reported in heavy smokers (Masora, 1977). The increased level of cholesterol is attributed to the increased activity of 3-hydroxy-3-glutaryl CoA reductase (HMG-CoA reductase) and increased incorporation of labeled acetate in to cholesterol by Brunzell, *et al.,* 1983. Nicotine decreased the activity of lipoprotein lipase resulting in elevated levels of triglycerides. Huttunen, *et al.,* 1976 envisages that this enzyme is involved in the uptake of circulating triglycerides rich in lipoprotein (chylomicrons or VLDL) by the extra hepatic tissues, while Cryer, 1981 stated that Chromaffin the cells of adrenal medulla synthesize catecholamines by the stimulation of nicotine and adipose tissue lipolysis which is carried out by catacholamines, which in turn elevates the levels of cholesterols, triglycerides and also increases the fatty acids.

Venkatesan *et al.,* 2006 have shown that the levels of plasma TC, LDLC, non- HDL-C and MDA significantly elevated in smokers in comparison with non-smokers. In an earlier study a significant increase in serum TC, phospholipids, and triglycerides as well as the amount of lipids associated with VLDL and LDL was recorded in nicotine-treated rats (Ashakumary and Vijayammal 1997). Present study has significant increase in levels of plasma TC, triglyceride, LDL-C and VLDL-C, and a significant decrease in plasma HDL-C of the nicotine treated rats under both dietary conditions are in agreement with the earlier studies. Cigarette smoking may induce functional and chemical change in the living systems. Treatment with *Emblica officinalis* rats showed decreased the TC, TG, LDL-C, VLDL-C levels and increased the levels of HDL-C in dose dependent manner.

CONCLUSION

Plants and plant products are widely used as agents for the prevention and cure of many diseases. Plants are generally considered to be less toxic and free from many of the side effects than synthetic drugs. Human diets constituting fruits, vegetables and spices have been shown to contain beneficial components, including phenolic compounds with antioxidant properties. And also, some important naturally occurring vitamins particularly vitamin C have been found to effective in reducing the toxic effects. It also contains a high antioxidant activity.

The present study was, on effect of nicotine which causes alteration in lipid profile. *Emblica officinalis* and vitamin C were used to combat toxicity due to nicotine, the results were satisfactory indicating the role of *Emblica officinalis,* since *Emblica officinalis* contains vitamin C, gallic acid, flavonoids, minerals, tannins, alkaloids, phenolic compounds, amino acids and carbohydrates, etc. which can detoxify the effect of Nicotine on lipid profile. The constitution of *Emblica officinalis* might be the causative factor as modifiers in the changed metabolism due to exposure of nicotine toxicity. It is hoped that the studies of this kind on cheap and readily accessible antidotes in future shall open up new awareness in finding remedies for a wide variety of diseases.

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