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SYNERGESTIC ROLE OF SELENIUM AND VITAMIN E IN AMELIORATING THE CIGARETTE SMOKE INDUCED BIOCHEMICAL ALTERATIONS IN ALBINO RAT

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ABSTRACT

Present study was undertaken to investigate the synergistic role of selenium and vitamin E in ameliorating the cigarette smoke induced biochemical alterations in albino rats. A total of thirty six (36) adult albino rats of the Wister strain were used, they were randomly divided into three sets of twelve rats each. Set A served as control (no exposure to cigarette smoke). While rats in set B were exposed to only cigarette smoke and rats in set C were exposed to cigarette smoke with pre-supplementation of selenium and vitamin E. The rats were subjected to whole body exposure of cigarette smoke of a filtered cigarette 1hr/day (delivered as 6 cigarettes, 6 times/day) for 28 days. At the end of each experimental period, blood was obtained from each rat for the determination of serum total protein, serum urea, serum creatinine and serum glucose. An increase in serum urea, serum creatinine and serum glucose levels was observed, however serum total protein showed a considerable decrease in cigarette smoked albino rats. Due to the synergistic effect of Selenium and Vitamin E, the intensity of inflammation caused by cigarette smoke was reduced by antioxidant defence mechanism and the said altered biochemical parameter levels were considerably restricted to their normal ranges.

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INTRODUCTION

Cigarette smoke has enormous negative health consequences worldwide and the use of tobacco is still rising globally (CDC, 1999). Cigarette smoke is a heterogeneous aerosol, which contains many thousands of chemicals (Phillips, 2002). These constituents include many that are known to be pharmacologically active, toxic, mutagenic, and/or carcinogenic. Some of these agents are nicotine, tar, cadmium, carbon monoxide, carbon dioxide, cyanides and various hydrocarbons (Goodman and Gilman, 2001). Cigarette smoke also includes various compounds, which are capable of causing an increase in the generation of various reactive oxygen species, such as O_2^- , H_2O_2 , OH^- , and ROO^- . These reactive oxygen species in turn are capable of initiating and promoting oxidative damage in the form of lipid peroxidation (Ozkan and Fiskin, 2004). Cigarette smoking may thus be associated with an increase in the incidence and severity of various diseases such as cancer.

The potential damage that can be caused by free radicals is normally minimized by a combination of biological antioxidant systems including enzymatic and non-enzymatic reactions (Kim *et al.*, 2003). Similarly, cellular damage and biochemical alterations caused by cigarette smoke exposure can be prevented by free radical scavengers or antioxidants, which further strengthens the hypothesis that free radicals play a key role in cigarette smoke induced toxicity. Antioxidants are the frontline of defence against free radicals. The antioxidants are used frequently as food supplements and can be effective in preventing oxidative damages. Damages that are caused by cigarette smoke may be prevented by selenium and vitamin E as their concurrent use has a synergistic protective effect against oxidative damages. Therefore, the present study was carried out to determine the possible synergistic and ameliorative effect of selenium and vitamin E against the cigarette smoke induced biochemical alterations in albino rats.

MATERIALS AND METHODS

The albino rat, *Rattus norvegicus* (Berkenhout) of both the sexes have been selected for the present investigation. The colony of the albino rats was inbred at the animal house of

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Zoology Department, Dr. B.R. Ambedkar, Agra. Thirty six healthy and adult rats ranging in weight from 100 to 120 g were kept in polypropylene cages at temperature $25 \pm 5 \text{ }^\circ\text{C}$, relative humidity $60 \pm 5\%$ and photoperiod 12hrs/day. The experimental protocol was in accordance with guidelines approved by the institutional ethics committee. The rats were fed on commercial food pellets (Golden Feed, New Delhi) and water *ad libitum*. For the exposure to cigarette smoke the experimental rats were kept in an isolated smoke chamber within their cages. The rats were subjected to whole body exposure of cigarette smoke of a filtered cigarette 1hr/day (delivered as 6 cigarettes, 6 times/day) for 28 days. Experimental animals were acclimated for one week prior to the experiment.

The experimental rats were grouped in three sets. One Control set 'A' and two experimental sets 'B' and 'C' of twelve rat each. Control set 'A' was exposed to ambient air, while experimental set 'B' was exposed to cigarette smoke and experimental set 'C' was exposed to cigarette smoke with pre-supplementation of antioxidants selenium (0.01mg/100g b. wt.) and vitamin E (2.5mg/100g b. wt.) in combination for 28 days. The rats were sacrificed by decapitation and dissected carefully for collection of blood directly from the ventricle of the heart and transferred to sterilize plain glass centrifuge tubes for the separation of serum. Serum total protein content was estimated by modified Biuret and Dumas method described by Dumas *et al.* (1971). Serum urea was estimated by GLDH – Urease method, as described by Young (1995). Serum creatinine was estimated by alkaline picrate method as described by Toro and Ackermann (1975) and Serum glucose activity was estimated by GOD/POD kit method (Trinder, 1969). All statistical calculations were performed by a statistical software Stat pac version 3.0.

RESULTS AND DISCUSSION

Biochemical analysis of blood serum showed a significant increase ($P < 0.05$) in the levels of urea and creatinine in rats exposed to the cigarette smoke but serum level of glucose was not significantly affected, while on the other hand serum total protein level showed a significant decrease ($P < 0.05$) in cigarette smoke exposed albino rats Table 1.

The alterations of these markers proved that cigarette smoke induce oxidative damages in albino rats. The damage to the organs by cigarette smoke is evidenced by the elevation of biomarkers in serum. These markers are the important indices for the diagnosis of renal dysfunction and these indicate the damage of the cells, cellular leakage and loss of functional integrity of cell membrane in the kidney (Vanisree and Sudha, 2006). The above results might suggest the inability of the kidney to excrete these products, indicating an impairment of kidney functions. These effects could be attributed to the changes in the threshold of tubular re-absorption, renal blood flow and glomerular filtration rate. Further, the observed decrease in serum total protein is attributed to activation of anabolism of protein due to lead toxicity which affected the enzymes of anabolism process, where as the elevated serum urea levels are due to the destruction of RBC's during lead administration and the elevation of serum creatinine may be due to impaired renal function and kidney damage, which may be attributed to the nephrotoxic effect of lead (Abdel-Aziz, 2010). However, an increase in serum glucose is attributed to nicotine, as it increases body metabolism by sympathoadrenal activation, increases energy expenditure and causes release of body stored fat and cholesterol into the blood stream (Okewumi *et al.*, 2012). The antioxidants act by scavenging free radicals, molecules with one or more unpaired electrons, which rapidly react with other molecules, starting chain reactions resulting in a process called oxidation, with the lack of antioxidant. Highly reactive free radicals can damage healthy DNA and have been linked to change that accompany aging and with other diseases. Antioxidants are intimately involved in the prevention of cellular damage (Halliwell and Gutteridge, 1999). Selenium is an essential micronutrient with important biological and biochemical functions due to its unique antioxidant properties. It acts as a free radical scavenger and plays an important biological role in living organisms, mainly through its presence in selenoproteins such as glutathione peroxidases, thioredoxin reductases, iodothyronine deiodinases (Moghadaszadeh and Beggs, 2006). Selenium is known due to its antioxidant role in living systems and its major function is as a cofactor for the enzyme GSH-Px. It is therefore essential in removing free oxygen radicals from the body and preventing oxidative stress. However, reports in the last decade have revealed that selenium protects cells and

Table 1. Effect of inhaling cigarette smoke on biochemical parameters of albino rat with supplementation of antioxidants (Selenium and Vitamin E)

Parameters	Control			Experimental sets (12)/Treatment		
	Set A		Set B		Set C	
	Ambient air	Cigarette smoke	Cigarette smoke + Selenium + Vitamin E			
	Range		Range		Range	
	Mean \pm S.Em		Mean \pm S.Em		Mean \pm S.Em	
Serum Total Protein (g/dl)	5.45 – 7.09 (6.47 \pm 0.31)	4.92 – 6.70 (5.46 \pm 0.32) ↓**	5.43 – 6.98 (6.38 \pm 0.22) ↑**			
Serum Urea (mg/dl)	13.71 – 19.73 (16.30 \pm 0.65)	16.94 – 19.11 (18.12 \pm 0.37) ↑**	14.11 – 19.61 (16.56 \pm 0.51) ↓**			
Serum Creatinine (mg/dl)	0.40 – 0.59 (0.49 \pm 0.03)	0.48 – 0.72 (0.62 \pm 0.04) ↑**	0.46 – 0.57 (0.51 \pm 0.02) ↓**			
Serum Glucose (mg/dl)	81.51 – 93.32 (87.88 \pm 2.01)	85.92 – 95.64 (92.62 \pm 1.56) ↑*	81.82 – 93.21 (88.12 \pm 1.98) ↓*			

* – Non significant

** – Significant

S.Em – Standard error of mean

↑ - Increase

(12) – Number of rats

↓ - Decrease

cell membranes from oxidative processes, facilitating reaction between oxygen and hydrogen and ions transfer at membrane level (Toman *et al.*, 2009). Vitamin E is a lipid soluble and free radical scavenger that help in stabilizing and protecting cell membrane and valuable in repairing tissues. The main function of vitamin E is to maintain the integrity of the body's intracellular membrane by protecting its physical stability and providing defense line against tissue damage caused by oxidation. Also, vitamin E is protective in nature as it helps to reduce the oxidation of lipid membranes and unsaturated fatty acids and also prevents the breakdown of other nutrients by oxygen. Selenium in combination with other antioxidants especially with vitamin E has proven to be more effective in mitigating the oxidative stress. These agents in combination are known to potentiate synergistically the effects of one another.

Serum total protein showed a significant increase while serum urea and serum creatinine showed a significant decrease, where as serum glucose showed a non-significant decrease in rats supplemented with combination of selenium and vitamin E in comparison to cigarette smoke exposed rats. Increased serum urea and serum creatinine levels due to cadmium-induced renal toxicity were decreased in rats given both the antioxidants (vitamin C, vitamin E and selenium) and cadmium (Karabulut-Bulan *et al.*, 2008), where as selenium, vitamin E and vitamin C in combination totally blocked the cadmium-induced stimulation of serum urea and serum creatinine (Obianime and Roberts, 2009). Supporting views to the present study are given by Dilsiz *et al.* (1999), who investigated the effects of selenium, vitamin C and vitamin E against oxidative stress of cigarette smoke in rats. Fiskin *et al.* (2005) reported the protective effect of selenium and vitamin E on lipid peroxidation in smoke exposed male mice. Similarly, Ozkan *et al.* (2007) stated that combined application of vitamin E and selenium had an additive protective effect against cigarette smoke induced oxidative stress in brain, kidney and liver of mice. This study concludes that after the supplementation of selenium and vitamin E in combination, the toxic effects of cigarette smoke can be curbed to a large extent in albino rats.

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