# Effects Of Oral Administration Of Nicotine On Blood Glucose, Electrolytes And Lipid Profile In Albino Rats

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**Abstract**

This study investigated the effect of oral administration of nicotine on glucose, serum electrolytes and lipid profile in albino rats. Forty rats were divided into five groups and treated orally for thirty days with nicotine. Group I, which served as the control received 0.2ml / kg normal saline, Group II and III received 0.5mg/kg and 1.0mg/kg body weight of nicotine respectively and were sacrificed on the 30th day. Group IV and V received 0.5mg/kg and 1.0mg/kg body weight of nicotine but were left untreated for another 30 days before sacrificing, these groups served as the recovery group. Blood glucose, low-density lipoprotein cholesterol (LDL-C), High-density lipoprotein cholesterol (HDL-C), total cholesterol (TC), triglyceride (Tg), sodium, potassium and calcium were measured in the serum at the end of the experiment. The result showed that blood glucose, LDL-C, TC, Tg, total cholesterol/high-density lipoprotein cholesterol ratio, low-density lipoprotein cholesterol/high- density lipoprotein cholesterol ratio were significantly higher ($P<0.05$), whereas sodium, potassium and calcium levels were significantly lower ($P<0.05$) in nicotine treated rats when compared with the control rats. HDL-C levels were similar in all the groups. However, mean value of the recovery groups for all the variable tends towards that of the control. The results suggest that nicotine induced reversible dyslipidaemia that is associated with decreased circulating levels of calcium, potassium and glucose.

**Key words:** ***Nicotine, glucose, lipoprotein, electrolyte, rat***

## Introduction

Nicotine use through cigarette smoking continues to be a widespread public health problem since millions of people smoke in the United States alone, with smoking-related deaths numbering over 440,000 each year [1]. Nicotine is considered the primary chemical in tobacco that is responsible for engendering tobacco use and dependence.

The level of cholesterol in the blood has been one of the considerable interests since the early 20th century. Although, it is well established that high levels of low-density lipoprotein cholesterol (LDL-cholesterol), total cholesterol, and several other lipoproteins are generally detrimental and growing body of evidence shows that increasing levels of high-density lipoprotein cholesterol (HDL-cholesterol) and/or its associated apolipoprotein has protective cardiovascular effects [2].Several epidemiological studies [3, 4] have established the importance of plasma levels of HDL-cholesterol as well as high LDL-cholesterol and triglyceride as an important predictor of the development of cardiovascular disease. Evidence from several lines of investigation strongly suggests that low HDL-cholesterol directly plays a role in the atherogenic process. It is important to keep in mind that low HDL-cholesterol is associated with other known cardiovascular risk factors, including hypertension, diabetes, insulin resistance, obesity, physical inactivity, and genetic factors [5]. Total cholesterol/HDL-cholesterol ratio [6, 7] and LDL-cholesterol/HDL-cholesterol ratio[8] have been suggested as atherogenic indices.

Several effects of nicotine on different biological systems have been documented ranging from cardiovascular, renal, and gastrointestinal to reproduction. The association between smoking and various cancers, particularly lung cancer is well known [9, 10]. Nicotine has recently been shown to stimulate angiogenesis in different pathological setting including wound healing tumor growth and vascularization of atherosclerotic plague [11] and effect of nicotine on blood flow, oxygen consumption and glucose uptake in the small intestine have been studied [12]. Several experimental studies on reproduction have revealed a consistent and highly significant incidence of infertility [13, 14]. **It was also previously demonstrated under experimental condition in rats that exposure to cigarette smoke resulted in reduced birth weight [15, 16] and oral administration of nicotine have been associated with testicular degeneration, disorganization of the cytoarchitecture and decreased serum testosterone levels [17] .**Nevertheless, studies that associated nicotine with altered lipid profile in rats did not account for its effect upon withdrawal on serum electrolytes and blood glucose to

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the best of our knowledge. In spite of the knowledge of adverse effect of nicotine on lipid profile, it is relatively unsettled whether nicotine affects blood glucose and electrolytes. The present study was therefore designed to investigate the effect of oral nicotine administration on blood glucose, serum electrolytes and lipid profile in adult albino rats and subsequent effect of cessation.

## Materials and Methods

### Nicotine preparation

Nicotine hydrogen tartrate (95% nicotine) was purchased from BDH chemical Ltd Poole England. The nicotine dosage freshly prepared in normal saline for each group of animals was delivered orally at 0.5mg/kg and 1.0mg/kg body weight. The working solutions were stored in foil-wrapped glass bottle at 4°C for no longer than ten days.

### Animals and treatments

Experiments were performed on 25 male and 15 female albino rats (8-10 weeks old weighing 150-180g) obtained from the Animal House, College of Medicine, University of Ibadan, Oyo State, Nigeria. Animals were divided into five equal groups with free access to rat chow and drinking water. Animals were also maintained in a well-ventilated room with a 12:12-hour light-dark at room temperature. The experiment was conducted in accordance with the Guidelines of the U.S. National Institute of Health (NIH) on the care and use of laboratory animals. The animals were divided into five groups; Control group (Group 1) that received 0.2 ml/kg normal saline (vehicle) for 30 days, Group II received 0.5mg/kg nicotine for 30 days, Group III received 1.0mg/kg nicotine for 30 days, Group IV and V received 0.5mg/kg and 1.0mg/kg nicotine respectively for 30 days but were left untreated for another 30 days.

### Blood sample collection

Blood (2ml) was collected from each animal via retro-orbital sinus with 70µl capillary tube [18] and put into plain sample bottles for analysis. The sample was centrifuged at 3000 rpm for five minutes. The serum was used to analyze the level of random blood glucose, electrolytes and lipid profile immediately.

### Determination of electrolyte levels

$Na^+$ and $K^+$ concentration of serum samples were done by flame photometry [19] (Corning model 410C). Serum calcium level was determined according to Merck Diagnostic (E. Merck, Darmstadt, Germany) using the methyl thymol blue method.

### Determination of *serum lipid*

Plasma levels of total cholesterol (TC), triglyceride (TG) and HDL-cholesterol were assayed by standard enzymatic-colorimetric method with assay kits supplied by Randox Laboratory Ltd (Co. Antrim,UK). LDL-cholesterol was calculated with the use of Friedewald's formula [20]. Plasma albumin level was measured by micro-biuret method using assay kit obtained from Randox Laboratory Ltd. (Co. Antrim, UK).

**Statistical analysis*:*** The results are presented as means±SEM for each group. Differences among groups were analyzed using ANOVA and post hoc analyses were done with the Turkey test for pairwise comparison. $P<0.05$ was accepted as significant.

## Results

### Effects of nicotine on electrolyte level in albino rats

There was a significant decrease ($p<0.05$) in the mean serum level of sodium, potassium and calcium of nicotine treated rats when compared with the control while an insignificant decrease in the mean serum level of sodium and potassium for the recovery groups was noticed. 1.0 mg/Kg body weight recovery group had a significant decrease ($p<0.05$) in the mean serum level

Table 1: **Effect of nicotine on mean serum electrolyte level in albino rat**

| DOSE | Sodium (mmol/l) | Potassium (mmol/l) | Calcium (mmol/l) |
|---|---|---|---|
| Control | 137.2 ± 2.0[a] | 6.2 ± 0.2[a] | 1.9 ± 0.5[a] |
| 0.5mg/kg BW | 124.2±2.2[b] | 4.8±0.3[b] | 1.4±0.4[b] |
| 1.0mg/kg BW | 113.2 ±2.6[b] | 4.4 ±0.6[b] | 1.2 ±0.2[b] |
| 0.5mg/kg BW recovery | 136.5 ± 2.4[a] | 6.0 ±0.4[a] | 1.8 ± 0.2[a] |
| 1.0mg/kg BW recovery | 135.2 ± 2.8[a] | 5.8± 0.4[a] | 1.5± 0.2[b] |

Values are expressed as means±S.E.M of 8 rats per group. Means in rows showing different superscript letters [a,b] are significantly different; $p<0.05$.

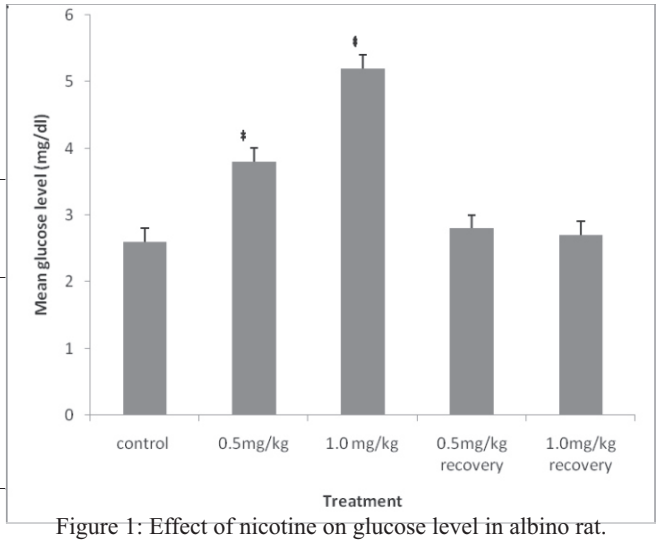


Figure 1: Effect of nicotine on glucose level in albino rat. Values are expressed as means±S.E.M of 8 rats per group. *p<0.05 significantly different from other groups

Table 2: **Effect of nicotine on mean serum lipid concentration in albino rats**

| DOSE | Control | 0.5mg/kg BW | 1.0mg/kg BW | 0.5mg/kg BW Recovery | 1.0mg/kg BW Recovery |
|---|---|---|---|---|---|
| Total cholesterol (mmol/l) | 2.31 ±0.23[a] | 3.62 ±0.22[b] | 3.91 ±0.27[b] | 2.44 ±0.24[a] | 2.50 ±0.31[a] |
| Triglyceride(mmol/l) | 0.64 ±0.02[a] | 1.01 ±0.02[b] | 1.42 ±0.03[b] | 0.73 ±0.04[a] | 0.67 ±0.2[a] |
| LDL- cholesterol(mmol/l) | 1.88 ±0.04[a] | 1.94 ±0.01[a] | 2.29 ±0.02[b] | 2.01 ±0.04[a] | 2.03 ±0.04[a] |
| HDL- cholesterol(mmol/l) | 0.84 ±0.01[a] | 0.86 ±0.03[a] | 0.85 ±0.02[a] | 0.89 ±0.03[a] | 0.88 ±0.01[a] |
| Total cholesterol /HDL cholesterol ratio | 2.75 ±0.12[a] | 4.21 ±0.15[b] | 4.60 ±0.17[b] | 2.97 ±0.12[a] | 3.18 ±0.14[a] |
| LDL-cholesterol /HDL cholesterol ratio | 2.24 ±0.08[a] | 2.26 ±0.07[a] | 2.69 ±0.09[b] | 2.26 ±0.06[a] | 2.31 ±0.04[a] |

Values are expressed as means±S.E.M of 8 rats per group. Means in columns showing different superscript letters [a,b] are significantly different; $p<0.05$.

of calcium when compared with the control group as shown in Table1

**Effects of nicotine on lipid profile level of albino rats**

There was a significant increase ($P<0.05$) in the mean TC level in nicotine treated rats when compared with the control group, while recovery groups showed an insignificant increase in TC during recovery (Table 2).There was also a significant increase ($P<0.05$) in serum TG level of nicotine treated group when compared with the control while a gradual recovery in TG level for both recovery groups was observed when compared with the control group as shown in Table 2.

There was no significant difference in the HDL-Cholesterol of nicotine treated, normal control and the recovery rats (Table2).

There was an insignificant increase in the mean serum LDL-C level for 0.5mg/kg BW treated rats while 1.0mg/kg. BW treated animals had a significant increase ($P<0.05$) in the mean serum level of LDL-C when compared with the control. The recovery groups for both treatments had an insignificant increase in the mean serum LDL-C when compared with the control rats as shown in Table 2.

The results also showed that there was also a significant increase ($P<0.05$) in the mean level of TC and HDL-C ratio of 0.5mg/kg BW and 1.0mg/kg BW treated group when compared with the control group. The recovery group showed an insignificant increase in the mean level of TC and HDL-C ratio for both recovery groups when compared with the control group as shown in Table 2. There was a significant increase ($p<0.05$) in the LDL-C and HDL-C ratio for 1.0 mg/kg BW treated animals when compared with the control group. The recovery groups had an insignificant increase when values were compared with the control group as shown in table 2.

**Discussion**

The results of the present study showed that oral nicotine administration could cause hyperglycemia, hyperlipidemia and electrolyte imbalances in rats.

The serum levels of sodium, potassium and calcium were significantly decreased in a dose-dependent manner by nicotine. The observed decrease in serum electrolyte level might be due to increased losses, reduced absorption or alteration in metabolism [21, 22]. The recovery groups had mean values of serum electrolyte tending towards that of the control due to nicotine withdrawal.

The blood glucose level also showed a significant dose dependent increase in the treated animals. This might be due to the suppressing effect of nicotine on pancreatic release of insulin and is consistent with other studies [23]. The significantly high glucose level must have also been responsible for the reduction in serum potassium level considering the role of blood glucose in potassium metabolism. High serum glucose enhances the movement of potassium from extracellular fluid into the cells. This role of glucose in potassium metabolism was evidenced by significantly lower serum potassium level in diabetes with poor glucose control [24, 25]. The recovery group had an insignificant increase in the serum glucose level.

Administration of nicotine to the animals also raised the serum cholesterol, triglyceride, LDL-cholesterol. This is consistent with other studies [26, 27] in which nicotine caused elevation of plasma free fatty acid which may serve as building blocks for the synthesis of both cholesterol and triglyceride. The hyperglycemia recorded may also be due to stimulation of adenylcyclase enzyme in tissue in the production of cAMP. The increased cAMP levels, in blood stimulate

glycogenolysis thus increasing the levels of glucose in the blood. It is worth noting that the various adverse effect of nicotine on serum glucose level, electrolyte and lipid profile was ameliorated by nicotine withdrawal.

Administration of nicotine led to significant decrease in plasma level of calcium. Low serum level of calcium has been shown to elicit an increase in the secretion of parathyroid hormone which stimulates dehydroxylation of 25-hydroxy vitamin D to the more biologically active 1,25-dihydroxyvitamin D in the kidney. 1, 25-dihydroxyvitamin D promotes glycogenesis and inhibits lipolysis [28]. In this study the decrease in plasma calcium could provide an explanation for disturbance in the lipid profile.

In conclusion, this study showed that abnormal lipid profile observed during nicotine administration is associated with reduced serum sodium, potassium and calcium. However, it is conceivable that nicotine cessation could ameliorate the observed adverse effects caused by nicotine in rats.

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**References**

1. Centers of Disease control and prevention. Annual smoking attributable mortality, years of potential life lost, and economic costs-United states. 2006; 51:300-303.
2. Wannamethee SG, Shapper AG, Ebrahim, S. HDL cholesterol, total cholesterol and risk of stroke in middle-aged British women. Stroke 2000; 31: 1882-1888.
3. Gordon DJ, Probstfield JL, Garrison RJ, Neaton JD, Catelli WP, Knoke J. High-density lipoprotein cholesterol and cardiovascular disease: four prospective American studies. Circulation 1989; 79: 8-15.
4. Wilson PW, D'Agostino RB, Levy D, Belanger, AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. Circulation. 1998; 97: 1837-1847.
5. Vega GL, Grundy SM. Hypoalpha lipoproteinemia (low high density lipoprotein) as a risk factor for coronary heart disease. Curr. Opin. Lipidol. 1996; 7: 209-216.
6. Castelli WP, Anderson K, Wilson PW, Levy D. Lipids and risk of coronary heart disease: the Framingham study. Ann. Epidemiol. 1992; 2: 23-28.
7. Criqui MH, Golomb BA. Epidemiologic aspects of lipid abnormalities. Am. J. Med. 1998; 105: 48S-57S.
8. Forst PH, Havel, RJ. Rationale for use of non-high-density lipoprotein cholesterol rather than low-density lipoprotein cholesterol as a tool for lipoprotein cholesterol screening and assessment of risk and therapy. Am. J. Cardiol. 1998; 81: 26B-31B.
9. Wynder EL, Hoffmann D. Tobacco and Tobacco smoke studies in experimental carcinogenesis *Academic press* New York.1987
10. Hecht SS, Murphy SE, Carmella SG, Zimmernon CL, Losey L, Kramarczuk I. Effect of reduced cigarette smoking on the uptake of a Tobacco specific long carcinogen. *J. Natt cancer Inst.* 2004; 96(2):107 – 115. 11. Li Z, Duckles SP. Acute effect of nicotine on rat mesenteric vasculature and tail artery. *J. Pharmacol Exp Ther*. 1993; 264: 1305 – 1310.
12. Grayson J, Oyebola DDO. Effect of nicotine on blood flow, oxygen consumption and glucose uptake in the canine small intestine. British Journal of Pharmacology. 1985; 85: 797 - 804.
13. Weisberg E. Smoking and reproductive health. Clinical reproduction and fertility. 1985; 3.75 – 186.
14. Aydos k, Guren M, Can B, Ergun. A. Nicotine toxicity to the ultra structure of the testis in rats. BJU international. 2001; 88.622 – 629.
15. Carmines EL, Gaworski CL, Faqi AS, Rajendaran N. In uterus exposure of IR4F reference cigarette smoke: Evaluation of developmental toxicity. Toxicol. Sci. 2003; 75: 134 – 147.
16. Garwoski CL, Carmines EL, Faqi AS, Rajerdaran N. In uterus and lacftation exposure of rats to IR4F reference cigarette mainstream smoke: Effect on prenatal and postnatal development. Toxicol. Sci. 2004; 79: 15 7 – 169.
17. Oyeyipo IP, Raji Y, Emikpe BO, Bolarinwa AF. Effects of oral administration of nicotine on organ weight, serum testosterone level and testicular pathology in adult male rats. Nigerian Journal of Physiological Science. 2010. 25:81-86.
18. Ezzai SD. Effect of intrathecal morphine on blood glucose, glucagons and tissue glucagons in rats, comparison with the effect of xanthan gum on blood glucose. *Journal of Islamic Academy of Science. 1995;* 8: 3-8.
19. Olatunji LA, Soladoye AO. Effect of increased calcium intake on cardiac and vascular $Na^+$ - $K^+$-ATPase activity in oral contraceptive-treated female Sprague-Dawley rats. Ind. J. Exp. Biol. 2006a 44: 875-879.
20. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma without use of the preparative ultracentrifuge. *Clin. Chem. 1972;* 18: 499-502.
21. Macallan DC. Wasting in HIV infection and AIDS. J. Nutr. 1999; 129: 238S-242S.
22. Basamento G, Kotler DP. Malnutrition in HIV infection. Gastroenterol.Clin. North Am.1997; 26:

393-415.

23. Alada RA. Effects of calcium channel blockers on nicotine-induced hyperglycaemia in the rat. African Journal of Medicine and Medical Sciences. 2001; 30: 57 - 59.

24. Walmsley RN, White GH. A guide to diagnostic clinical chemistry. Blackwell Scientific Publication Melbourne, Oxford, London. Edinburgh Boston. Palo Alto, 1983; Pp220-222

25. Sudhakar K, Sujatha M, Ramesh BS, Padmavthi P, Reddy PP. Serum calcium levels in patients with essential hypertension and their first-degree relatives. Indian Journal of Clinical Biochemistry, 2004; 9 (1): 1-23.

26. Maida V, Howlett GJ. Effect of Cigarrette Smoking and Dietary Lipids on Rats. Lipoprotein Metabolism. Atherosclerosis. 1990; 80 (3)209 – 216.

27. Latha MS, Vijayammal PL, Kurup PA. Effect of nicotine administration on lipid metaboliem in rat. Indian J. Med. Res. 1993; 98:48-4

928. Zemel MB. Calcium modulation of hypertension and obesity: mechanisms and implications. J. Am. Coll. Nutr. 2001; 20: 4285-4355.