

Short communication

Changes in Serum Electrolytes, Urea and Creatinine in *Nicotiana tabacum*-treated Rats

* Nwaji A.R.^{1,2}, Ante I.A.², Nwoke F.K.¹, Inwang U.¹

¹Department of Physiology, Faculty of Basic Medical Sciences, Alex Ekwueme Federal University, Ndufu-Alike, Ebonyi State-Nigeria

²Department of Physiology, Faculty of Basic Medical Sciences, University of Calabar, Calabar-Nigeria.

Summary: Tobacco, a product of *Nicotiana tabacum* (*N. tabacum*) is composed of nicotine as its primary active ingredient. Nicotine has been reported to be the major cause of tobacco addiction with consequent renal implications. Therefore, this study was conducted to investigate the effect of the aqueous extract of *N. tabacum* on serum electrolytes, urea and creatinine levels as indices of renal function in male Wistar rats. Eighteen male Wistar rats weighing between 140 to 230g were used for this study. The animals were divided randomly into three groups: A, B and C; with each group containing 6 rats. Group A served as control while Group B and C were orally administered sublethal doses of 20 and 30 mg/kg body weight of the *N. tabacum* extract respectively once per day for 21 days. At the end of the experimental observations, the animals were sacrificed and blood samples were collected for biochemical assay. The results showed a significant increase ($p < 0.05$) in the serum concentration of sodium, potassium and urea levels of rats treated with the extract when compared with the control. However, serum concentrations of chloride, bicarbonate and creatinine showed no significant appreciable differences between the treated groups and the control group ($p < 0.05$). In conclusion, the study showed that aqueous extract of *Nicotiana tabacum* is associated with renal dysfunction with consequent hypernatremia and hyperkalemia, and may also suggest impaired urea clearance by the kidneys in male Wistar rats.

Keywords: Creatinine, electrolytes, kidney, *Nicotiana tabacum*, urea, Wistar rats

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*Address for correspondence: E-mail: zubbynwaji@yahoo.com; Tel: +2348114105954

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INTRODUCTION

The kidney plays a primary role in homeostasis by excreting urea and creatinine (Walter, 2004 and Stuart, 2011). This it achieves through filtration of waste products from the blood stream and converting the ultra-filtrate to urine. Also, by regulating blood volume, and maintaining the acid-base balance (pH) and levels of electrolytes, especially sodium and potassium. Thus, according to Valerie and Scanlon, (2007), compromising kidney function can cause pernicious health effects due to build-up of unwanted substances in the body system.

The most commonly requested biochemical tests are urea and electrolytes because they provide crucial information on renal function, chiefly in homeostasis and excretion. The major factor in determining the estimated glomerular filtration rate, which is the gold standard marker of kidney health are the levels of creatinine (Blann, 2014). Also, glomerular filtration rate and levels of electrolytes, urea and creatinine give a strong indication of kidney function and can guide treatment (Blann, 2014).

Tobacco is a product of *Nicotiana tabacum* and has nicotine as its main phytochemical (Di-Chiara, 2000 and Harvey et al., 2004). Nicotine has been reported to be an addictive drug and the leading cause of tobacco addiction. Tobacco is derived from any plant of the genus *Nicotiana* of the Solanaceae family and has been reported to affect several

vital organs of the body. For instance, Nwaji et al., (2021) reported that *Nicotiana tabacum* impaired serum testosterone and testicular weight in rats. The smokeless tobacco has different names in Nigeria. It is called Anwuru in Igbo, Taba in Yoruba and Hausa languages (Thomson, 2008).

Smokeless tobacco is in two forms according to Aduema et al., (2012), viz: 'Tobacco snuff' and 'Chewing tobacco'. Also, according to Ureme et al., (2007), tobacco snuff is the powdered form blended with potash as the main additive in Nigeria and is being recommended as a substitute for cigarette since it is free of hazardous elements such as tar and carbon monoxide (Russel et al., 1980). For this sole reason, people now believe that using smokeless tobacco is safer than smoking it. However, this assumption is false because smokeless tobacco can as well induce nicotine addiction. (Dempsey, 2001).

An understanding of tobacco's effects on renal function can clearly point towards novel approach to its use or disuse at both social and clinical settings with references to renal implications. However, there is dearth of literature on the sub-lethal effects of its graded doses on the renal system. This study thus sought to investigate the effect of *Nicotiana tabacum* on serum electrolytes, urea, and creatinine as indicators of renal function.

MATERIALS AND METHODS

Collection and Identification of plant

Leaves of *Nicotiana tabacum* were collected, identified and authenticated by experts at the Alex Ekwueme Federal University, Ndufu-Alike, Ebonyi State.

Extraction of Sample: 100grams of the plant material was extracted by maceration in 1000ml of distilled water with intermittent agitation (8hrs/day) for 3days using mechanical shake. The mixture was filtered afterwards using Whatman no. 1 filter paper. The filtrate concentrate by rotary evaporation to dryness and solid residue was obtained. The dark brown paste residue was transferred to an airtight bottle and refrigerated until use. The concentration of the aqueous extract was determined using this formula:

$$\text{Concentration} = \text{Weight of leaves (g)} / \text{Quantity of water (ml)}$$

And the actual dose administered was obtained using this formula:

$$\text{Dose (ml)} = \text{Dosage (mg)} / \text{Body weight (kg)} / \text{Concentration (mg/ml)}$$

Experimental Design: 18 male rats of Wistar strain weighing between 140 to 230g were used for this experiment. The animals were acclimatized for two weeks at the Animal House of the Department of Physiology, Alex-Ekwueme Federal University, Ndufu-Alike. The animals were divided randomly into three groups, containing 6 rats each. The experimental design consisted of three groups denoted Group A, B and C. Group A served as the control while groups B and C were orally treated with 20 and 30 mg/kg body weight doses of the *N. tabacum* extract respectively.

The experiment was conducted following the humane treatment for the care and use of laboratory animals.

The animals were kept under optimal laboratory conditions with 12 hour light/dark cycle. The animals were fed with normal rat chow and allowed access to water *ad libitum* for three weeks.

Blood sample collection: The extracts were administered orally for three weeks using oropharyngeal cannula. On the last day of the experimental protocol, the animals were sacrificed and blood samples were collected via cardiac puncture into sample bottles. Serum was obtained by centrifuging at 3000 rpm for 15 minutes.

Determination of serum electrolytes, urea, and Creatinine: Serum levels of sodium and potassium were

determined using the Flame photometry method (Chiron Diagnostics) by strictly following the manufacturer's guidelines. Serum bicarbonate, urea, and creatinine levels were determined by titrimetry, diacetyl monoxime, and alkaline picrate methods respectively using the standard assay kit. These assays were carried out at the Chemical Pathology unit of the Alex-Ekwueme Federal University Teaching Hospital, Abakaliki (AE-FUTHA), Ebonyi State.

Statistical Analysis

Data were expressed as mean \pm SEM. Data were analyzed using Graph pad prism 7.0 software. Differences in means were compared using ANOVA and Students T-test. P-values < 0.05 were taken as statistically significant.

RESULTS

Changes in Serum Electrolyte, Urea and Creatinine in

***Nicotiana tabacum*-treated Rats:** The effect of *Nicotiana tabacum* on serum electrolytes (Na^+ , K^+ , Cl^- and HCO_3^-), urea and creatinine concentration are shown in Table 1 below. Administration of *Nicotiana tabacum* extract has no significant effect ($p < 0.05$) on the serum chloride ion, bicarbonate and creatinine concentrations. There was a significant increase in the serum sodium ion concentration of rats fed with 30mg/kg body weight of the extract when compared with the control group. Also, there was a significant increase ($P < 0.05$) in the potassium ion concentration of all the treated groups when compared with the control. There was also a significant increase in the serum urea concentration of the treated group which received higher dose (30mg/kg body weight) of the extract when compared with the control group.

DISCUSSION

Nicotine is the primary and most important bioactive constituent of Tobacco (*Nicotiana tabacum*) (Harvey *et al.*, 2004). Electrolytes at the right levels are required for the proper functioning of the central nervous system, endocrine and musculoskeletal and digestive systems. The kidney is the principal organ that regulates electrolytes, urea and creatinine levels thereby maintaining homeostasis. Thus, making urea and electrolytes the most commonly requested biochemical tests to assess renal function, principally in excretion and homeostasis. According to Blann, (2014), the serum levels of electrolytes, urea and creatinine give a strong indication of kidney function and can guide diagnostics and medical treatment.

Table 1:

Changes in serum electrolyte, urea and creatinine in *Nicotiana tabacum*-treated rats. Values are expressed as mean \pm SEM (n=6)

Group	Parameters				Urea (mmol/l)	Creatinine (mmol/l)
	Electrolytes					
	Na ⁺ (mmol/l)	K ⁺ (mmol/l)	Cl ⁻ (mmol/l)	HCO ₃ ⁻ (mmol/l)		
A	143.7±0.3	4.6±0.1	108.7±0.8	24.0±0.5	4.4±0.1	76.0±1.1
B	142.5±1.1	5.1±0.1**	109.8±0.5	21.2±1.2	4.7±0.4	77.0±2.4
C	145.2±0.4*	5.2±0.2*	108.5±0.6	24.2±1.4	5.1±0.2**	79.3±1.1

Key: n=6, ** $P < 0.01$, * $P < 0.05$ vs. ctrl group, Na^+ (sodium ion), K^+ (potassium ion), Cl^- (chloride ion), HCO_3^- (bicarbonate)

The result of this study shows that aqueous leaf extract of *Nicotiana tabacum* caused elevated serum sodium, potassium as well as increased serum urea concentrations. However, serum levels of chloride, bicarbonate and creatinine concentrations showed no appreciable differences between the treated groups and the control group.

The result of this study is in pact with previous findings (Eliasson *et al.*, 1993; Yuka *et al.*, 2012; El-Sayed *et al.*, 2013 and Munzir *et al.*, 2015) who reported an increase in serum levels of sodium, magnesium, potassium and urea levels amongst smokers.

Some researchers also reported decreased serum and urinary creatinine values amongst smokers (Eliasson *et al.*, 1993). However, Munzir *et al.*, (2015) reported that there was an elevated value of serum creatinine amongst smokers. This is not consistent with our findings. Eliasson *et al.*, (1993) also reported decreased urinary creatinine, increased serum phosphate and increased urinary potassium amongst snuff users.

Hypernatraemia (Raised sodium) can be caused by a salt-rich diet or dehydration. It can also be caused by low blood volume, resulting from insufficient drinking or excessive loss of water in urine, sweat or diarrhoea (Blann, 2014). Also, raised potassium (hyperkalaemia) may be due to renal problems such as failure to excrete, acidosis (high pH) or potassium being released from damaged cells, such as red bloods cells. HCO_3^- (bicarbonate) is also important in determining the pH of the blood, thus, indicating acidosis or alkalosis.

The main excretory product of body's biochemical metabolism is urea, while creatinine is a more specialized product of the breakdown of protein. Thus, urea and creatinine molecules help with the excretion of excess nitrogen in the body. Urea is a good marker of acute renal disease while creatinine is useful as a longer-term marker of renal function (Blann, 2014). Moreso, the elevated serum urine concentration according to Ritz *et al.*, (1998) might be due to the fact that nicotine (an active ingredient in *Nicotiana tabacum*) increases renovascular resistance which will lead to the fall in renal plasma blood, filtration fraction and glomerular filtration rate (GFR)

The decrease in GFR will, therefore, lead to a decrease in distal tubular flow rate and thus, it is not surprising that it may bring about increased urea reabsorption in the distal convoluted tubule of the kidney (JoAnn and Robert, 2011). It has been suggested that several mechanisms may be involved in inducing renal vasoconstriction and vascular damage. For instance, nicotine has been reported by Ritz *et al.*, (1998) and Gambaro *et al.*, (1998) to increase plasma levels of vasoconstrictors such as catecholamines, vasopressin, endothelin-1 and arginine.

In conclusion, the results of the study suggest that aqueous extract of *Nicotiana tabacum* impaired renal handling of electrolytes with consequent hypernatremia and hyperkalemia and may also suggest impaired urea clearance by the kidneys in male Wistar rats.

REFERENCES

- Aduema W, Lelei S.A, Osim E.E, Koikoibo W, Nneli R.O (2012). Effect of chronic consumption of powdered tobacco (snuff) on anxiety, fear and social behaviours. *Int. J. Basic Appl. Inno. Res*; 1:161-169.
- Blann A (2014). Routine blood tests 1: why do we test for urea and electrolytes? *Nursing Times*; 110: 5, 19-21.
- Dempsey A.K (2001). Absorption of nicotine in cigarette and effect of cigar smoke. *Nature* 226:1231-1232.
- Di-Chiara G (2000). Role of dopamine in the behavioral actions of nicotine related to addiction. *Eur J. Pharmacol.*; 393:295-314
- Eliasson M, Hagg E, Lundblad D, Karlsson R, Bucht E (1993). Influence of smoking and snuff use on electrolytes, adrenal and calcium regulating hormones. *Acta Endocrinologica*; 128: 35-40.
- El-Sayed SM, Mahmoud HS, Nabo, MMH. (2013). Medical and Scientific Bases of Wet Cupping Therapy (Alhijamah): in Light of Modern Medicine and Prophetic medicine. *Ltern Integ Med.* 2-5.
- Gambaro G, Verlato F, Budakovic A. (1998). Renal impairment in chronic cigarette smokers. *J Am. Soc Nephrol* 9. 562-567.
- Harvey D.M, Yasar J, Heishman S.J, Panlilio L.V, Henningfield J.E, Goldberg S.R (2004). Nicotine serves as an effective reinforcer of intravenous drug-taking behaviors in human cigarette smoking. *Psychopharmacology*; 175:134 - 142.
- JoAnn L, Robert W.S. (2011). Blood Urea Nitrogen A Marker for Adverse Effects of Loop Diuretics. *Journal of the American College of Cardiology.* 58-4.
- Johannes J, Jawes J.J, Uma S, Hayan D, F-Farjado L, John P.L (2002). Nicotine accelerates angiogenesis and wound healing in genetically diabetic mice. *Am J Pathology*;161:97-104
- Munzir M.E.A, Al-Obosi S.A.J, Osman H.M, Shayoub M.E (2015). The effect of smoking cigarettes on kidney functions among Sudanese peoples. *International Journal of Development Research*; 5:4473-4475.
- Nwaji AR, Ante IA, Nwoke FAK (2021). Aqueous extract of *Nicotiana tabacum* impaired serum testosterone and testicular weight in male Wistar rats. *Niger J Exp Clin Biosci* ;9:182-5.
- Ritz E, Benck U, Franek E, Keller C, Seyfarth M, Clorius J. (1998). Effects of smoking on renal hemodynamics in healthy volunteers and in patients with glomerular disease. *J Am Soc Nephrol.* 9(10).1798-804
- Russel M.A.H, Tarvis M, Feyerabent C (1980). A view age for Snuff. *Lancet*; 1:474-475.
- Stuart F (2011). *Human Physiology*, 12th ed., McGraw-Hill.
- Thomson M (2008). Health effects of smokeless Tobacco products. SCENIHR (Scientific Committee on Emerging and Newly -Identified Health Risks) paper Brussel.
- Ureme S.O, Ibeagha I.D, Maduka I.G, Ibeagbulam O.G (2007). The concentrations of methaemoglobin, carboxyhaemoglobin and some haematological parameters in tobacco snuff addicts in Igbo of Nigeria. *Niger. J. Physiol. Sci.*; 22:27-30. York: Chapman and Hall. 266-84.
- Valerie C, Scanlon T.S (2007). *Essentials of Anatomy and Physiology*, 5th ed., F.A. Davis Company, Philadelphia.
- Walter F.B (2004). *Medical Physiology: A Cellular and Molecular Approach*, 1st ed., Elsevier, Saunders.
- Yuka N, Masao I, Minori N, Yuichi Y, Ryumon H, Hitoshi Y, Masaru M, Masaji T. (2012). Cigarette smoking, proteinuria, and renal function in middle-aged Japanese men from an occupational population. *Environ Health PrevMed.* 17. 147-156.