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Effect of Aqueous Corn Silk (Stigma maydis) Extracts on Serum Electrolytes in Male Albino Wistar Rats

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Abstract
Excretion of water and active solutes such as Na^+ and K^+ have an effect in regulating blood pressure, as diuretic effects can result in loss of water and solutes in the blood. Thus, the decrease in blood volume will reduce the blood pressure. The diuretic effects of Corn silk (CS) have been reported by many literatures. This study investigated the mechanism through which CS exerts its diuretic effects, by investigating its effects on serum electrolyte levels. Twenty (20) normal male albino rats were divided into four groups as; control (normal saline), Spironolatone (0.002mg/kg/day) treated, CS (aqueous extract) 200mg/kg/day and CS (aqueous extract) 600mg/kg/day, treated rats. Blood samples were drawn at baseline, after 10 days and 21days for the estimation of Serum Na^+, K^+, Cl^-, $HCO3^-$, Urea, Billirubin and Creatinine. Twenty one days administration of CS extracts resulted in a significant ($p<0.05$) increase in serum K^+, $HCO3^-$ and Creatinine levels compared with the control. However administration of CS extract significantly ($p<0.05$) lowered the serum Na^+ concentrations compared with the control. There were no significant ($p>0.05$) differences in serum urea, billirubin and serum Cl^-, level between all groups at the end of 21 days. This study revealed that Corn silk extract may be a useful tool of considerable therapeutic importance in lowering blood pressure due to its sodium lowering and its potassium sparing properties.
Keywords: Corn silk, Diuretics, Spironolactone, Electrolytes, Albino Wistar rats

1. Introduction

Hypertension (HTN) or high blood pressure is a chronic medical condition in which the blood pressure in the arteries is elevated. As of 2000, nearly one billion people or ~26% of the adult population of the world had hypertension (Kearney, *et al*, 2005). It was common in both developed (333 million) and undeveloped (639 million) countries (Kearney, *et al*, 2005). Antihypertensive drugs fall into four major categories which include; the diuretics, sympathoplegic agents, direct vasodilators and agents that block the production or action of angiotensin. Diuretics are drugs which lower blood pressure by depleting the body of sodium and reducing blood volume by inducing urine flow and through other mechanisms (Agrawal and Pandhavi, 2007). The increased renal excretion of water is accompanied by depletion of sodium in the body and thus a reduction in blood volume. This decreases cardiac workload, oxygen demand and plasma volume, thus decreasing blood pressure. Hence, diuretics play an important role in hypertensive patients (Jain et al., 2007), and in the treatment of congestive heart failure, glaucoma, diabetes insipidus and liver aliments. There are different categories of diuretics these include; Loop diuretics (which inhibits Na^+-K^+-Cl^- symport), Thiazides (which inhibits Na^+-Cl^- symport), Carbonic anhydrase inhibitors (inhibits hydrogen secretion and HCO_3^-), Osmotic diuretics (they inhibit water and solutes reabsorption), Potassium-sparing diuretic (these group inhibits Na^+channel and aldosterone receptor). Potassium-sparing diuretics are diuretic drugs that do not promote the secretion or excretion of potassium in the urine. They are used as adjunctive therapy, together with other drugs, in the treatment of hypertension and management of congestive heart failure (Kokko, 1984; Stuart, 2002; John, 2011).

Corn silk (CS) is made from stigmas, the yellowish thread like strands from the female flower of maize. It is a waste material from corn cultivation and available in abundance (Maksimovic et al., 2005). Corn silk is an excellent source of many bioactive compounds such as volatile oils, steroids, alkaloids, sitosterol and stigmasterol and natural antioxidants such as flavonoids, alkaloids, saponins, tannins and other phenolic compounds with beneficial effects on human health (Liu *et al*., 2011, Valazquez *et al*., 2005). The phenolic compounds present in Corn silk are anthocyanins, p-coumaric acid, vanillic acid, protocatechuic acid, derivatives of hesperidin and quercetin, and bound hydroxycinnamic acid forms composed of p-coumaric and ferulic acid (Kaur et al., 2006). Corn silk has been used in many parts of the world for herb treatment of hypertension, tumor, hyperglycemia, hepatitis, cystitis, gout, kidney stones, diabetes nephritis and prostatitis (Hu and Deng, 2011; Grasses et al., 1993; Newal et al., 1996). Diuretic, as well as antilithiasic, uricosuric, and antiseptic, properties are traditionally attributed to corn silk (Grases etal., 1993; Newal et al., 1996). Several studies have reported the diuretic activities of corn silk through the estimation of urine electrolyte levels (Velazquez et al., 2005; Caceres et al ., 1987, Dat et al 1992), this study investigated the effects of aqueous corn silk extract on serum electrolytes in normal albino rats.

2. Materials and Methods

2.1 Chemicals and Drugs

Carbon dioxide, Potassium, Sodium, Chloride assay kits, were obtained from Teco diagnostics Anaheim CA U.S.A.

Urea test kit, was obtained from Biosystems S.A. Spain. Creatinine and Bilirubin assay kit were obtained from Randox laboratory U.K. Spironolactone was obtained from (Jiangxi' erkangtal Pharmaceutical Co. Ltd. China).

2.2 Methods

2.2.1 Plant preparation

The fresh corn silks were purchased from Oja oba market in Owo, Ondo State Nigeria. They were dried under the shade for one week and cut into smaller pieces. 350 grams of the corn silk was soaked with 3500mls of distilled water for 72hours (3days). The extract was filtered using a muslin cloth and evaporated to dryness in water bath at 70°C. The extract was then kept in glass bottles and refrigerated until use.

2.2.2 Drug preparation

Rats in group 2 received spironolactone by a single intramuscular (i.m.) injection per day, prepared in 10 mls volume of normal saline and corn oil (ratio 1:1). Animals received 0.002mg/kg body weight.

2.2.3 Experimental Animals

Twenty-five male albino wistar rats weighing between 160-190g were obtained from the Animal house, Achievers University Owo. The animals were housed and maintained under normal laboratory conditions (maintained at 24 ± 1^0C on a 12:12 h light-dark cycle) and were fed a standard animal feed (vital animal feeds) and free access to water in stainless plates, *ad libitum*. The animals were used according to guidelines of committee on care and use of Experimental Animals Resources of the University. All animals were acclimatised for 14 days before the commencement of the experiment. The animals were divided into four groups of five animals each.

Group 1 –Control given only normal saline orally.
Group 2 – Rats given Spironolactone (0.002mg/kg/day) intramuscularly.
Group 3 – Rats given aqueous CS extract (200mg/kg/day) orally.
Group 4 – Rats given aqueous CS extract (600mg/kg/day) orally.

2.2.4 Experimental protocol

Blood sample was drawn by the tail vein after 2 weeks of acclimatization for the determination of baseline parameters. Second blood sample were collected through the same method after 10 days of treatment. The rats were killed using chloroform, after 21 days of treatment and the last blood sample were collected through heart puncture into plain bottle, for serum. The samples were centrifuged at 3000 x g for 10min to obtain the serum. The samples were stored at -20 ^{o}C for further use.

2.2.5 Statistical analysis

Values are expressed as the mean ± SD. Results were statistically analyzed by one-way analysis of variance (ANOVA) for differences between means of different groups. All data were analyzed using SPSS statistical package (SPSS Inc.) version 13.0.

3. Results

The effect of aqueous corn silk extracts on serum electrolytes levels of normal rats are presented in Tables 1,2, 3and 4. Table 1 shows the effects of aqueous corn silk extract on serum Potassium (mEq/L) in experimental rats. At day 10 there was a significant ($p<0.05$) increase in the serum potassium level of the spironolatone treated and the 600mg/kg/day OC extract treated groups compared with the control. After 21days treatment, the serum potassium level of rats treated with 600mg/kg/day CS was significantly high ($p<0.05$) compared with control and other treated groups. The result in table 2 shows that after 10 and 21 days of treatment there were no significant difference in the serum sodium (mEq/L) level in the experimental rats ($p > 0.05$) except for those who received 600mg/kg/day of the OC extract. Treatment of rats with 600mg/kg/day of the OC extract resulted in a reduction in the serum sodium concentration compared with control and other treated groups although not significantly different ($p>0.05$) from the control. In Table 3, the administration of aqueous Corn silk extract for 21 days resulted in a significant ($p<0.05$) increase in the CO_2 (mmol/L) level of rats given 600mg/kg/day OC extract compared with the control and the spironolactone treated group. However as shown in Table 4, there was no significant difference in the serum concentration of chloride (mEq/L) of experimental rats throughout the period of experiment.

As presented in Table 5, administration of aqueous corn silk extracts of 200 and 600mg/kg/day for 21 days resulted in a significant ($p< 0.05$) increase in the serum Creatinine (mg/dl), compared with the control and the spironolactone treated group. The effect of aqueous corn silk extract on serum billirubin was presented in table 6, there was an increase in the in serum billirubin (mg/dl) in rats who received 600mg of OC extracts after 21 days of treatment compared with the spironolactone treated group, however the difference was not significant ($p>0.05$) compared with the control group. Table 7 Shows there was no significant ($p>0.05$) difference in the serum urea (mmol/l) concentrations of experimental rats throughout the period of experiment.

Table 1: Effects of corn silk on serum potassium (mEq/L) in Albino wistar rats

Groups/treatment	Baseline	10 Days	21 Days
1(Normal saline)	1.40 ± 0.64	1.24 ± 0.26	1.90 ± 0.30
2(Spironolactone 0.002mg/kg/day)	4.04 ± 0.12[a]	3.59 ± 1.04[a]	3.92 ± 1.35
3(200mg/kg aqueous CO extract)	3.27 ± 0.48[a]	3.12 ± 0.63	3.08 ± 0.46
4(600mg/kg aqueous CO extract)	2.75 ± 0.31	4.41 ± 0.94[a]	4.41 ± 0.69 [a]

The results are shown as means ± SE. (n=5). The different letters in the same column indicates a statistical difference ($p<0.05$). Subscripts [a, b, c] and [d] indicates a statistical difference ($p<0.05$) from groups 1, 2, 3 and 4 respectively.

Table 2: Effects of Corn silk on serum sodium (mEq/L) in Albino wistar rats

Groups/treatment	0 Day	10 Days	21 Days
1(Normal saline)	54.80 ± 7.86	63.97 ± 6.65	115.48 ± 10.78
2(Spironolactone 0.002 mg/kg/day)	60.28 ± 21.37	79.13 ± 8.28	123.09 ± 7.45
3(200mg/kg aqueous CO extract)	58.90 ± 3.39	80.60 ± 4.06	113.98 ± 5.76
4(600mg/kg aqueous CO extract)	75.06 ± 5.23	90.76 ± 1.38[a]	89.55 ± 9.71[b]

The results are shown as means ± SE. (n=5). The different letters in the same column indicate a statistical difference ($p<0.05$). Subscripts [a, b, c] and [d] indicates a statistical difference ($p<0.05$) from groups 1, 2, 3 and 4 respectively.

Table 3: Effects of corn silk on serum carbon dioxide (mmol/L) in Albino wistar rats

Groups/treatment	Baseline	Day 10	Day 21
1 (Normal saline)	32.00 ± 20.12	21.73 ± 6.35	26.73 ± 8.03
2 (Spironolactone 0.002mg/kg/day)	13.03 ± 2.91	10.04 ± 3.40	43.89 ± 12.14
3 (200mg/kg aqueous CO extract)	10.63 ± 0.49	18.83 ± 2.69	59.52 ± 10.52
4 (600mg/kg aqueous CO extract)	10.43± 5.95	12.40 ± 4.78	88.05± 26.77 [ab]

The results are shown as means ± SE. (n=5). The different letters in the same column indicate a statistical difference ($p<0.05$). Subscripts [a, b, c] and [d] indicates a statistical difference ($p<0.05$) from groups 1, 2, 3 and 4 respectively.

Table 4: Effects of corn silk on serum chloride (mEq/L) in Albino wistar rats

Groups/treatment	Day 0	Day 10	Day 21
1(Normal saline)	101.98 ± 19.10	108.15 ± 17.41	89.67 ± 3.38
2(Spironolactone 0.002mg/kg/day)	98.83 ± 15.06	119.00 ± 10.65	86.95 ± 1.61
3(200mg/kg aqueous CO extract)	109.98 ± 9.51	118.60 ± 27.39	88.96 ± 2.30
4(600mg/kg aqueous CO extract)	116.25 ± 12.00	98.20 ± 5.36	96.47 ± 2.59

The results are shown as means ± SE. (n=5). The different letters in the same column indicate a statistical difference ($p<0.05$). Subscripts [a, b, c] and [d] indicates a statistical difference ($p<0.05$) from groups 1, 2, 3 and 4 respectively.

Table 5: Effects of corn silk on serum creatinine (mg/dl) in Albino wistar rats

Groups/treatment	Day 0	Day 10	Day 21
1(Normal saline)	2.03 ± 0.31	2.39 ± 0.44	2.14 ± 0.52
2(Spironolactone 0.002mg/kg/day)	2.11 ± 0.12	2.08 ± 0.09	3.36 ± 0.57
3(200mg/kg aqueous CO extract)	2.17 ± 0.47	2.70 ± 0.26	4.00 ± 0.83$_a$
4(600mg/kg aqueous CO extract)	2.90 ± 0.27	2.77 ± 0.09	3.96 ± 0.31[a]

The results are shown as means ± SE. (n=5). The different letters in the same column indicate a statistical difference ($p<0.05$). Subscripts [a, b, c] and [d] indicates a statistical difference ($p<0.05$) from groups 1, 2, 3 and 4 respectively.

Table 6: Effects of corn silk on serum Bilirubin (mg/dl) in Albino wistar rats

Groups/treatment	Day 0	Day 10	Day 21
1(Normal saline)	2.87 ± 0.08	3.08 ± 0.97	4.56 ± 0.09
2(Spironolactone 0.002mg/kg/day)	3.33 ± 0.67	3.50 ± 0.75	3.76 ± 0.20[d]
3(200mg/kg aqueous CO extract)	3.60 ± 0.64	2.69 ± 0.42	4.54 ± 0.04
4(600mg/kg aqueous CO extract)	3.10 ± 0.35	2.04 ± 0.16	6.85 ± 0.10

The results are shown as means ± SE. (n=5). The different letters in the same column indicate a statistical difference ($p<0.05$). Subscripts [a, b, c] and [d] indicates a statistical difference ($p<0.05$) from groups 1, 2, 3 and 4 respectively.

Table 7: Effects of corn silk on serum urea (mmol/L) in Albino wistar rats

Groups/treatment	Day 0	Day10	Day 21
1(Normal saline)	22.77 ± 1.65	26.97 ± 3.32	42.20 ± 2.94
2(Spironolactone 0.002mg/kg/day)	23.06 ± 0.94	31.30 ± 4.39	40.31 ± 4.30
3(200mg/kg aqueous CO extract)	22.34 ± 1.60	24.42 ± 3.57	44.12 ± 10.29
4(600mg/kg aqueous CO extract)	25.03 ± 3.69	25.47 ± 1.94	43.93 ± 5.87

The results are shown as means ± SE. (n=5).

4. Discussion

Excretion of water and active solutes such as Na+ and K+ has an effect in regulating blood pressure (Khairunnisa et al., 2012). Diuretics work by increasing the loss of water and solutes in blood (mainly sodium). Major purposes of diuretic therapy are to decrease fluid volume of the body, and to adjust the water and electrolyte balance. Thus, the decrease in blood volume will reduce the blood pressure; hence they are tools of considerable therapeutic importance because they effectively reduce blood pressure. Although the antihypertensive actions of some diuretics (thiazides and loop diuretic in particular) are independent of their diuretic effects, however in the treatment of hypertension, the most common adverse effect of diuretics (except for potassium-sparing diuretics) is potassium depletion. Potassium-sparing diuretics are useful both to avoid excessive potassium depletion, particularly in patients taking digitalis, and to enhance the natriuretic effects of other diuretics. The concentrations of potassium in the serum of experimental rats were presented in table 1. The higher serum level of potassium observed in the 600mg/kg body wt. CS treated rats after 21 days of treatment may be due to potassium-sparing activities, which is one of the mechanisms through which some diuretic drugs exerts their effects.

Most diuretics exert their effects by inhibiting tubular sodium and water reabsorption by epithelial cells lining the renal tubule system (Xiaoping, 2013). Some diuretic drugs inhibit Na+ reabsorption in the collecting tubule thus also inhibits K+ secretion, these drugs are called K+-sparing diuretics.. The concentrations of sodium in the serum of experimental animals were presented in table 2. The reduction in serum sodium concentration was in a dose dependent manner in the CS treated rats although not significantly different from the control. Diuretic activity also has been investigated by Dat et al., (1992) who reported there were no significant difference in urine, sodium and potassium excretion when CS (600 ml water extract) were tested on 38 volunteers for one week. However the reduction in the serum sodium concentration of rats, who received 600mg/kg body wt. CS, may be an indication of increased urinary excretion of sodium which may result due an exchange between K^+ and Na^+.

Carbon Dioxide (CO_2) in serum or plasma exists primarily as dissolved CO_2 and bicarbonate anion (HCO_3^-) (Kaplan, 1984). The plasma CO_2 content is decreased in metabolic acidosis and respiratory alkalosis, whereas the level is increased in metabolic alkalosis and respiratory acidosis (Trumper, 1975). In pathologic conditions such as diabetes mellitus, glomerulonephritis, pyloric obstruction, diarrhoea e.t.c. Acidosis or Alkalosis could be anticipated (Tietz, 1986) therefore, determination of plasma CO_2 content as part of electrolyte profile can help establish to degree, the anticipated change in the patient. As shown in table 3, a significant increase in the serum CO_2 of rats who received 600mg/kg body wt was observed compared to its water control ($p < 0.05$), the increase in the serum CO_2 of CS treated rats was in a dose dependent manner. The result showed that administration of high dose of CS extract may have protective effects against metabolic acidosis. This is unexpected because drugs that inhibit Na+ reabsorption in the collecting tubule and thus also inhibit K+ secretion results in metabolic acidosis.

Both extracellular fluid (ECF) and intracellular fluid (ICF) contain electrolytes, a general term applied to bicarbonate and inorganic anions and cation. The electrolytes are unevenly distributed between compartments; $Na^+$and Cl^- are the major electrolytes in the ECF (plasma and interstitial fluid), and K^+ and phosphates such as HPO4-2 are the major electrolytes in cells. This distribution is maintained principally by energy-requiring transporters that pump Na^+ out of cells in exchange for K^+. Chloride, a major anion, is important in the maintenance of the cation/anion balance between intra- and extra-cellular fluids. This electrolyte is therefore essential to the control of proper hydration, osmotic pressure, and acid/base equilibrium. Low serum chloride values are found with extensive burns, excessive vomiting, intestinal obstruction, nephritis, metabolic acidosis, and in addisonian crises. Elevated serum chloride values may be seen in dehydration, hyperventilation, congestive heart valve and prostatic or other types of urinary obstruction (Tietz, 1976; White 1970). Table 4 shows the serum concentration of chloride (mEq/L). There was no significant difference in the serum chloride level after 21 days between the study groups.

Bilirubin is formed by breakdown of haemoglobin in the spleen, liver and bone marrow. In the liver, bilirubin is conjugated with glucuronic acid to form a soluble compound. This conjugated bilirubin passes down the bile duct and is excreted into the gastrointestinal tract. An unconjugated albumin bound form is also present in the circulation. It is insoluble and those not normally pass through the kidneys into the urine. Elevated plasma level of billirubin is an indication of jaundice which can result from liver disease (Sherlock, 1951). Table 4.6 Shows the Serum concentration of Bilirubin (mg/dl) of experimental rats. After 21days of CS treatment there was

no significant (p> 0.05) difference in serum billirubin level of CS treated compared with the control group. This is an indication that CS may not have hepathotoxic effect on rats even at high dose (600mg/kg/day).

Creatinine is derived from creatine and creatine and phosphate in muscle tissue and may be define as nitrogenous waste product. Creatinine is not reutilised but is excreted at a constant rate which is proportional to the body muscle mass. As a consequence of the way in which Creatinine is excreted by the kidney, Creatinine measurement is used almost exclusively in the assessment of kidney function .Creatinine is regarded as the most useful endogenous marker in the diagnosis and treatment of kidney disease (Bartels and Bohmer, 1972). Hence increased plasma concentration of creatinine is an indication of kidney disease. Table 4.7 Shows the Serum concentration of creatinine (mg/dl) of experimental rats. There was a significant increase in serum creatine level observed in the CS treated rats compared with the control; this may be an indication of nephrotoxicity. But comparison with a standard drug spironalactone showed no significant difference. A study by Sepehri et al., (2011) reported that the consumption of CS methanol extract (80%) at concentrations of 200 and 300 mg/kg showed a significant decrease of serum creatinine levels in Gentamicin-induced nephrotoxicity. This indicates a reduction in GM-induced nephrotoxicity. While CS administration with GM treatment significantly prevented GM-induced interstitial nephritis in a dose-dependent manner at up to 500 mg/kg, showing a protective effect against GM-induced interstitial nephritis compared to the GM group. However, at higher doses of CS (400 and 500 mg/kg) it caused nephrotoxicity such as hyaline cast formation, apoptosis, congestion and cell swelling.

Urea is synthesized in the liver as a by-product of the deamination of amino acids. Its elimination in the urine represents the major route for nitrogen excretion. Elevated urea concentration in plasma is found as a result of high-protein diet, increase protein catabolism, after a gastrointestinal haemorrhage, mild dehydration, shock and heart failure or treatment with glucocorticoids (pre-renal uraemia) (Young, 2000). Table 4.8 Shows the Serum concentration of Urea (mmol/l) of experimental rats. However, there were no significant differences in the serum urea levels in all the study groups throughout the period of experiment. This may be due to the maintenance of constant weight gain throughout the period of experiment by the animals i.e there was no significant weight loss which is associated with increased protein catabolism.

In conclusion this study revealed that while corn silk extract may possess potent antihypertensive and diuretic effects, however long term intake of high dose of the extract may have nephrotoxic effects.

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