

ASSESSMENT OF THE ADMINISTRATION OF WATERMELON (*CITRULLUS LANATUS*) JUICE ON PLASMA POTASSIUM, SODIUM, CHLORIDE AND ZINC IN RABBITS OVERDOSED WITH ACETAMINOPHEN EXTRA

Mathew Folaranmi Olaniyan*, Lagundoye Sherifat Bolade and Olagundoye Serifat

Department of Medical Science, Achievers University, Owo-Nigeria.

Corresponding Author: Dr. Mathew Folaranmi Olaniyan

Department of Medical Science, Achievers University, Owo-Nigeria.

Article Received on 16/12/2016

Article Revised on 06/01/2017

Article Accepted on 26/01/2017

ABSTRACT

Background: Watermelon juice has many non- scientific health beneficial claims due to its bioactive chemical constituents. Acetaminophen Extra contains paracetamol (500mg) and caffeine(65mg) used to relieve pain. **Aim and Objective:** This work was designed to evaluate the effect of watermelon juice in rabbits overdosed with acetaminophen extra using plasma zinc, potassium, chloride and sodium. **Materials and Method:** Thirty rabbits classified into six experimental groups labeled A-F (with C1, C2, E1 and E2) with A as control were investigated. An overdose of acetaminophen extra of 1,500mg/Kg was administered for 5 days into some of the rabbits to induce toxicity. 15ml/kg of watermelon juice was used to prevent and treat acetaminophen extra toxicity. Plasma potassium, zinc, chloride and sodium were analysed biochemically by spectrophotometry. **Result:** The result obtained showed that a significant reduction in plasma potassium and a significant increase in plasma sodium and chloride following the administration of 1500mg/Kg of acetaminophen extra for 5 days which was significantly normal after the administration of 15mg/Kg of watermelon juice ($P<0.05$). The result also showed a significant decrease in plasma zinc following the administration of acetaminophen extra overdose and watermelon juice. **Conclusion:** Abnormal plasma alterations in the concentration of Potassium, Sodium, Chloride and Zinc In rabbits overdosed with acetaminophen extra for 5 days was significantly reduced following the administration of 15ml/Kg BW.

KEYWORD: Watermelon juice has many non- scientific paracetamol (500mg) and caffeine(65mg) used to relieve pain.

INTRODUCTION

Acetaminophen commonly referred to as paracetamol is used as an over the counter analgesic to relief of pains and headache. Acetaminophen Extra contains paracetamol (500mg) and caffeine(65mg).^[1] Acute overdose can cause potentially liver damage. Oral administration of the drug is rapidly adsorbed from the gastro-intestinal tract, but when taken in excess can lead to toxicity; causing renal and liver necrosis.^[2] Caffeine in acetaminophen constituent is a mild stimulant.^[3] Coffee oil raises serum levels of the liver enzyme alanine aminotransferase (ALT) and to lesser extent, aspartate aminotransferase (AST). Elevation of these liver enzymes may indicate injury of hepatocytes.

However, co-administration of acetaminophen extra drug is increasingly gaining popularity. Caffeine acts as an analgesic adjuvant which enhances efficacy of acetaminophen. Despite the benefit of rapid analgesic effect and the probable decrease in toxicity,

coadministration with these agents is still a cause of concern.^[4]

Watermelon juice contains vitamins, minerals and other nutrients. This include Vitamins and minerals such as potassium, B vitamins, vitamin A as beta carotene. Watermelon also contains antioxidants, including lycopene, which may help reduce the risk of some cancers

JUSTIFICATION

Acetaminophen extra is referred to as an analgesic (pain reliever) and antipyretic (fever reducer), available and accessible to the populace hence the temptation of abuse. It contains two active ingredients, paracetamol and caffeine. The 'extra' in acetaminophen refers to the addition of caffeine.

Watermelon is gaining popularity in Nigerian beverage. It is cheap and affordable by Nigerians but its health benefits specifically on plasma zinc, potassium, sodium

and chloride has not been documented. There is little or no information on the effects of watermelon in rabbits overdosed with acetaminophen extra on these parameters hence the need for this research work

AIM OF STUDY

This research study will be conducted to assess the administration of watermelon on plasma potassium, calcium, chloride and zinc in rabbits overdosed with Acetaminophen extra.

MATERIALS AND METHODS

Study area

The study was conducted at the animal farm of Achievers University Owo, Ondo state. Ondo state lies on the Northern senatorial district of Ondo States, Nigeria within latitude 70100N and longitude 70100E.

Study population

Healthy rabbits of the same strains, were purchased in Owo through the Department of Biological Sciences, Achievers University, Owo-Nigeria.

Sample size

Thirty apparently healthy rabbits were classified into six(6) groups of five(5) rabbits each. The rabbits were maintained at room temperature under alternating natural light/dark photoperiod and had access to standard laboratory food and fresh water for a period of 2weeks for adaptation to their new environment before administration of watermelon and overdose acetaminophen extra. Care was taken to minimize discomfort, distress and pains to the animals. Body weight of the rabbits before and after the experiment was measured using Mettler sensitive balance (number 202845).

Biological sample

After two weeks of acclimatization, basal blood sample was collected from the veins on the ear of each of the rabbits in the six (6) groups.

Group A(control group): Five millilitres of blood sample was collected from the five rabbits into a Lithium heparinized before and after 7 days feeding with normal meal and water.

Group B: Five millilitres of blood sample was collected into Lithium heparinized bottle from each of the five rabbits before and after 7 days of normal meal and 15ml/Kg of watermelon juice.

Group C: Five millilitres of blood sample was collected into Lithium heparinized bottle from each of the five rabbits after 5 days of post 1500mg/kg of panadol extra administration and thereafter five millilitres of blood sample was collected into Lithium heparinized bottle from each of the five rabbits after 7 days of administration of 15ml/kg of watermelon juice daily.

Group D: Five millilitres of blood sample were collected into Lithium heparinized bottle from each of the five rabbits before and after 7 days of post-administration of 1500mg/kg of panadol extra per oral for 5 days and fed with normal meal and water.

Group E: Five millilitres of blood sample was collected into Lithium heparinized bottle from each of the five rabbits before and after 7 days feeding with normal meal and 15ml/Kg of watermelon juice and administration of 1500mg/kg of panadol extra for 5 days.

Group F: Five millilitres of blood sample was collected into Lithium heparinized bottle from each of the 5 rabbits before and after 7 days of the administration of 1500mg/kg of panadol extra per oral for 5 days and with simultaneous administration of 15ml/kg of watermelon juice

Materials

The following standard materials were used in the cause of this scientific research study and Standard Operating Procedures (SOP) were absolutely observed.

Apparatus

Electric blender, sterile universal bottle, clean white cotton cloth, hand gloves, weighing balance, cotton wool, plastic tray, bucket, bowl, measuring cylinder, plastic sieve, lithium heparin bottles, cutting knife, spatula.

METHODS

The following methods were applied in the cause of this study and Standard Operating Procedures (SOP) were absolutely observed.

Treatment of normal control and experimental rabbits

Group A: (control group): Five rabbits were fed with normal meal and water for 7days.

Group B: Five rabbits were fed with normal meal and 15ml/Kg of watermelon juice daily for 7 days.

Group C: Five rabbits were given 1500mg/kg of panadol extra per oral for 5 days and thereafter were fed with normal meal and 15ml/kg of watermelon juice daily for 7 days

Group D: Five rabbits were given 1500mg/kg of panadol extra per oral for 5 days and thereafter were fed with normal meal and water for 7 days

Group E: Five rabbits were fed with normal meal and 15ml/Kg of watermelon juice daily for 7 days after which each rabbit were given 1500mg/kg of panadol extra per oral for 5 days and fed with normal meal and water. The rabbits were observed for another 7 days post panadol extra administration.

Group F: Five rabbits were given 1500mg/kg of panadol extra per oral for 5 days and were simultaneously fed with normal meal and 15ml/Kg of watermelon juice daily for 7 days.

Preparation of watermelon juice

Watermelon fruits (green skin, red flesh) were procured from a fruit vendor in a local market in Owo, Ondo state, Nigeria and was presented to the Department of biological sciences, Achievers University, Owo for confirmation and certification. The back was washed clean and peeled with a knife.

The seeds were aseptically removed and the mesocarp of the ripe fruit was chopped into thin slices and kept in a sterile bowl. The remaining succulent red part of the watermelon was crushed to juice with an electric blender. The watermelon juice obtained was filtered undiluted through a fine mesh muslin cloth to get the fresh watermelon fruit juice. 15ml of the filtrate was then administered to the rabbits as watermelon juice

Preparation of Acetaminophen extra powder

Acetaminophen extra tablets were purchased and ground into powder using Laboratory pestle and mortar. 1500mg of the ground acetaminophen extra tablets was weighed and poured into a sterile universal bottle, about 2ml of distilled water was added to it and administered to the rabbits

Blood Sample preparation

Whole blood samples were collected from each of the rabbits and preserved in Lithium heparinized tubes for plasma zinc, potassium, chloride and sodium estimations. The blood samples were spun using bench/macro centrifuge for the extraction of the plasma.

Processing of specimen

The samples were analysed appropriately in the laboratory according to Standard Operating Procedures.

Estimation of plasma zinc

METHOD: PRECIPITATION.

PRINCIPLE

Nitro-PAPS reacts with zinc in alkaline solution to form a purple colored complex, the absorbance of which is measured at 560nm using a spectrophotometer, interference from copper and iron are virtually eliminated by PH and chelating additives.

Reference range: 70-150ug/dl (10.7-22.9umol/L).

METHOD: ION SELECTIVE ELECTRODE

Principle of the method

An ion selective electrode is a sensor which converts the activity of a specific ion (dissolved in a solution) into a voltage (potential), which can be measured by a mV or ion

meter. The voltage is theoretically dependent on the logarithm of the ion activity as described by the Nernst Equation.

$$E = E_0 + (2.303 \cdot RT/nF) \log(A)$$

The sensing part of the electrode is usually made from an ion specific membrane, coupled together with a reference electrode (either separate or as a combination)

Normal range for plasma potassium: 4.3-5.8mmol/L

Normal range for plasma sodium: 140-160mmol/L

Normal range for plasma chloride: 90-110mmol/L

STATISTICAL ANALYSIS

A statistical package for social sciences [SPSS] 19.0 was used for the analysis of the data appropriately. Continuous variables were displayed as means and standard deviation [SD] and categorical variables were displayed as percentage. The level of significance was taken at 95% confidence interval and $P \leq 0.05$ was considered significant.

RESULTS

The results showed a statistical significant decrease in the plasma zinc level in all the rabbits administered with acetaminophen extra and watermelon than the control that were not administered with it when the groups were compared throughout the period of study with $P < 0.05$. There was no significant difference in the plasma potassium level with the comparison of group A versus group B,

group A versus C1, group A versus C2, group A versus group E1, group A versus group E2, group A versus group F, group C1 versus group C2, group E1 versus (P < 0.05) but a statistical significant decrease was found in group A versus group D. There was no significant difference in the plasma levels of sodium when group A versus group B, group A versus group C2, group A versus group E1, group A versus group F were compared but there was statistical significance difference in group A versus group C1, group A versus group D, group A versus group E2, group C1 versus C2, group E1 versus E2.

There was no statistical significant decrease in the plasma levels of chloride in one experimental group; Group C2 [Treatment with watermelon juice after acetaminophen extra overdose] and a statistical significant increase was found in one experimental group; Group E2 [Treatment with acetaminophen extra after watermelon juice administration] when compared with the normal control.

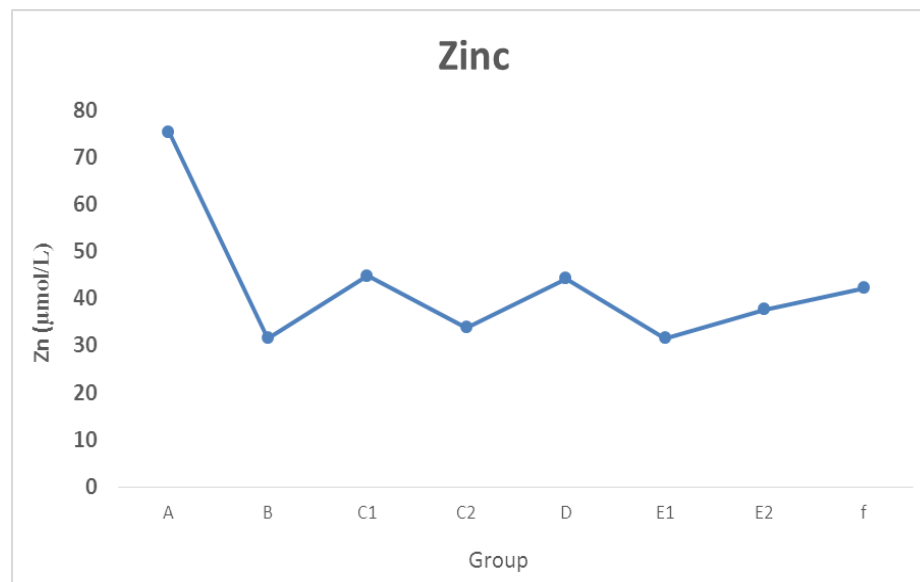
TABLE 1: mean ± standard deviation of plasma potassium, zinc, sodium and chloride Living

	GROUP A	GROUP B	GROUP C1	GROUP C2	GROUP D	GROUP E1	GROUP E2	GROUP F
Plasma potassium	5.30 ± 0.55	4.95 ± 0.61	5.16 ± 0.29	4.52 ± 0.23	5.16 ± 0.29	4.96 ± 0.61	5.34 ± 0.26	5.26 ± 0.75
Plasma zinc	75.46 ± 6.22	31.54 ± 5.29	44.88 ± 6.29	33.82 ± 3.59	44.30 ± 6.14	31.58 ± 5.34	37.72 ± 2.66	42.28 ± 4.74

Plasma sodium	134.48 ± 3.96	135.52 ± 3.78	142.24 ± 4.37	132.14 ± 1.80	142.44 ± 4.27	133.04 ± 2.37	142.30 ± 6.01	133.92 ± 3.43
Plasma chloride	105.50 ± 11.84	113.42 ± 4.96	110.22 ± 6.99	98.44 ± 5.05	110.58 ± 7.31	96.14 ± 1.75	115.96 ± 3.92	105.42 ± 6.16

TABLE 2: Comparative analysis of the effects of acetaminophen extra and watermelon on value of plasma zinc, potassium sodium and chloride ions.

		A Vs B	A Vs C1	A Vs C2	A Vs D	A Vs E1	A Vs E2	A Vs F	C1 Vs C2	E1 Vs E2
Plasma potassium	"t"	0.24	0.33	0.22	3.45	0.39	0.11	0.55	0.35	0.13
	P	0.34	0.57	0.39	0.03*	0.46	0.89	0.12	0.56	0.85
Plasma Zinc	T	9.05	9.85	9.56	8.88	9.88	9.56	9.24	6.66	5.56
	P	0.001*	0.001*	0.001*	0.001*	0.001*	0.001*	0.001*	0.01*	0.01*
Plasma Sodium	T	0.38	3.99	0.19	6.45	0.25	6.00	0.44	6.99	6.98
	P	0.43	0.02*	0.78	0.01*	0.39	0.01*	0.27	0.01*	0.01*
Plasma Chloride	T	0.46	0.45	0.43	0.45	0.33	0.55	0.11	5.99	8.85
	P	0.22	0.28	0.27	0.28	0.48	0.21	0.83	0.01*	0.001*

**Figure 1: Shows the comparative analysis of the effect of acetaminophen extra overdose and watermelon juice on plasma zinc (µmol/L).**

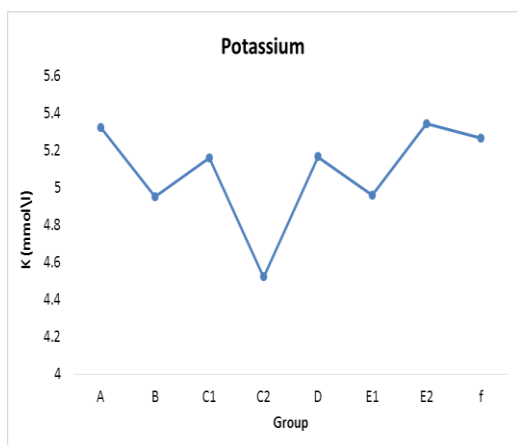


Figure 2: Shows the comparative analysis of the effect of acetaminophen extra and watermelon on plasma potassium (mmol/L).

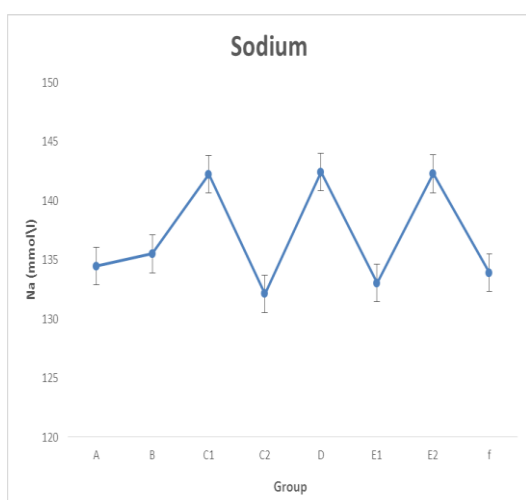


Figure 3: Shows the comparative analysis of the effect of acetaminophen extra and watermelon on plasma sodium (mmol/L).

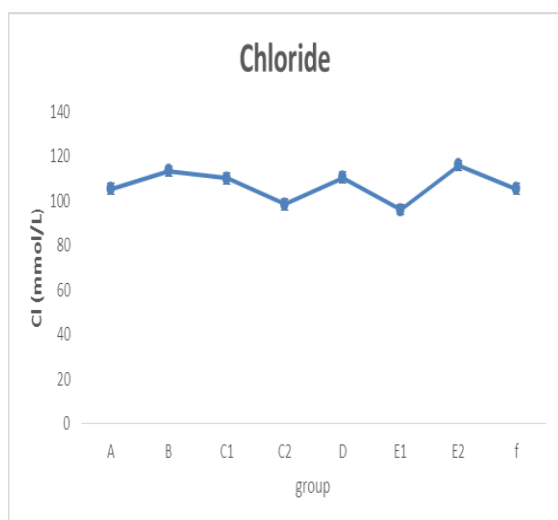


Figure 4: Shows the comparative analysis of the effect of acetaminophen extra and watermelon on plasma chloride (mmol/L).

DISCUSSION, CONCLUSION AND RECOMMENDATION

Discussion

This present study aimed at investigating whether the administration of watermelon juice in rabbits overdosed with acetaminophen extra is effective by evaluating the plasma concentrations of zinc, potassium, sodium and chloride. The result obtained from this study showed a significant higher mean value of plasma sodium in three experimental groups compared to the control group: Group C1(5days post acetaminophen extra overdose administration), Group D (Treatment with acetaminophen extra overdose only), Group E2(Treatment with acetaminophen extra after watermelon juice administration).

Also, a significant decrease was found in the plasma level of potassium in only one experimental group: Group D (Treatment with acetaminophen extra overdose only) and two experimental groups of plasma sodium: Group C2(treatment with watermelon juice after acetaminophen extra overdose) and Group E1(Treatment with watermelon juice only before acetaminophen extra overdose). The significant results seen in Group C1, Group E2 and Group D of both plasma potassium and sodium concur with the study by Goddard *et al.*,^[5] who explained that acetaminophen overdose could cause similar tubular effects to NSAIDs (Non-steroidal anti-inflammatory drugs) via inhibition of prostaglandin synthesis, vasoconstriction and activation of renin-angiotensin-aldosterone system causing electrolyte changes(increase fractional excretion of potassium and sodium retention). The significant decrease seen in Group C2 and Group E1 is in accordance with fact that watermelon juice contain high level of antioxidants which help to mop out free radicals that was generated by acetaminophen extra overdose and more than 90% water that could help replenish body fluids and restore electrolyte leading to decrease level of plasma sodium in these groups thus supporting the report by Braide, *et al.*,^[6]

There was a significant decrease in plasma chloride in one experimental group: Group C2(Treatment with watermelon juice after acetaminophen extra overdose) and a statistical significant increase was found in one experimental group E2(Treatment with acetaminophen extra after watermelon juice administration).The result seen in group E2 is in accordance with the study of Schiano *et al.*,^[7] who reported that acetaminophen overdose can lead to mitochondrial poisoning that could result in lactic acidosis, a cause of anion gap metabolic acidosis.

Also, the result seen in Group C2 which concur with the study by Rimando *et al.*,^[8] that watermelon contains more than 90% water that helps replenish body fluids and restore electrolyte.

The administration of acetaminophen extra together with watermelon juice has significantly decreased the levels of plasma zinc in all the experimental groups compared to the control group. Acetaminophen overdose could lead to increased production of cellular reactive oxygen species leading to decrease in plasma zinc which could cause activation of zinc transporter leading to change in intracellular environment from a reductive to a more oxidative state and make cells vulnerable to oxidative stress, increase the risk for oxidative damage to DNA, protein and lipid. In addition and according to Majhi *et al.*,^[9] acetaminophen enhanced the risk of arsenic-mediated oxidative stress in kidney. Discontinuation of acetaminophen administration also increased the susceptibility of kidney to nephrotoxic effect of arsenic. It appeared ROS were primarily responsible for oxidative stress in both the phases. No may have a minor role in Phase-I, but does not contribute to redox signalling mechanism in Phase-II.

Significant reduction in the levels of plasma zinc after the administration of watermelon juice could be attributed to regulatory actions of metallothioneins that contains Zn constitute antioxidant defences which reserves excess zinc to avoid increase in the production of zinc in the circulation and to prevent toxicity. In addition accordance to Fosmire^[10] and Blake.^[11] Zinc may be held in metallothionein reserves within microorganisms, and in the intestines or liver of animals. Metallothionein in intestinal cells adjusts absorption of zinc by 15–40%. Consequently, inadequate or excessive zinc intake can be harmful; excess zinc particularly impairs copper absorption because metallothionein absorbs both metals.^{[10] [11]}

CONCLUSION

In a nut shell, the results indicates a significant reduction in plasma zinc and potassium and a significant increase in sodium and chloride after acetaminophen extra overdose.

Also, watermelon juice contain more than 90% water that could help replenish body fluids and restore electrolyte like sodium, potassium and chloride.

RECOMMENDATION

Estimation of plasma zinc, potassium, sodium, and chloride is essential for the treatment of any disease condition using watermelon juice.

LIST OF REFERENCES

1. Aronoff DM, Oates JA, Boutaud O (2006). "New insights into the mechanism of action of acetaminophen: Its clinical pharmacologic characteristics reflect its inhibition of the two prostaglandin H₂ synthases". *Clin. Pharmacol. Ther.* 79 (1): 9–19. doi:10.1016/j.clpt.2005.09.009. PMID 16413237

2. Allen, A.L. (2003). The diagnosis of acetaminophen toxicosis in a cat. *Can. Vet. J.* 44(6): 509–510
3. Baumann T.W, (1997). "Metabolism and Excretion of caffeine during germination of coffee Arabica L". *Plant and cell physiol Journal*, 25(8): 1431 – 36.
4. Lawrence J, Moore E, port L, Danchini M, Counel T, (2009) "Paracetamol as a risk factor for allergic disorders". *The Lancet*, 373(9658): 119 – 120.
5. Goddard J., Mitchell A. J., Pakravan N. (2003) Effect of acute paracetamol overdose on changes in serum electrolytes. *Journal of Clinical Toxicology* 3: 741-747.
6. Braide W, Odiong I.J and Oranusi S (2012). Phytochemical and antibacterial properties of the seed of watermelon (*Citrulus lanatus*). *Prime J. Microbiol. Res.* 2: 99-10.
7. Schiano, T.D., Hernandez S.H, Howland, M. (2004) Acetaminophen poisoning following a single acute ingestion. *J. of Clin. Toxicol.* 42: 133-136.
8. Rimando, A. M., Perkins-Veazie, P. M. (2005). Determination of citrulline in watermelon rind. *J. Chromatogr. A*, 1078(1–2): 196–200.
9. Majhi CR, Khan S, Leo MD, Manimaran A, Sankar P, Sarkar SN. Effects of acetaminophen on reactive oxygen species and nitric oxide redox signaling in kidney of arsenic-exposed rats. *Food Chem Toxicol.* 2011 Apr; 49(4): 974-82. doi: 10.1016/j.fct.2011.01.003. Epub 2011 Jan 8.
10. Fosmire, G. J. (1990). Zinc toxicity. *American Journal of Clinical Nutrition.* 51: 225–227.
11. Blake, Steve (2007). *Vitamins and Minerals Demystified. McGraw-Hill Professional.* 242: 148901-148907.