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Original Research Article

# Assessment of the Administration of Watermelon (*Citrullus lanatus*) on Lipid Profile in Rabbits Overdosed with Acetaminophen Extra

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**Abstract:** Water melon juice contain potent antioxidants such as lycopene in addition to other health promoting bioactive phytochemicals. Overdoses of the analgesic and antipyretic acetaminophen extra represent one of the most common pharmaceutical product poisonings worldwide today. This work was designed to evaluate the effect of watermelon juice in rabbits overdosed with acetaminophen extra using Total cholesterol, Triglyceride, HDL and LDL. Thirty rabbits classified into 6 groups labeled A-F (with C1, C2, E1 and E2) with A as control were investigated. Acetaminophen extra overdosed (1500mg/kg) was administered into some of the rabbits to induce toxicity. Fifteen milliliter of watermelon juice was used to prevent the toxicity. The blood sample collected was used to determine the plasma level of Total cholesterol, Triglyceride, HDL cholesterol and LDL cholesterol were analyzed biochemically by spectrophotometry**.** The result showed no significant alteration in the plasma level of Total cholesterol, Triglyceride, HDL cholesterol and LDL cholesterol when the rabbits were given 1500mg/Kg of Acetaminophen Extra body weight and also when the rabbits were given water melon juice before or after they were given 1500mg/Kg of Acetaminophen Extra( $p>0.05$). Ho**w**ever, there was a significant increase in the level of plasma Cholesterol following the administration of 1500mg/kg body weight of acetaminophen extra and 15ml/Kg of watermelon juice simultaneously ($p<0.05$). co-adminisration of 15ml/Kg of watermelon juice and 1500mg/Kg acetaminophen extra could have a synergetic and defective metabolic effect leading increase in plasma cholesterol in rabbits.
**Keywords:** Water melon, cholesterol, Triglyceride, HDL cholesterol, acetaminophen

## INTRODUCTION

Acetaminophin extra is a combination of acetaminophen(panadol) and caffeine which is used to treat mild to moderate pain (from headaches, menstrual periods, toothaches, backaches, osteoarthritis, or cold/flu aches and pains) and to reduce fever [1]. Overdoses of the analgesic and antipyretic acetaminophen extra represent one of the most common pharmaceutical product poisonings worldwide today [2, 3]. Acetaminophen extra is generally safe at recommended doses [2, 3]. An overdose can result in liver failure [4].

Watermelon juice is a nutrient dense juice a juice that provides a high amount of vitamins, minerals and antioxidants for a low amount of calories. Many studies have suggested that increasing consumption of plant foods like watermelon decreases the risk of obesity and overall mortality, diabetes, heart disease and promotes a healthy complexion and hair, increased energy, overall lower weight. Watermelon extract supplementation reduced ankle blood pressure, brachial blood pressure and carotid wave reflection in obese middle-aged adults with prehypertension or stage 1 hypertension and that watermelon extract improved arterial function. Watermelon, because of its water and fiber content, helps to prevent constipation and promote regularity for a healthy digestive tract. watermelon contains more lycopene than any other fruit or vegetable [5].

Watermelon is made up of 92% water and full of important electrolytes, watermelon is a great snack to have on hand during the hot summer months to prevent dehydration. Watermelon also contains thiamin, riboflavin, niacin, vitamin B-6, folate, pantothenic acid, magnesium, phosphorus, potassium, zinc, copper, manganese, selenium, choline, lycopene and betaine [6].

Choline is a very important and versatile nutrient in watermelon that aids our bodies in sleep, muscle movement, learning and memory. Choline also helps to maintain the structure of cellular membranes, aids in the transmission of nerve impulses, assists in the absorption of fat and reduces chronic inflammation. As

an excellent source of the strong antioxidant vitamin C as well as other antioxidants, watermelon can help combat the formation of free radicals known to cause cancer. Lycopene intake has been linked with a decreased risk of prostate cancer prevention in several studies [7, 8].

Metabolism Total cholesterol, Triglyceride, HDL cholesterol and LDL cholesterol take place in the hepatocytes. This function could be affected by drug toxicity and inflammation [4].

## JUSTIFICATION OF THE STUDY

Recent studies have shown the effect of overdosed acetaminophen extra on human and some animals such as Dogs, Cats and snakes [9].

This present study is aimed to measure the levels of lipid profile in rabbits overdosed with acetaminophen extra and treated with water melon juice. This is because acute overdosed of acetaminophen extra can cause hepatocellular damage.

## AIM AND OBJECTIVES

This present study is designed to determine biochemical alteration in lipid profile of rabbits overdosed with acetaminophen extra and treated with water melon juice.

## MATERIALS AND METHOD

### Study area

This experimental study was carried out in the animal house of Achievers University, Owo. Ondo State.

### Study Population

Rabbits of either sex were used in the experiment. Thirty rabbits were purchased in Owo through the Department of Biological Sciences, Achievers University, Owo – Nigeria. Before performing the experiment, ethical clearance was obtained from institutional animal ethics committee (IAEC).

### Sample size

Thirty apparently healthy rabbits were bought and classified into 6 groups of 5 rabbits each. Body weight of animals before and after the experiment was measured using Mettler sensitive balance (number 202845).

### Study design

Experimental and observational study involves thirty rabbits divided into six (6) groups:

Group A: five (5) rabbits were fed with normal meal for 7days. (Control)

Group B: five (5) rabbits were fed normal meal and 15ml/kg of water melon juice for 7 days

Group C: five (5) rabbits were given 1500mg/kg of acetaminophen extra for 5 days orally thereafter, they were fed with normal meal and 15ml/kg of watermelon juice daily for 7 days after 5 days of post acetaminophen extra administration.

Group D: five (5) rabbits were given 1500mg/kg of acetaminophen extra for 5 days orally thereafter; they were fed with normal meal and water for 7days.

Group E: five (5) rabbits were fed with normal meal and 15ml/kg of water melon juice daily for 7days, thereafter; they were given 1500mg/kg of acetaminophen extra for 5 daysorally and fed with normal meal and water. The rabbits were observed for another 7days post acetaminophen extra administration.

Group F: five (5) rabbits given 1500mg/kg acetaminophen extra orally and they were fed simultaneously with normal meal and 15ml/kg of water melon juice daily for 7days.

### 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 6 groups.

**Group A:**Five milliliters of blood sample was collected from 5 rabbits before and after 7 days feeding with normal meal and water (control group)

**Group B:** Five millilitres of blood sample was collected into Lithium heparinized bottle from each of the 5 rabbits before and after 7 days normal meal and 15ml/kg of watermelon juice.

**Group C:** Five millilitrescof blood sample was collected inti Lithium heparinized bottle from each of the 5 rabbits after 5 days post administration of 1500mg/kg acetaminophen extra. Five millilitres of blood samole was also bcollected into Lithium heparinized bottle from each of the 5 rabbits after 7 days of the administration of 15ml/kg of watermelon juice daily.

**Group D:** Five millilitres of blood sample was collected into Lithium heparinized bottle from each of the 5 rabbits before and after 7 daysof post administration of 1500mg/kg of acetaminophen extra for 5 days given orally and fed with normal meal and water.

**Group E:** Five millilitres of blood sample was collected into Lithium heparinized bottle from each of the 5 rabbits before and after 7 days normal meal and 15ml/kg of watermelon juice and adminitration of 1500mg/kg of acetaminophen extra for 5 days given orally.

**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 acetaminophen extra for 5 days given orally and with simultaneous administration of 15ml/kg of watermelon juice.

**Materials**

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

**Preparation of watermelon juice**

Water melon were purchased from Owo market and presented to the Department of biological sciences, Achievers University, Owo for confirmation and certification.

The succulent red part was removed and kept in a sterile bowl. The seeds were aseptically removed. The remaining succulent red part of the watermelon was blended using electric blender and thereafter was filtered undiluted. Fifteen milliliter of the filtrate was administered to each rabbit as watermelon juice orally.

**Preparation of Acetaminophen extra powder**

Panadol extra tablets of Glaxo Smithkline were purchased and grinded into powder using Laboratory pestle and mortal.

**Blood Sample preparation**

Whole blood samples collected from each of the rabbit. It was collected in Lithium heparinized bottle. The blood sample was spun using bench/macro centrifuge and the plasma was separated in a plain bottle.

**Animal behavioral study**

Some behaviors such as vomiting, drowsiness, loss of appetite, dark urine, were monitored for up to 2-3hours after overdosing the animals with acetaminophen extra

**Assay Methodology**

Analysis of Lipid Profile:
The lipid profile estimated includes:
Total cholesterol (TC)
Total triglyceride (TG)
High density lipoprotein (HDL)
Low density lipoprotein (LDL)

**Method and Principle**

**Cholesterol Estimation**

This is based on an enzymatic assay described by Allain *et al.,* [10].

**Principle of Assay**

The cholesterol esters are hydrolyzed to free cholesterol by cholesterol esterase (CE). The free cholesterol is then oxidized by cholesterol oxidase (CO) to cholesten-3-one with the simultaneous production of hydrogen peroxide. The hydrogen peroxide produced couples with 4- aminoantipyrine and phenol, in the presence of peroxidase, to yield a chromogen with maximum absorbance at 505nm. The intensity of the color produced is directly proportional to the concentration of total cholesterol in the sample.

**Triglycerides estimation**

Method as described by Fossati and Prencipe [11] associated with Trinder reaction.

**Principle of Assay**

Triglycerides are measured enzymatically in serum or plasma using a series of coupled reactions in which triglycerides are hydrolyzed to produce glycerol. Glycerol is then oxidized using glycerol oxidase, and $H_2O_2$, one of the reaction products, is measured as described above for cholesterol. Absorbance is measured at 500 nm.

The reaction sequence is as follows:

Reaction scheme is as follows:

Triglycerides → Glycerol + free fatty acids

Glycerol + ATP→ Glycerol 3 phosphate + ADP

glycerol 3 phosphate + $O_2$→ Dihydroxyacetone phosphate + $H_2O_2$

$H_2O_2$ + 4-Chlorophenol + PAP → Quinoneimine (pink) +$H_2O$

The absorbance of the colored complex (Quinoneimine) is proportional to the amount of triglycerides in the specimen, measured at 500nm wavelength

**HDL-Cholesterol Estimation**

**Principle of Assay**

Low density lipoprotein (LDL), very low density lipoprotein (VLDL) and chylomicrons from specimen and precipitated by phosphotungstic acid (PTA) and magnesium chloride HDL-cholesterol obtained in supernatant after centrifugation is then measured with total cholesterol reagent.

**LDL-cholesterol estimation**

Most of the circulating cholesterol is found in three major lipoprotein fractions: Very Low Density Lipoproteins (VLDL), LDL and HDL.

[Total chol] = [VLDL-chol] + [LDL-chol] + [HDL-chol]

Plasma low density lipoprotein was calculated using Freidwald formula [12].

LDLC=TC-(TG/5+HDLC) where all values are expressed in mg/dl, or

[LDL-chol] = [total chol] - [HDL-chol] - [TG]/2.2

Where, [TG]/2.2 is an estimate of VLDL-cholesterol and all values are expressed in mmol/L.

**Statistical analysis of data**

A statistical package for social sciences (SPSS) version 17.0 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. Analysis of

variance (ANOVA) was used to determine significance difference between the six groups. The level of significance was taken at 95% confidence interval and P ≤ 0.05 was considered significant

## RESULTS

The data obtained is organized and subjected to statistical analysis using statistical package for social science (SPSS) 18.0 to determine the level of significance.

The table shows the result on lipid profile of rabbits overdosed with Acetaminophen Extra and treated with watermelon juice. The results show no significant difference in plasma triglyceride, HDL and LDL in all the groups.

It also shows a significant difference in one experimental group (group F) of rabbit overdosed with Acetaminophen Extra and treated with watermelon juice simultaneously compared to the control group.

**Table 1: Mean± Standard Deviation of Triglyceride, Cholesterol, HDL and LDL**

| | GROUP A | GROUP B | GROUP C1 | GROUP C2 | GROUP D | GROUP E1 | GROUP E2 | GROUP F |
|---|---|---|---|---|---|---|---|---|
| TRIGLYCERIDE | .3220 ± .12194 | .9100± .71460 | 1.2540± .24552 | .6580± .15498 | 1.5020± .90458 | .9100± .71460 | 1.2340± .36596 | 1.4740± .28571 |
| CHOLESTEROL | .8400± .42573 | 1.1800± .48616 | 1.2100± .18868 | .9060± .05320 | 1.3200± .61298 | 1.1800± .48618 | 1.5940± .25755 | 1.6700±0.331 |
| HDL | .9180± .16022 | .8940± .18623 | .8880± .16177 | .8540± .25667 | 1.1420± .24468 | .8740± .14755 | .9200± .14663 | 1.0420± .11760 |
| LDL | .7140± .11830 | .5300± .14577 | .7500± .16248 | .9560± .16965 | .8680± .15336 | .6280± .07259 | .7340± .18202 | .8220± .08226 |

**Table 2: Comparative analysis of mean and standard deviation of Total cholesterol, Triglyceride, HDL and LDL obtained in the rabbits**

| | | GROUPA VERSUS B | GROUP A VERSUS D | GROUP C1 VERSUS C2 | BGROUP E1 VERSUS E2 | GROUP A VERSUS F |
|---|---|---|---|---|---|---|
| TRIGLYCERIDE | T-TEST | -1.982 | -2.728 | 6.959 | -.933 | -7.691 |
| | P- VALUE | .401 | .430 | .259 | .898 | .716 |
| | COMMENT | NS | NS | NS | NS | NS |
| CHOLESTEEROL | T-TEST | -1.754 | -1.245 | 4.193 | -1.746 | -16.372 |
| | P- VALUE | .332 | .555 | .279 | I..YUUN 890 | .002 |
| | COMMENT | NS | NS | NS | NS | S |
| HDL | T-TEST | .168 | -1.158 | .299 | -.480 | -1.157 |
| | P- VALUE | .191 | .627 | .586 | .801 | .869 |
| | COMMENT | NS | NS | NS | NS | NS |
| LDL | T-TEST | 3.090 | -1.448 | -2.024 | -1.481 | -1006 |
| | P-VALUE | .383 | .361 | .922 | .410 | .975 |
| | COMMENT | NS | NS | NS | NS | NSC |

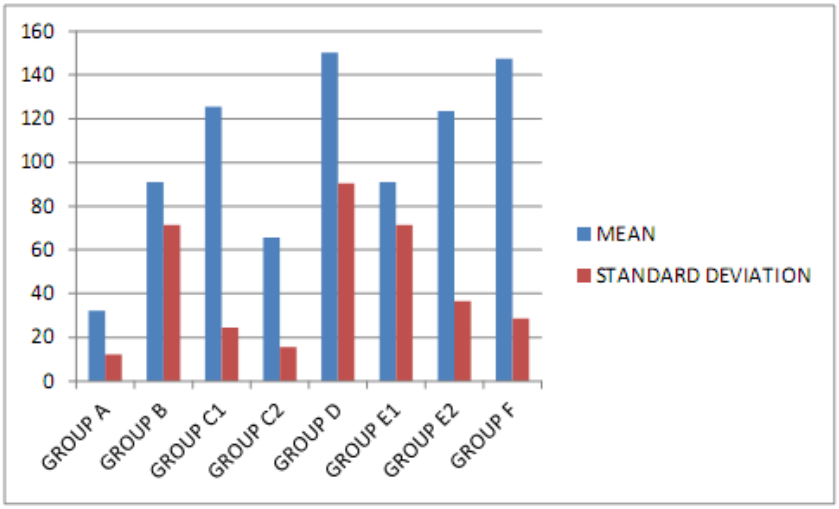


**Fig-1: shows the comparative analysis of the effect of Acetaminophen Extra overdosed and treated with Watermelon juice of plasma Triglyceride (mmol/L)**

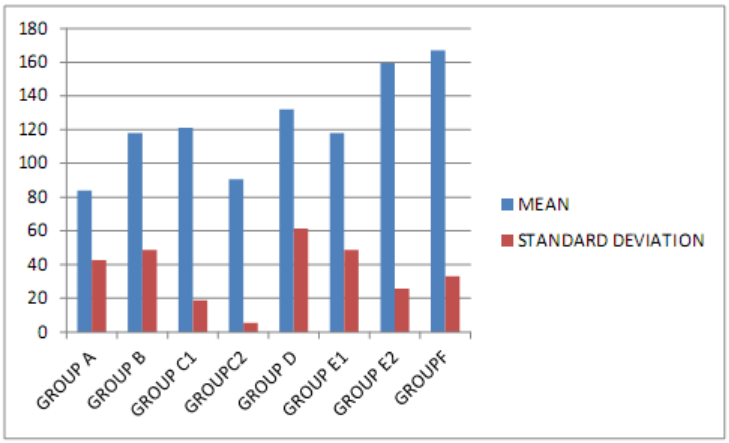


**Fig-2: Shows the comparative analysis of the effect of Acetaminophen Extra overdosed and treated with Watermelon juice of plasma Cholesterol (mmol/L)**

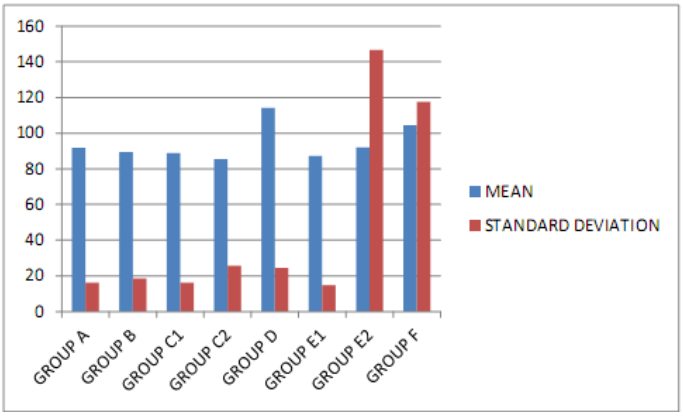


**Fig-3: Shows the comparative analysis of the effect of Acetaminophen Extra and Watermelon juice of plasma HDL (mmol/L)**

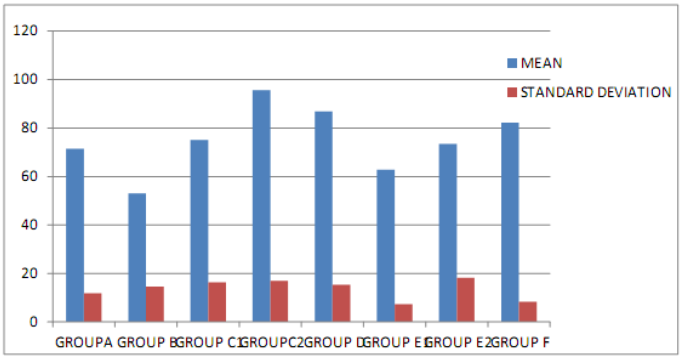


**Fig-4: Shows the comparative analysis of the effect of Acetaminophen extra overdosed and treated with watermelon juice. (mmol/L)**

## DISCUSSION

The result showed no significant alteration in the plasma level of Total cholesterol, Triglyceride, HDL cholesterol and LDL cholesterol when the rabbits were given 1500mg/Kg of Acetaminophen Extra body weight and also when the rabbits were given water melon juice before or after they were given 1500mg/Kg of Acetaminophen Extra. There could be associated with a significant relationship of acetaminophenexra and watermelon with plasma lipids because acetaminophen extra, a widely used analgesic and antipyretic agent, has significant antioxidant properties [13]. Meraland Aysun [13] demonstrated that the LDL isolated from serum was oxidized by Cu++ ions and this oxidation reduced in the presence of acetaminophen. The reduced oxidative modification of LDL by acetaminophen may be of therapeutic value in preventing the development and progression of atherosclerosis. At this point, Meral andAysun [13] concluded that acetaminophen might have a therapeutic value as an alternative drug for prevention of atherosclerosis which is one of the main causes of

human death in industrialized countries because high plasma total cholesterol and low density lipoproteins (LDL) levels showed a significant positive correlation to the development of atherosclerosis and cardiovascular diseases [14, 15]. Massa *et al.*, [16] reported that supplementation with Watermelon Extract Reduces Total Cholesterol and LDL Cholesterol in Adults with Dyslipidemia under the Influence of the MTHFR C677T Polymorphism. The use of watermelon extract reduced plasma total cholesterol and low-density lipoprotein without modifying triglycerides, high-density lipoprotein, and very low-density lipoprotein values [16].

However there was a significant increase in the plasma level of cholesterol when watermelon juice and 1500mg/Kg of Acetaminophen Extra were co-administered into the rabbits. This could be as a result of the synergetic effect of acetaminophen extra and watermelon juice cholesterol lowering bioactivities as reported by Meral and Aysun [13] and Massa *et al.*, [16] respectively. The co administration of acetaminophen extra with watermelon juice was found to increase plasma cholesterol. This could be attributed to hepatotoxicity caused by the administration of 1500mg/kg body weight. Metabolism of cholesterol takes place in the liver. Consequently, the metabolism of cholesterol in the liver will be affected due to acetaminophen extra induced hepatotoxicity [17]. In accordance with Aruna *et al*., [18] the consumption of watermelon (*C. lanatus*) led to reduced body weight gain, decreased plasma cholesterol concentrations which does not agree with findings of this research work.

## CONCLUSION

The result obtained from this study showed no significant alteration in the plasma level of Total cholesterol, Triglyceride, HDL cholesterol and LDL cholesterol when the rabbits were given 1500mg/Kg of Acetaminophen Extra body weight and also when the rabbts were given water melon juice before or after they were given 1500mg/Kg of Acetaminophen Extra. However there was a significant increase in the level of plasma Cholesterol following the administration of 1500mg/kg body weight of acetaminophen extra and 15ml/Kg of watermelon juice simultaneously

## RECOMMENDATION

Watermelon juice could be used in the treatment of fat accumulation to lower heart disease risk and also can improve Lipid Profile.

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