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Potentials of Aqueous Extract of Gnetum Africanum (Okazi) Tendril in Counteracting Hepatotoxic Effect of Acetaminophen in Wistar Rats

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ABSTRACT

This study was designed to evaluate the potentials of Gnetum africanum tendrils in counteracting the hepatotoxic effect of acetaminophen in Wister rats. Twenty five male Wister rats which were randomly divided into five groups were used for the study. Group 1 (Negative control) was treated with distilled water only while group 2 (positive control) was treated with 1500mgkg of acetaminophen only. Group 3-5 were first treated with 1500mg of acetaminophen, and two hours later, graded doses of the extract were administered. Treatment with the extract continued for four days. After the period of treatment, blood samples were collected for assay of alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), serum proteins and bilirubin. The results of laboratory analysis showed an increase in AST, ALT, ALP, total and conjugated bilirubin in group 2, 3, 4, and 5 when compared with group 1. The increase was greater in group 3-5 than in group 2. This suggests that acetaminophen and the extract induced an increase in ALT, ALP, total and conjugated bilirubin in the wister rats. It can therefore be concluded that Gnetum africanum tendrils did not counteract the hepatotoxic effect of acetaminophen but rather exacerbated it.

Keywords: Hepatotoxic, Acetaminophen, transaminase, induce, Extract, counteract and Tendrils

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INTRODUCTION

The liver is a large, complex organ that is well designed for its central role in carbohydrate, protein and fat metabolism (Asmaa *et al*, 2009). It is the site where waste products of metabolism are detoxified through processes such as amino acid deamination, which produces urea. In conjunction with the spleen it is involved in the destruction of spent red blood cells and the reclamation of their constituents. It is responsible for synthesizing and secreting bile and synthesizing lipoproteins and plasma proteins, including clotting factors (Zhou *et al*, 2006). It maintains a stable blood glucose level by taking up and storing glucose as glycogen (glycogenesis), breaking this down to glucose when needed (glycogenolysis) and forming glucose from noncarbohydrate sources such as amino acids (gluconeogenesis). Many of these biosynthetic functions use the products of digestion. With the exception of most lipids, absorbed food products pass directly from the gut to the liver through the hepatic portal

vein. At the microscopic level, the primary functional unit of the liver is the liver acinus, which is defined by the territory supplied by each terminal branch of the hepatic artery and hepatic portal vein (Cheung *et al*, 2009). Liver disease is often reflected by biochemical abnormalities of liver function. Although tests that measure the level of serum liver enzymes are commonly referred to as liver function tests, they usually reflect hepatocyte integrity or cholestasis rather than liver function. A change in serum albumin level or prothrombin time may be associated with a decrease in liver functioning mass, although neither is specific for liver disease (Asmaa *et al,* 2009).

Secondary plant metabolites are numerous chemical compounds produced by the plant cell through metabolic pathways derived from the primary metabolic pathways (Rehab and El-Anssary, 2017). In the middle of the twentieth century, advances of analytical techniques such as chromatography allowed the recovery of more and more of these molecules, and this was the basis for the establishment of the discipline of phytochemistry (Bjeldanes and Shibamoto, 2009). Secondary metabolites have shown to possess various biological effects, which provide the scientific base for the use of herbs in the traditional medicine in many ancient communities (Pagare *et al*, 2015). They have been described as antibiotic, antifungal and antiviral and therefore are able to protect plants from pathogens (Pichersky and Gang, 2000).

Tropical shrubs have been in use as medicinal and ornamental plants by tradtinal herbalists in Southern Nigeria in the management and treatment of various illnesses (Onyegeme-Okerenta and Essien, 2021).

A bioactive compound is a compound having some biological activity (Walia *et al*, 2019). As the name suggests (Greek ‘bios’ means life and Latin‘activus’ means dynamic or full of energy), a bioactive compound (or substance) has its direct physiological or cellular effects on a living organism. Such effects may be positive or negative depending on the nature of the substance, its dose, and its bioavailability (Walia *et al*, 2019). Accordingly, bioactive food components are components in foods or dietary supplements, other than those necessary to meet the basic nutritional needs, which can change the health status of the humans or animals that consume them (Bernhoft, 2010). In plants, nutrients are generally not included in the term “plant bioactive compound”. Typically, bioactive compounds in plants are produced as secondary metabolites that are not necessary for the daily functioning of the plant (such as growth); however, they play an important role in the competition, defense, attraction, and signalling (Korkina *et al*, 2018). These compounds can then be defined as secondary plant metabolites eliciting pharmacological or toxicological effects in humans and animals. A wealth of available scientific evidence demonstrates that natural bioactive compounds render a number of diversified biological effects, such as antioxidant, antibacterial, antiviral, antiinflammatory, antiallergic, antithrombotic and vasodilatory actions, as well as antimutagenicity, anticarcinogenicity and antiaging effects (Chandrasekara and Shahidi, 2018).

In Africa, phytomedicine has been in existence for several years and about 80% of the population depend on herbal medicine for its primary health care delivery (Okigbo and Mmeka, 2006). Although modern medicine may be available but treatment of diseases with traditional medicine is more preferable, perhaps, for historical or cultural reasons (Balogun *et al*., 2016). In Nigeria, medicinal plants are potential sources of new antimicrobials and with renewed interest in phytochemicals, avalanche of researches have been undertaken to screen antimicrobial activities of these plants (Anyanwu and Okoye, 2017).

It has long been recognized that naturally occurring substances in plants have antioxidant activity (Sunday *et al*, 2016). In recent times, there has been a growing interest in oxygen-containing free radicals in biological systems and their implied roles as causative agents in the aetiology of a variety of chronic disorders (Sunday *et al*, 2016). Consequently, attention is being focused on the therapeutic potentials of medicinal plants as sources of antioxidants in protecting biochemical functions in the cells of the organisms containing them (Gautam *et al*, 2011). *Gnetum africanum*, an African plant known for its antioxidant and anti-inflammatory properties, has been traditionally used in herbal medicine and is suggested to have potential liver-protective benefits. However, there is limited empirical data on the effectiveness of *Gnetum africanum* in counteracting liver damage specifically caused by acetaminophen toxicity.

MATERIALS AND METHODS

Sample collection and identification

The tendrils of *Gnetum africanum* were collected, authenticated and deposited at Captain Elechi Amadi Herbarium (Plate 1). They were air-dried at room temperature (29±1°C) for 3 weeks and then pulverized with the aid of MarlexExcellent grinder (Mumbai, India). The ground samples were then passed through a sieve of 0.5mm pore size to obtain a fine uniform powder. The powdered samples were kept in an airtight container until required.

Plate 1: *Gnetum africanum plant*

Sample extraction

Ten grams (10 g) of the powdered samples were weighed into a well-stoppered bottle and 20 mls of distilled water was added. The mixtures were vigorously agitated and were left to stand for 3 days. The mixture was filtered to remove solid plant material leaving behind the aqueous solution. The solution was then heated to evaporate water and concentrate the extract.

Experimental design

Twenty five (25) male wistar rats were used for the study. The rats were randomly divided into 5 groups of five rats in each group. Group 1, (control A) comprised 5 uninduced and untreated rats. Group 2 (control B) comprised 5 rats which were induced with a single dose of acetaminophen, 1500Mg/kg body weight. Group 3 comprised 5 rats which were induced with 1500mg of acetaminophen, and afterward, treated with 100mg of the extract per kg of body weight. Group 4 comprised 5 rats which were induced with 1500mg of acetaminophen, and then treated with 200mg of the extract per kg of body weight. Group 5 comprised 5 rats, which were induced with 1500mg of acetaminophen, and later treated with 300mg of the extract per kg of body weight. For group 3- 5, the acetaminophen was first administered. Thereafter, treatment with the extract commenced two hours post acetaminophen administration. The treatment continued for four days. On the fifth day, blood samples were collected from group 1-5 for laboratory analysis.

Determination of bilirubin

Total bilirubin was determined in the presence of caffeine, which releases albumin bound biliirubin by the reaction with diazotized sulphanilic acid using the following steps:
The test tubes were labelled as sample and blank tubes, and 0.2 ml of the reagent was pipetted into all the tubes.
Then, one drop of sodium nitrate was added to the tube label sample. One ml of caffeine was then added to all the tubes. Thereafter, 0.02 ml of the sample was added to the tubes, mixed and incubated for 10 mms at 25 ^{O}C. Again one ml of tarterate to all the tubes mixed and incubated for 5-30 mins at 25 ^{O}C. Then absorbance was read at 590 nm.To determine the direct-reacting bilirubin, the serum was mixed with water and diazo reagent. The reaction was terminated by ascorbic acid and then caffeine is added. Again the azobilirubin was made alkaline with tartrate buffer. When blanks are run, the serum is mixed with water and ascorbic acid.

Determination of serum albumin

Dye-binding Method was used. Ten ml (10.0 ml.) of working dye reagent was dispensed into a series of cuvets. One cuvet for the albumin blank, one each for the standards, and one for each of the unknowns. Thereafter, 0.20 ml. of saline, standards, sera was transferred to the respective cuvets. After mixing by gentle inversion, the cuvets were allowed to stand for 20 minutes. Afterwards, the absorbance of the standard and serum specimens against the blank at 540 nm were read. Absorbance readings were converted to albumin concentration by use of the calibration curve, which follows Beer's law.

Determination of total protein

Biuret method was used. Different test tubes were labeled test as the standard, blank and sample. Then, 1ml of reagent was pipetted into all the tubes. Thereafter 0.02ml of the standard, sample and d/w was added into appropriate tubes. The content of the test tubes were Mixed and incubated for 30mins at 25'c. The spectrophotometer was set at 540nm with the blank and the absorbance was read and recorded.

Determination of aspartate transaminase (AST)

Reitman and Frankel method was used. This method measures AST by monitoring the concentration of oxoloacetate hydrazones formed with 2, 4 dinitrophenyl – hydrazine. The test tubes were labelled as sample blank and sample, and 0.5 ml of reagent 1 (R1) was pipetted into all the test tubes. Afterwards, 0.1ml of the sample was added to the tubes labeled sample. It was then mixed and incubation for exactly 30 mins of 37 ^{O}C. Thereafter, 0.5 ml of reagent 2 (R2) was pipetted to all the test tubes, and 0.1ml of the sample was added to the tube labeled sample blank. The tube was mixed and allowed to stand for exactly 20 mins at 25 ^{O}C. Thereafter, 5.0 ml of NaoH was pipetted into all the test tubes. The tubes were mixed and the absorbance of the sample against the sample blank after 5 mins at 540 mm was read (Reitman and Frankel, 1957).

Determination of alanine transaminase (ALT)

Reitman and Frankel method was used, and the test was based on monitoring the concentration of pyruvate hydrazone formed with 2, 4 dinitrophynyl-hydrazine. The test tubes were labelled as sample blank and sample, and 0.5ml of reagent 1 (R1) was pipetted into all the test tubes. Afterwards, 0.1ml of the sample was added to the tubes labeled sample. It was then mixed and incubation for exactly 30 mins of 37 ^{O}C. Thereafter, 0.5 ml of reagent 2 (R2) was pipetted to all the test tubes, and 0.1 ml of the sample was added to the tube labeled sample blank. The tube was mixed and allowed to stand for exactly 20 mins at 25 ^{O}C. Later, 5.0ml of NaoH was pipetted to all the test tubes. The tubes were mixed and the absorbance of the sample against the sample blank after 5 mins at 540 mm was read (Reitman and Frankel, 1957).

Determination of alkaline phospatase (ALP)

Kochmar, J.F and moss, D.W method was used. Alkaline phosphatase acts upon buffered sodium thymolphthalein monophoshate. The addition of an alkaline reagent stops

Table 1: Bilirubin and Serum Proteins in the Experimental and Control Wista Rats.

Dosage (mg/kg b.w.)	Total Bilirubin (umol/L)	Conjugated Bilirubin (umol/L)	Albumin (g/L)	Total Protein (g/L)
Group 1 (Distilled Water)	11.50±0.00	7.10±0.00	39.33±0.14	59.33±0.00
Group 2 (A =1500)	13.40±0.05	10.33±0.55	42.67±0.51	61.33±0.53
Group 3 (A=1500, E= 100)	14.60±0.24	11.37±1.00	44.67±0.00	63.00±0.27
Group 4 (A= 1500, E= 200)	17.17±0.57	13.67±0.40	38.00±0.05	57.33±0.13
Group 5 (A=1500, E=300)	22.37±0.02	15.63±0.54	33.33±0.03	53.00±0.05

Data presented as ± standard deviation
A= Acetaminophen
E= Extract
b.w =Body Weight

Table 2: Liver Function Enzymes in the Experimental and Control Wistar Rats.

Dosage (mg/kg b.w.)	AST (u/l)	ALT(u/l)	ALP(u/l)
Group 1 (Distilled Water)	57.33±0.20	16.00±0.00	38.33±0.21`
Group 2 A =1500	64.33±0.40	19.66±0.04	56.33±0.00
Group 3 A=1500, E= 100	72.00±0.00	28.33±0.09	43.33±0.01
Group 4 A= 1500, E= 200	87.33±0.50	26.00±0.00	56.33±0.12
Group 5 A=1500, E=300	97.00±0.30	27.33±0.01	60.33±0.60

Data presented as ± standard deviation
A= Acetaminophen
E= Extract
b.w =Body Weight

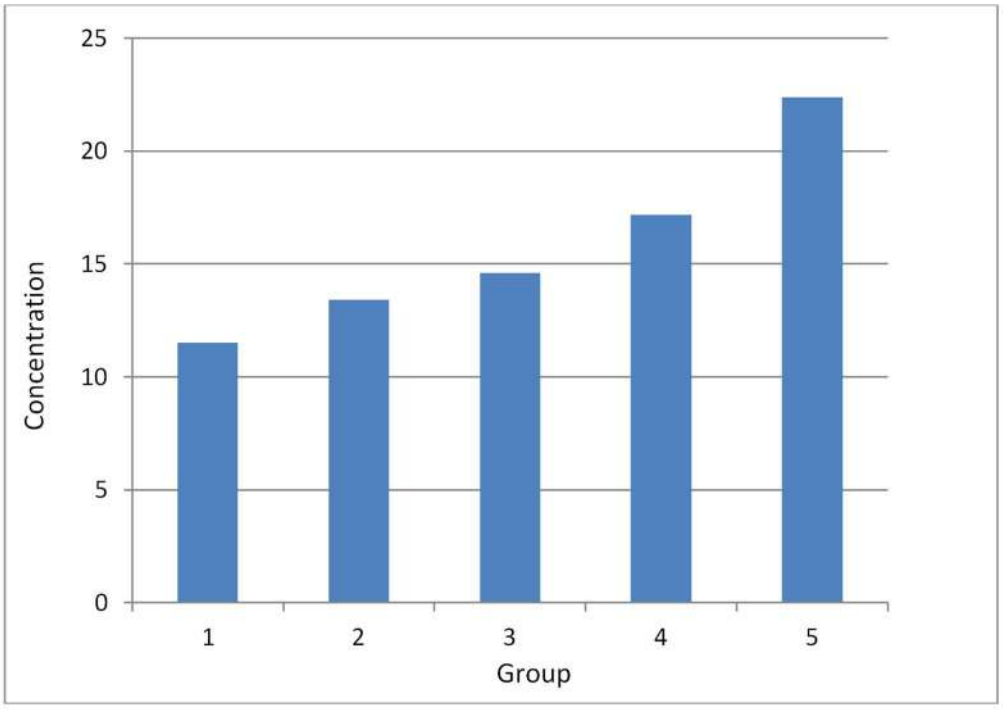

Figure 1: Total Bilirubin of Experimental and Control Groups
Group 1: Distilled water only
Group 2: Acetaminophen only
Group 3: Acetaminophen and 100mg of the Extract
Group 4: Acetaminophen and 200mg of the Extract
Group 3: Acetaminophen and 300mg of the Extract

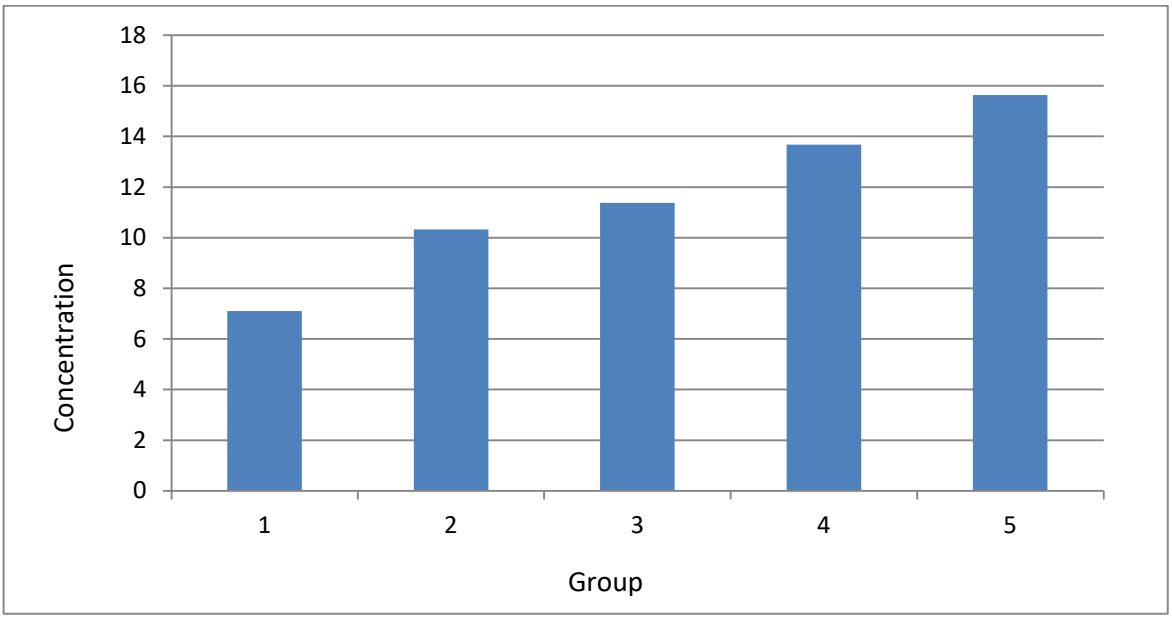

Figure 2: Conjugated Bilirubin of Experimental and Control Groups

Group 1: Distilled water only
Group 2: Acetaminophen only
Group 3: Acetaminophen and 100mg of the Extract
Group 4: Acetaminophen and 200mg of the Extract
Group 3: Acetaminophen and 300mg of the Extract

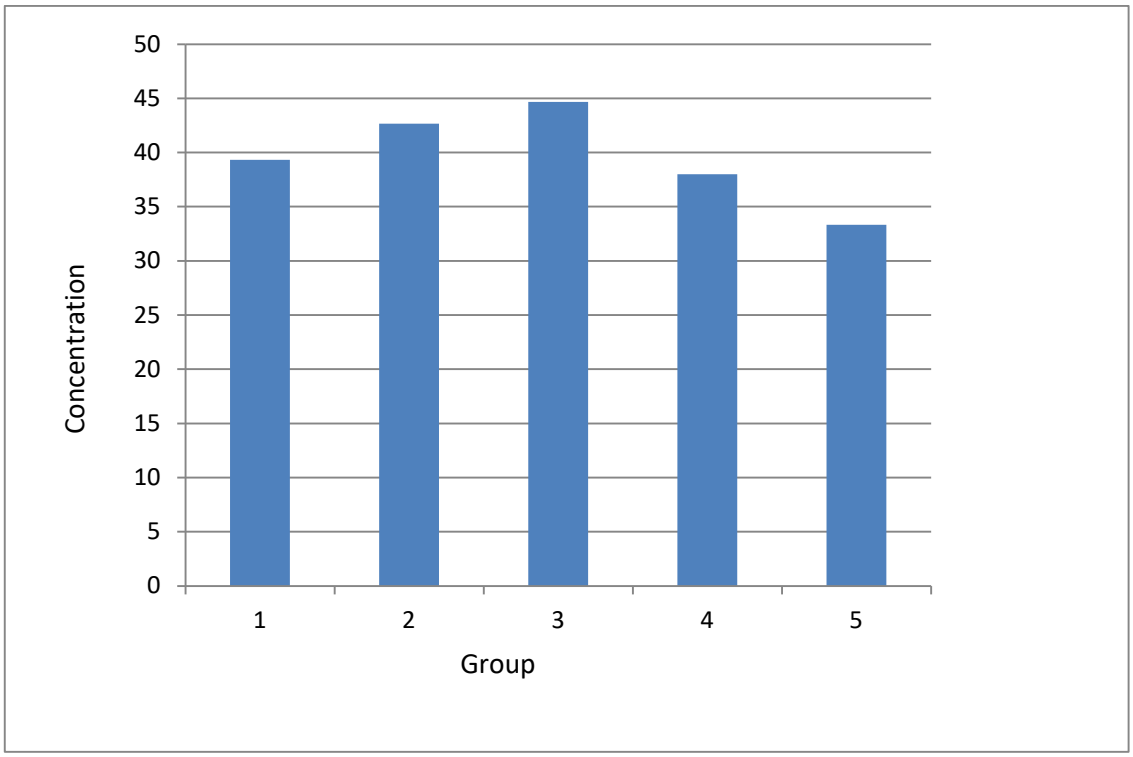

Figure 3: Serum Albumin of Experimental and Control Groups
Group 1: Distilled water only
Group 2: Acetaminophen only
Group 3: Acetaminophen and 100mg of the Extract
Group 4: Acetaminophen and 200mg of the Extract
Group 3: Acetaminophen and 300mg of the Extract

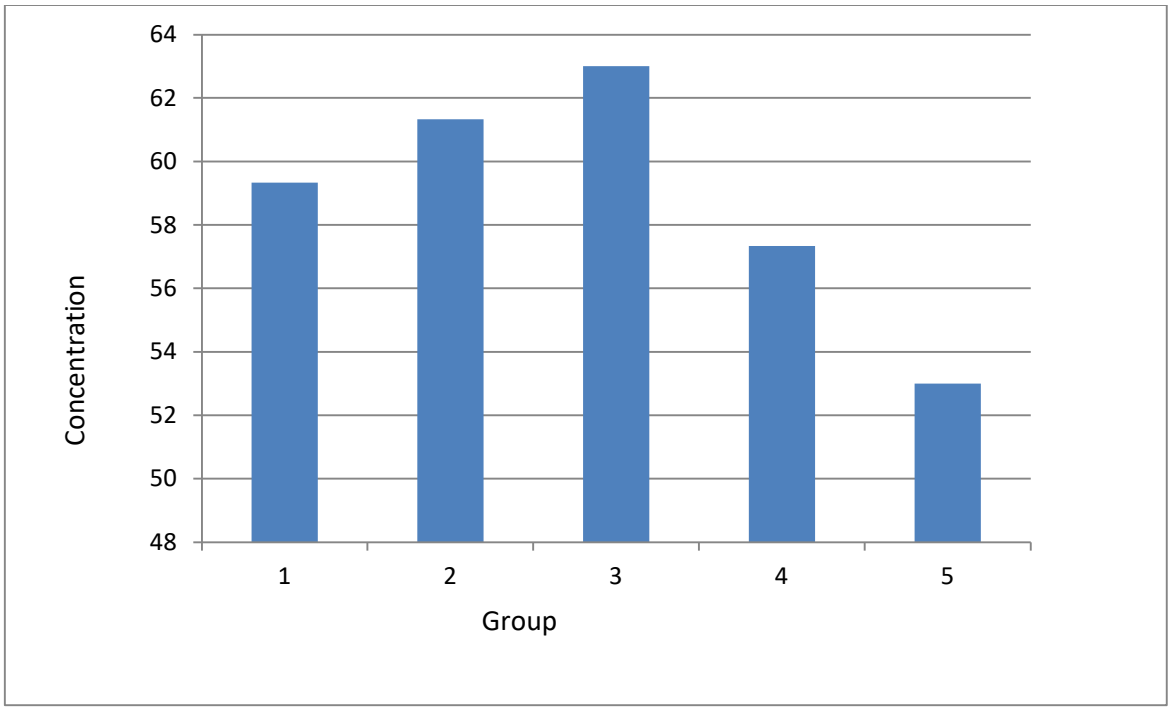

Figure 4: Total Serum Proteins of Experimental and Control Groups
Group 1: Distilled water only
Group 2: Acetaminophen only
Group 3: Acetaminophen and 100mg of the Extract
Group 4: Acetaminophen and 200mg of the Extract
Group 3: Acetaminophen and 300mg of the Extract

enzyme activity and simultaneously develops a blue chromogen which is measured photometrically. Test tubes were labeled as STD, blank and test. Afterwards, 0.5ml of Alp substrate was pipetted into all the test tubes and incubated at 37'c for 3mins. Thereafter, 50ul of the Std sample and d/w were added into appropriate tubes. They were incubated for exactly 10mm at 37°C. Then 2.5ml of Alp colour developer was pipetted into all the test tubes and mix-well. The spectrophotometer was zeroed with the blank, and absorbance read at 590nm.

RESULTS AND DISCUSSION

The results of this study is presented in (Tables 1 and 2 and Figures 1-5). The results of the study as presented in (Table 2, and Figures.5-7) showed that animal subjects who were not induced (Group 1) had the lowest levels of serum AST, ALT and ALP when compared with other groups. The results also showed that AST, ALT and ALP levels in the animal groups induced with acetaminophen, and concomitantly treated with the extract (group 3-5) were higher than those of the animals treated with distilled water only, as well as those treated with acetaminophen only (group 1 and 2). The results of the study as presented in (Table 1 and Figures1-4) showed that animal subjects who were not induced (Group 1) had the lowest levels of total and conjugated bilirubin when compared with other groups. The results also showed that total and conjugated bilirubin levels in the animal groups induced with acetaminophen, and concomitantly treated with the extract (group 3-5) were higher than those of the animals treated with distilled water only as well as those treated with acetaminophen only (group 1 and 2).

Liver enzymes, alanine aminotransferase (ALT), aspartate aminotransferase, and alkaline phosphatase (ALP), are some of the most commonly ordered blood tests in a physician's practice. These enzymes have been valuable in screening for liver disease, as well as in diagnosing and monitoring patients with acute and chronic hepatobiliary disorders (Green and Flamm, 2002). Patients with a marked increase in aminotransferase levels (> 10 times the upper reference limit) typically have acute hepatic injury (Tzong-His *et al*, 2005). Aminotransferases catalyze the redistribution of nitrogen between amino acids and corresponding Oxo acids participating in both protein metabolisms (Wedemeyer *et al*., 2004)

ALT is found in plasma and in various body tissues but is most common in the liver. It catalyzes the two parts of the alanine cycle. AST catalyzes the reversible transfer of an α-amino group between aspartate and glutamate and, as such, is an important enzyme in amino acid metabolism (Djakpo *et al*, 2020). The enzyme alkaline phosphatase (ALP, alkaline phenyl phosphatase, also abbreviated PhoA) is a phosphatase with the physiological role of dephosphorylating compounds. The enzyme is found across a multitude of organisms, prokaryotes and eukaryotes alike, with the same general function, but in different structural forms suitable to the environment they function in (Kim and Wyckoff, 1991).

The results of the study as presented in (Table 2, and

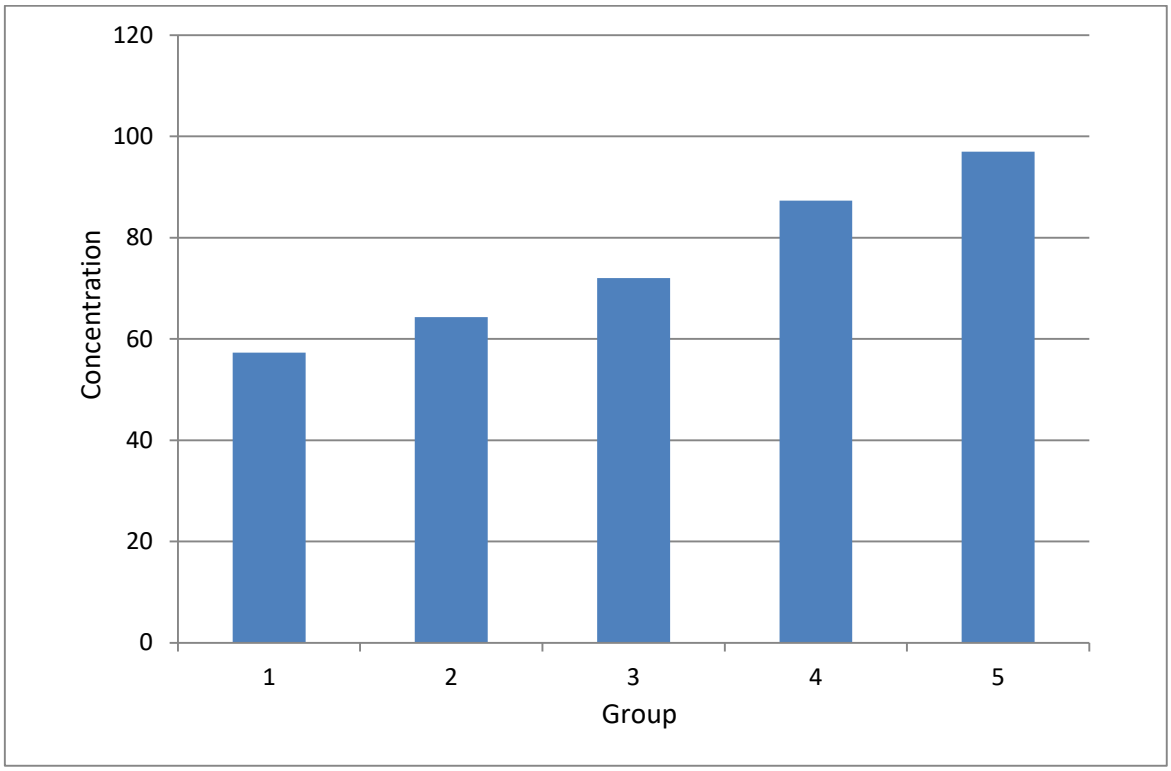

Figure 5: Aspartate Transaminase of Experimental and Control Groups
Group 1: Distilled water only
Group 2: Acetaminophen only
Group 3: Acetaminophen and 100mg of the Extract
Group 4: Acetaminophen and 200mg of the Extract
Group 3: Acetaminophen and 300mg of the Extract

Figure 5-7) showed that animal subjects who were not induced (Group 1) had the lowest levels of serum AST, ALT and ALP when compared with other groups. This clearly indicates that acetaminophen and the extract induced an increase in the aforementioned enzymes which are biomarkers of hepatic injury.

The results also showed that AST, ALT and ALP levels in the animal groups induced with acetaminophen, and concomitantly treated with the extract (group 3-5) were higher than those of the animals treated with distilled water only, as well as those treated with acetaminophen only (group 1 and 2). This suggests that the extract did not counteract the hepatotoxic effect of acetaminophen but rather potentiated it.

AST is found in the liver, heart, skeletal muscle, kidneys, brain, red blood cells and gall bladder Serum ALT level, serum AST (aspartate transaminase) level, and their ratio (AST/ALT ratio) are routinely measured clinically as biomarkers for liver health (Djakpo *et al*, 2020).

The primary clinical application of serum AST and ALT measurement is the detection and differential etiologic diagnosis of hepatic disease (Tripathi and Jialal, 2022). Hepatic cell injury is manifested by elevated serum transaminase activity prior to the appearance of clinical symptoms and signs (such as jaundice). The similar serum transaminase levels in these conditions are thought to be caused by cellular release of only cytoplasmic enzymes associated with reversible hepatic cell damage (Tripathi and Jialal, 2022). In chronic hepatitis and cirrhosis, serum AST levels are higher than ALT; this may reflect hepatic cell necrosis with release of mitochondrial AST. ALP plays an integral role in metabolism within the liver and development within the skeleton. Due to its widespread prevalence in these areas, its concentration in the bloodstream is used by diagnostician as a biomarker in helping determine diagnoses such as hepatitis or osteomalacia (Kim and Wyckoff, 1991).

The results of the study as presented in (Table 1 and Figure 1-4) showed that animal subjects who were not induced (Group 1) had the lowest levels total and conjugated bilirubin when compared with other groups. This explicitly underscores the fact that acetaminophen and the extract induced a spike in total and conjugated bilirubin which is indicators of hepatic and biliary injury.

The results also showed that total and conjugated bilirubin levels in the animal groups induced with acetaminophen, and concomitantly treated with the extract (group 3-5) were higher than those of the animals treated with distilled water only as well as those treated with acetaminophen only (group 1 and 2). This equally implies that the extract did not mitigate or annul the hepatotoxic effect of acetaminophen but rather amplified it.

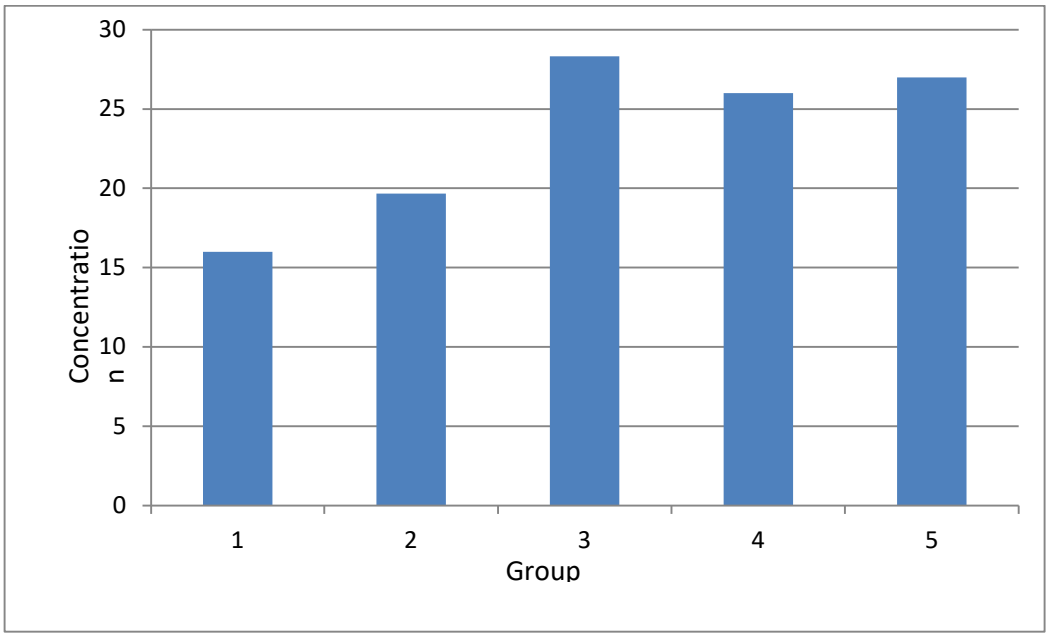

Figure 6: Alanine Transaminase of Experimental and Control Groups
Group 1: Distilled water only
Group 2: Acetaminophen only
Group 3: Acetaminophen and 100mg of the Extract
Group 4: Acetaminophen and 200mg of the Extract
Group 3: Acetaminophen and 300mg of the Extract

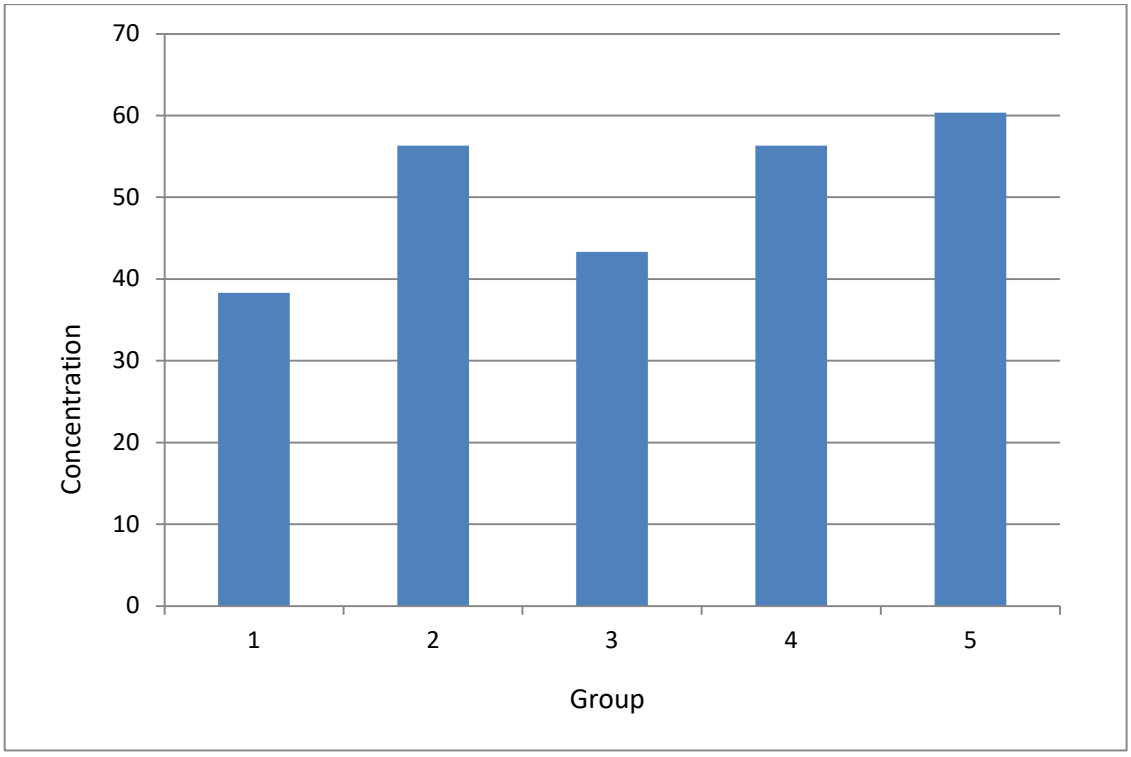

Figure 7: Alkaline Phosphatase of Experimental and Control Groups
Group 1: Distilled water only
Group 2: Acetaminophen only
Group 3: Acetaminophen and 100mg of the Extract
Group 4: Acetaminophen and 200mg of the Extract
Group 3: Acetaminophen and 300mg of the Extract

The observed increase in total and conjugated bilirubin followed a dose-dependent fashion. Animal subjects treated with 300mg/kg body weight had the highest while those that received the lowest dose had the lowest conjugated and total bilirubin.

Bilirubin is the end product of heme breakdown, and about 80% of bilirubin originates from degradation of erythrocyte haemoglobin in the reticuloendothelial system; while the remaining 20% comes from inefficient erythropoiesis in bone marrow and degradation of other heme proteins (Eva and Milan, 2013). Bilirubin is conjugated within the hepatocyte to glucuronic acid by a family of enzymes, termed uridine-diphosphoglucuronic glucuronosyltransferase (UDPGT). Conjugation is mandatory to render bilirubin aqueous soluble and facilitate its secretion across the canalicular membrane and excretion into bile (Owens *et al*, 2005).

Once unconjugated bilirubin arrives in the liver, liver enzyme UDP-glucuronyl transferase conjugates bilirubin with glucuronic acid to form bilirubin diglucuronide (conjugated bilirubin). Bilirubin that has been conjugated by the liver is water-soluble and excreted into the gallbladder (Owens et al, 2005).

Elevation of conjugated or direct bilirubin is termed conjugated hyperbilirubinemia and is a biochemical marker of cholestasis and hepatocellular dysfunction (Tripathi and Jialal, 2022).

On the average, animals that were treated with acetaminophen and the extract combined had higher AST, ALT, ALP, total and conjugated bilirubin than those treated with acetaminophen only. This observation could be attributed to adverse acetaminophen-extract interaction.

Drug-drug interactions (DDIs) refer to the effects produced when two or more drugs interact, potentially impacting the behavior of the drugs (Miranda *et al,* 2011). In certain circumstances, DDIs can cause adverse drug reactions (ADRs), which pose serious health hazards and life-threatening issues. The use of multiple drugs simultaneously increases the risk of DDIs, which can endanger patients' lives and lead to fatalities. DDIs pose a significant bottleneck for drug administration and patient safety, making them a critical factor affecting drug-related side effects and patient health (James *et al.,* 2006).

The results of this study did not agree with the result of Abirami *et al*, 2015. In 2015, Abirami and others conducted a research on Hepatoprotective effect of leaf extracts from *Citrus hystrix* and C. *maxima* against paracetamol induced liver injury in rats. All profiles of hepato-protective analysis indicate the *C. hystrix* and *C. maxima* (Red and White) leaves can serve as hepato-protectants as they restore all the liver function and oxidative stress markers to the desirable levels. Thus, the results of AST, ALT, ALP, total and conjugated bilirubin assay in this study have clearly demonstrated that the aqueous extract of *G. africanum* tendrils did not protect the liver.

Serum total protein, also known as total protein, is a clinical chemistry parameter representing the concentration of protein in serum. Serum contains many proteins including serum albumin, a variety of globulins, and many others. While it is possible to analyze these proteins individually, total protein is a relatively quick and inexpensive analysis that does not discriminate by protein type (Walker et al., 1990).

The measurement of protein is done on serum, which is the fluid that remains after plasma has clotted, thus removing fibrinogen and most of the clotting factors. Total protein content provides some information regarding a patient's general status; more clinically useful data are obtained from fractionating the total protein. The normal serum protein level is 6 to 8 g/dl. Albumin makes up 3.5 to 5.0 g/dl, and the remainder is the total globulins (Walker *et al,* 1990).

The only clinical situation that causes an elevation in serum albumin is acute dehydration. Variety of clinical entities result in a decreased albumin level, either from depressed synthesis or increased losses. A decrease in albumin synthesis is caused by end-stage liver disease, intestinal malabsorption syndromes, and protein-calorie malnutrition. Examples of albumin loss are nephrotic syndrome and severe burns because the skin is the most important extra storage pool for albumin. The consequence of a decrease in serum albumin is a shift of fluid from the intravascular to the interstitial space, resulting in intravascular volume depletion and edema formation (Walker *et al.,* 1990).

The results of total proteins and albumin analysis showed no decrease in the experimental animal subjects (group 1-3) when compared with the control. This suggests that acetaminophen and the extract did not induced hypoproteinaemia and hypoalbuminaemia. Further research into optimal extract dosages and the mechanisms underlying this dose-response relationship would be valuable for understanding the extract's potential as a hepatoprotective agent.

Conclusion

The results of this study have demonstrated that the co-administration of acetaminophen and the aqueous extract of *Gnetum africanum* tendrils to Wister rats induced the elevation of AST, ALT, ALP, total and conjugated bilirubin which are biomarkers of hepatic injury. It can therefore be concluded that the aqueous extract of *Gnetum africanum* tendrils did not counteract the hepatotoxic effect of acetaminophen but rather heightened it.

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