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RESEARCH ARTICLE

COMPARATIVE EVALUATION OF THE HEMATOLOGICAL AND HEPATIC EFFECTS OF ENERGY DRINKS AND CAFFEINE IN SPRAGUE-DAWLEY RATS

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ABSTRACT

The consumption of energy drink among youths and some adults has been on the increase in recent time, this has called for concerns over the possible effects these drink might have on some organs. This study therefore aimed to comparatively evaluate the effects of non-alcoholic energy drinks and caffeine on haematological and hepatic parameters as well as the histology of the liver. Fifty female Sprague Dawley rats (164–250 g) were divided into five groups (n=10 each): a control group, two energy drink treated groups (5 ml and 10 ml respectively), and two caffeine treated groups (0.89 mg/kg and 2.0 mg/kg respectively). Treatments were administered orally for six weeks. Hematological indices and liver function tests (ALT, AST, ALP, bilirubin, albumin, total protein, and globulin) were assessed at the end of the experimental period. Histopathological analysis of the liver was also performed. Findings showed no significant changes in liver enzymes or bilirubin levels. However, globulin levels significantly decreased in the treated groups. Most of the Hematological parameters, were not affected except for significant reductions in WBC, MID, RBC, HGB, MCV, MCHC, MPV, and P-LCR in the groups administered high doses of caffeine and non-alcoholic energy drinks , suggesting dose dependent bone marrow suppression. Histological analysis revealed normal liver architecture in controls, while treated groups showed vascular congestion, periportal inflammation, and Kupffer cell activation features consistent with portal hepatitis. In conclusion, frequent consumption of energy drinks and caffeine even in low concentrations pose health risks to the synthesis of liver proteins, alters liver histology and may impair haematopoiesis. These alterations are dose dependent; there is therefore need for caution to be taken in the frequent consumption of these substances and need for further study into their safety.

KEYWORDS

Energy drink, caffeine, liver function test, hematological indices, Sprague-Dawley rats

1. INTRODUCTION

The major constituents of Energy drinks (EDs) include caffeine, sugar, some kinds of sweeteners, in some cases herbal extracts. Occasionally vitamins, amino acids such as taurine are also included. They are often marketed as mental and physical performance enhancers, separating them from drinks that are designed to restore electrolytes, some macro nutrients and vitamins during exercise (Orru et al., 2018). Several brands and formulations exist globally, and the the most active ingredients caffeine, is largely responsible for the cognitive enhancing effects such as increased alertness and reaction time (McLellan, 2012; Van et al., 2008).

According to some studies EDs pose various health concerns even with the popularity of these drinks, especially among young adults under 25 years (Reissig et al., 2009; Seifert et al., 2011). Caffeine powder side effects According to a 2010 study by Higgins et al., extremely high levels of caffeine — far beyond the levels contained in a can of cola — can cause cardiac, neurological and psychological problems. Guarana, yohimbine and B vitamins, which are sometimes added to caffeine powder, can increase the effects of caffeine, as studied (Reissig et al., 2009; Sanchis-Gomar et al., 2015). Taking EDs with alcohol or taking large doses can also cause cardiac arrhythmias, hypertension and other behavioural problems as studied (Sanchis-Gomar et al., 2015).

The consumption of ED and Caffeine over a long period have been associated with hematological and hepatic dysfunction. Components of whole blood such as white blood cells, red blood cells, mean corpuscular volume and hemoglobin indices provide insights into bone marrow suppression and alterations in immune response (Isaac et al., 2013). The liver is an important organ in metabolism, protein synthesis and detoxification, and is particularly vulnerable to damage to components of energy drinks. Some studies have observed that excessive consumption of caffeine and energy drinks can result in inflammation of hepatic cells, necrosis and steatosis. Caffeine is also known to promote oxidative stress and trigger hepatocyte injury, which can progress to liver fibrosis. In addition, high doses of caffeine exposure in rats led to an increase in lipid droplet formation and increased liver enzymes, all markers of hepatic injury as reported by (Arroyave-Ospina et al., 2025).

There is growing evidence showing energy drink related health risks, with increasing studies focusing primarily on cognitive performance and to some extent acute and chronic cardiovascular responses. But there remains need for more comprehensive research data into other possible systemic effects especially on hematological and hepatic damage biomarkers from consumption of energy drinks and caffeine.

1.1 Justification of the Study

The recent increase in the emergency department (ED) use by nonprofessional populations has become a topic of great interest and is a

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major public health issue. Although EDs are considered to be safe for certain groups of populations, they may cause adverse effects to non-tolerant individuals. It is widely accepted that EDs serve to enhance physical performance and consist of large amounts of caffeine along with mixtures of other ingredients such as taurine, guarana and B-vitamins which were evaluated (Higgins et al., 2010; Reissig et al., 2009). While the noxious effects of EDs on cognition and cardiovascular systems have been studied extensively, there is a lack of information regarding their adverse effects on blood and liver functions.

Caffeine which is the primary stimulant in most EDs, have been associated with damage to liver tissue (hepatocellular damage), oxidative stress, mostly when present in high concentration and consumed over a long time (chronic use) (Arroyave-Ospina et al., 2025). Alterations in some hematological indices like altered blood cell counts may indicate bone marrow suppression and immune system can be compromised (Isaac et al., 2013). The liver is an important organ involved in both detoxification and synthesis of plasma proteins, investigating the systemic effects of EDs and caffeine is important is very crucial due to increase in their consumption. Furthermore, histopathological assessment provides important insights into organ specific damage that biochemical tests alone may not reveal. This study therefore aims to bridge these knowledge gaps with a comprehensive comparative analysis.

1.2 Aim of the Study

This primary aim of this study is to determine the effects of non-alcoholic EDs drinks and caffeine on some haematological indices, liver function and histopathological changes in the liver of female Sprague Dawley rats.

2. Materials And Methods

2.1 Experimental Animals

Fifty (50) healthy Sprague Dawley rats weighing between 164 - 250 g, obtained from the University of Ibadan were used in this study. The animals were housed in the Department of Pharmacology and Toxicology animal house of the University of Benin. They were allowed to acclimatize to their new environment for two (2) weeks under standard laboratory conditions with free access to food and water, and treated in line with the National Research Council (NRC) guidelines for the use of laboratory animals (NRC, 2011).

2.2 Experimental Design

After the acclimatization process all animals were randomly selected into five groups (n=10). Group 1 served as control, receiving water and standard rat pellets; Group 2 and 3 were administered 5 and 10 ml of non-alcoholic energy drink respectively; while Groups 4 and 5 received 5- and 10-ml caffeine (0.89 mg/kg and 2 mg/kg, respectively). Treatment with the non-alcoholic energy drink and caffeine was administered orally with an orogastric gavage for four weeks.

2.3 Sample Collection

At the end of the study period, all rats were anesthetized using chloroform fume in an airtight glass chamber and whole blood collected via cardiac puncture into plain and EDTA bottles for hematological and biochemical analysis. The liver was collected after dissection of the whole animal under anesthetize and fixed in 10% formalin for histological evaluation.

2.3.1 Hematological Analysis

Full blood count (FBC) was conducted using automated hematology analyzers based on electrical impedance and laser flow cytometry (Dacie and Lewis, 2017; Kim et al., 2020).

2.3.2 Liver Function Tests

Serum biochemical markers were analyzed to assess liver function. ALT and AST levels were measured using the Reitman-Frankel method (Reitman and Frankel, 1957). ALP activity was determined via the colorimetric method using p-nitrophenylphosphate substrate (Rec. GSCC, 1972). Total and conjugated bilirubins were quantified using the diazotized sulphanilic acid method (Jendiasik and Grof, 1939; Tripathi and Jialal, 2024). Total protein was measured by the Biuret method, while albumin was determined using the bromocresol green (BCG) dye-binding method (Weichselbaum, 1887; Grant et al., 1987). Globulin was calculated by subtracting albumin from total protein (Jolles et al., 2014).

2.3.3 Histological Procedures

Harvested organ were fixed in 10% formalin, and dehydrated in varying grades of alcohol, xylene cleared and embedded in paraffin. Section of about 4 - 5 µm were cut using a microtome a method described (Carson, 2002). The tissues were then stained with Hematoxylin and Eosin dyes (H&E). The slides were viewed under a light microscope at x400 magnification and photomicrographs captured.

2.4 Statistical Analysis

Statistical analysis was carried out using GraphPad prism 10.0.1. One-way analysis of variance was utilized to compare the means and result presented as mean±SEM. Dunnett's post hoc text was carried out to access the differences among the means, and a P value of less than 0.05 was considered statistically significant.

3. Results

Table 1: Effect of Energy Drink and Caffeine on Liver Function Parameters

Parameter		Control	Energy Drink (5 ml)	Energy Drink (10 ml)	Caffeine (5 ml)	Caffeine (10 ml)
Total bilirubin (mg/dL)	Mean± SEM	0.26±0.02449	0.24±0.02449	0.26±0.02449	0.22±0.02	0.26±0.02449
Conjugated bilirubin (mg/dL)	Mean± SEM	0.1±0.0	0.1±0.0	0.1±0.0	0.1±0.0	0.1±0.0
Alkaline phosphatase (U/L)	Mean± SEM	231.4±6.431	290.4±52.14	225.6±37.43	286.8±3.353	227±12.93
Aspartate aminotransferase (U/L)	Mean± SEM	251±24.55	282.4±78.61	315.8±73.58	264.2±10.94	274±17.56
Alanine aminotransferase (U/L)	Mean± SEM	21.4±0.9274	22.2±2.035	25.6±2.694	20.2±1.02	25.4±3.881

*p<0.05 compared to control; [a]p<0.05 compared to energy drink (5 ml); [b]p<0.05 compared to energy drink (10 ml); [c]p<0.05 compared to caffeine (5 ml)

Effect on Liver Function Parameters: total and conjugated bilirubin levels remained unchanged across all groups.

Alkaline phosphatase (ALP) levels increased in both the 5 ml energy drink and the 5 ml caffeine groups compared to the control, though not significantly. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels showed mild, non-significant elevations in all treated groups, with the 10 ml energy drink group having the highest AST value (315.8 ± 73.58 U/L). No statistically significant alterations in liver function enzymes were observed between groups.

Table 2: Effect of Energy Drink and Caffeine on Red Blood Cell Indices

Parameters		Control	Energy Drink (5 ml)	Energy Drink (10 ml)	Caffeine (5 ml)	Caffeine (10 ml)
Red blood cell count (10^6/µL)	Mean± SEM	6.276±0.253	5.526±0.5749	5.678±0.3389	6.59± 0.1854	4.9± 0.4069^{c}
Haemoglobin concentration (g/dl)	Mean± SEM	13.96±0.6038	12.32±1.115	12.74±0.7698	15.04± 0.6266^{c}	10.76± 1.216^{c}
Haematocrit (%)	Mean± SEM	38.28±1.532	34.52±2.917	35.64±1.965	39.02± 1.215	31.54± 3.353
Mean corpuscular volume (µm^3)	Mean± SEM	61.08±0.372	63.26±1.54	62.92±0.8576	57.3± 2.284^{ab}	61.6± 0.5357
Mean corpuscular haemoglobin (pg)	Mean± SEM	22.2±0.1304	23.6±1.163	22.38±0.2154	22.54± 0.4622	21.06± 0.5609
Mean corpuscular haemoglobin concentration (g/dl)	Mean± SEM	36.4±0.2588	35.56±0.3203	35.66±0.4106	38.26± 0.5016^{aab}	34.14± 0.7865^{*cccc}
Red Blood Cell Distribution Width-Standard Deviation (µm^3)	Mean± SEM	34.6±1.261	36.74±2.826	103.9±70.28	31.38± 0.9372	31.84± 1.653
Red Blood Cell Distribution Width - Coefficient of Variation (%)	Mean± SEM	15.92±0.5352	16.42±0.9578	45.34±29.92	14.88± 0.3121	14.62± 0.4705

*p<0.05 compared to control; ^{a}p<0.05 compared to energy drink (5 ml); ^{b}p<0.05 compared to energy drink (10 ml); ^{c}p<0.05 compared to caffeine (5 ml)

3.1 Red Blood Cell Indices

Administration of energy drinks and caffeine produced varying effects on red blood cell indices.

There was a statistically significant decrease in red blood cell count in the 10 ml caffeine treated group compared to control and the other treatment groups (4.9 ± 0.4069 × 10^6/µL, p<0.05). at the same time, 5 ml caffeine showed no statistically significant increase in red blood cell count compared to control (6.59 ± 0.1854 × 10^6/µL). Also, Haemoglobin concentration followed a similar trend, showing a statistically significant decrease in the 10 ml caffeine group (10.76 ± 1.216 g/dL, p<0.05) and a significant increase in the 5 ml caffeine group (15.04 ± 0.6266 g/dL, p<0.05) compared to control.

Haematocrit levels remained relatively stable, although the 10 ml caffeine group showed a marked reduction (31.54 ± 3.353%) compared to the control (38.28 ± 1.532%). At the same time, there was a significant decrease in mean corpuscular volume in the 5 ml caffeine group (57.3 ± 2.284 µm^3, p<0.05 vs. energy drink groups). Mean corpuscular haemoglobin concentration (MCHC) was significantly increased in the 5 ml caffeine group (38.26 ± 0.5016 g/dL, p<0.05), while it was statistically significantly decreased in the 10 ml caffeine group (34.14 ± 0.7865 g/dL, p<0.05 vs. control). No significant changes were observed in mean corpuscular haemoglobin (MCH) or red cell distribution width (RDW) across most groups. However, a there was marked increase in RDW-SD and RDW-CV in the 10 ml energy drink group, although this was not statistically significant due to high variability.

Table 3: Effect of Energy Drink and Caffeine on white Blood Cell and platelet Indices

		Control	Energy Drink (5 ml)	Energy Drink (10 ml)	Caffeine (5 ml)	Caffeine (10 ml)
Platelet count (10^3/µL)	Mean± SEM	752.2±97.07	2496±1240	978.2±195.8	625±73	429.6± 163
Mean platelet volume (µm^3)	Mean± SEM	7.66±0.1536	7.82±0.1828	7.66±0.2977	6.78±0.201^{a}	7.18± 0.2223
Platelet Distribution Width (%)	Mean± SEM	9.44±0.5671	8.78±0.5453	8.05±0.0866	8.78±0.2059	8.74± 0.172
Plateletcrit (%)	Mean± SEM	0.572±0.07984	0.716±0.1457	0.762±0.1699	0.406±0.06911	0.256± 0.1263
Platelet Large Cell Ratio (%)	Mean± SEM	8.98±1.974	11.88±1.568	11.26±2.112	1.8±0.9874$^{*aab b}$	8.58± 1.347
White blood cell count (103/µL)	Mean± SEM	10.14±1.756	7.56±0.7567	6.48±1.03	9.74± 1.168	2.92± 0.1068^{**cc}
Lymphocyte (%)	Mean± SEM	67.12±2.611	61.56±6.161	47.46±11.09	66.92± 1.269	61.56± 0.397
mid-sized white blood cells (%)	Mean± SEM	15.34±0.9212	17.24±1.026	13.92±3.012	16.84± 0.6757	18.1± 0.5908
Granulocyte count (%)	Mean± SEM	17.54±2.115	21.2±6.349	15.44±2.508	16.02± 0.72	21.42± 0.414
Lymphocyte (103/µL)	Mean± SEM	6.800±1.361	4.680±0.7193	4.000±0.8562	6.620± 0.7819	5.300± 3.426
mid-sized white blood cells (103/µL)	Mean± SEM	1.520±0.1828	1.320±0.1744	1.160±0.1470	1.720± 0.2800	0.3600± 0.05099^{**abcc}
Granulocyte count (103/µL)	Mean± SEM	1.760±0.3187	1.560±0.4578	1.320±0.3072	1.720± 0.3555	0.5600± 0.05099

*p<0.05 compared to control; ^{a}p<0.05 compared to energy drink (5 ml); ^{b}p<0.05 compared to energy drink (10 ml); ^{c}p<0.05 compared to caffeine (5 ml)

3.2 White Blood Cell and Platelet Indices

Significant alterations in white blood cell (WBC) and platelet parameters

were also observed following treatment. Platelet count was markedly elevated in the 5 ml energy drink group (2496 ± 1240 × 10^3/µL), although with high variability, while it was substantially reduced in the 10 ml caffeine group (429.6 ± 163 × 10^3/µL). Mean platelet volume (MPV) was significantly decreased in the 5 ml caffeine group (6.78 ± 0.201 µm^3, p<0.05 vs. 5 ml energy drink group), with no significant differences in platelet distribution width (PDW) or plateletcrit. There was a sigificant decrease in platelet large cell ratio (P-LCR) in the 5 ml caffeine group (1.8 ± 0.9874%, p<0.05 compared to all groups). WBC count was also significantly reduced in the 10 ml caffeine group (2.92 ± 0.1068 × 10^3/µL, p<0.01 vs. control and other groups). A similar pattern was observed in mid-sized white blood cells (mid WBC), with the 10 ml caffeine group showing a significant reduction (0.3600 ± 0.05099 × 10^3/µL, p<0.01 vs. control, 5 ml energy drink, and 5 ml caffeine). Lymphocyte percentages remained relatively stable across groups, though absolute lymphocyte counts declined with increasing energy drink dose. Granulocyte counts also decli.

3.3 Histology of the liver

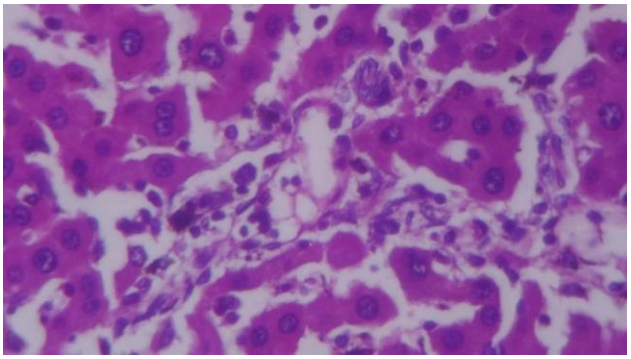

Plate 1: Rat liver control, show: normal architecture: hepatocytes (HC), sinusoids (SI), portal vein (PV) and bile ducts (BD): H&E 400 X

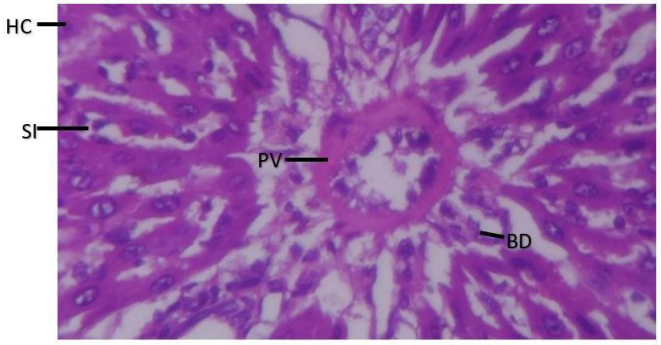

Plate 2: Rat liver control, show: normal architecture: hepatocytes (HC), sinusoids (SI), portal vein (PV) and bile ducts (BD) : H&E 400 X

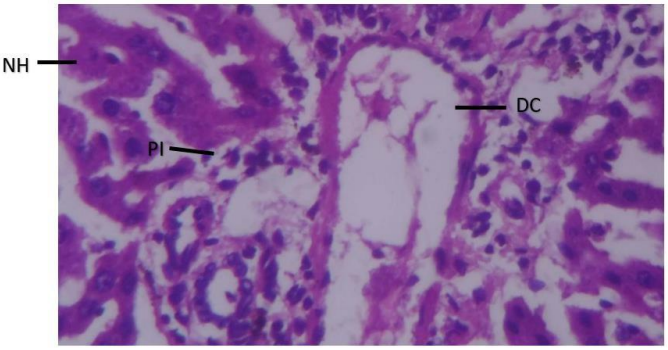

Plate 3: Rat liver given 5ml energy drink show: hepatocytes (HC), congestion and marked vasodilatation (DC) and periportal Infiltrates of inflammatory cells (PI): H&E 400 X

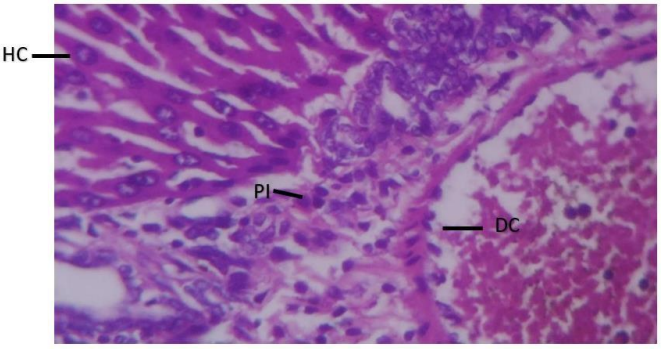

Plate 4: Rat liver given 5ml energy drink show: hepatocytes (HC), congestion and marked vasodilatation (DC) and periportal Infiltrates of inflammatory cells (PI): H&E 400 X

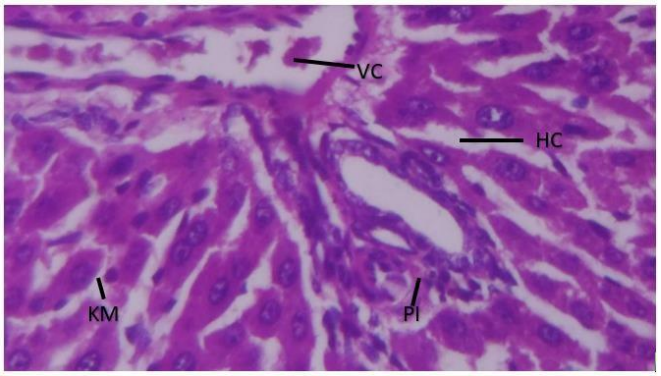

Plate 5: Rat liver given 10ml energy drink show: hepatocytes (HC), vascular congestion (VC), mild periportal infltrates of inflammatory cells (PI), kupffer cell activation (KM): H&E 400 X

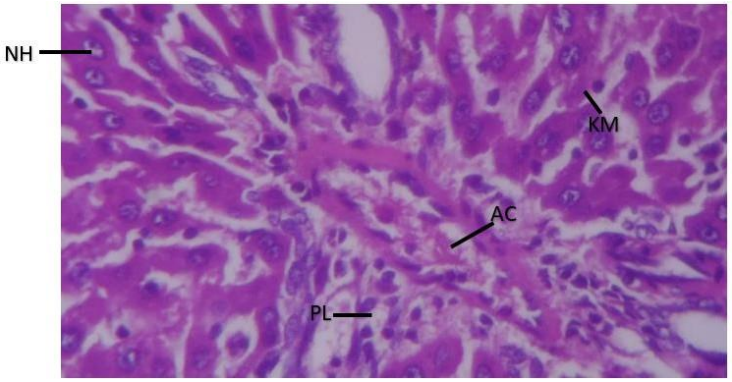

Plate 6: Rat liver given 10ml energy drink show: hepatocytes (HC), vascular congestion (VC), mild periportal infltrates of inflammatory cells (PI), kupffer cell activation (KM): H&E 400 X

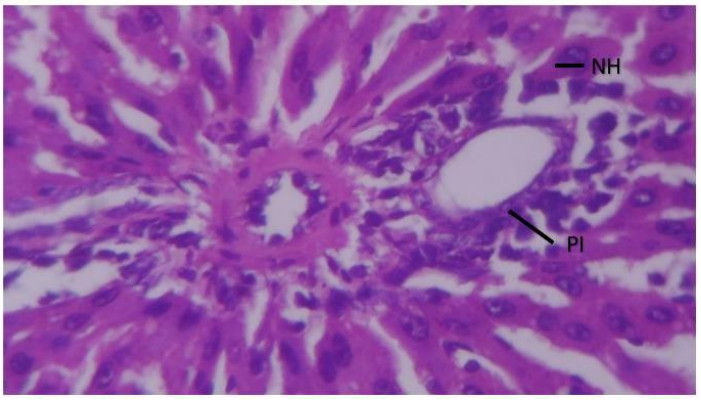

Plate 7: Rat liver given 5ml Caffeine show: normal hepatocytes (NH), periportal infiltrates of inflammatory cells (PI): H&E 400 X

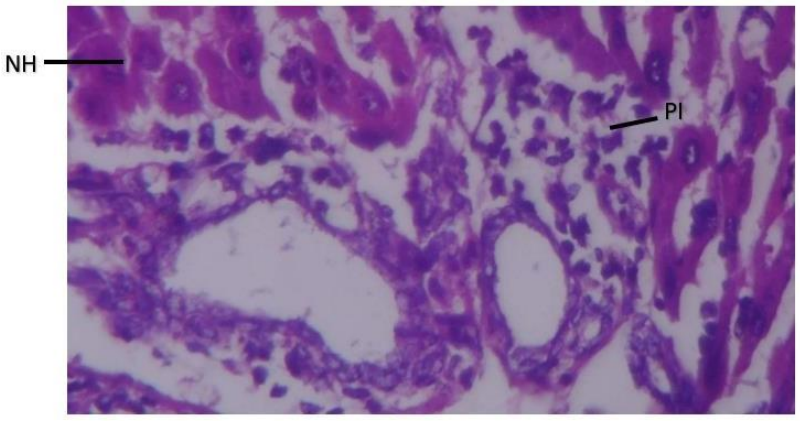

Plate 8: Rat liver given 5ml Caffeine show: normal hepatocytes (NH), periportal infiltrates of inflammatory cells (PI) : H&E 400 X

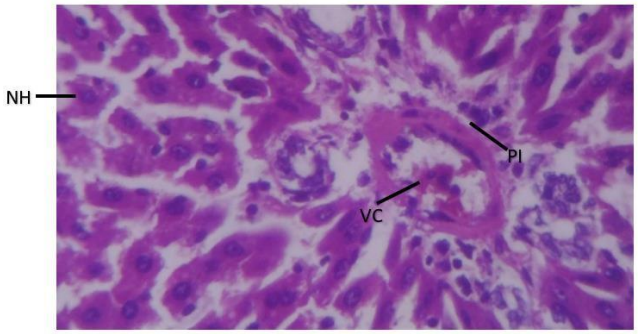

Plate 9: Rat liver given 10ml Caffeine show: normal hepatocytes (NH), vascular congestion (VC) and mild periportal infiltrates of inflammatory cells (PI): H&E 400 X

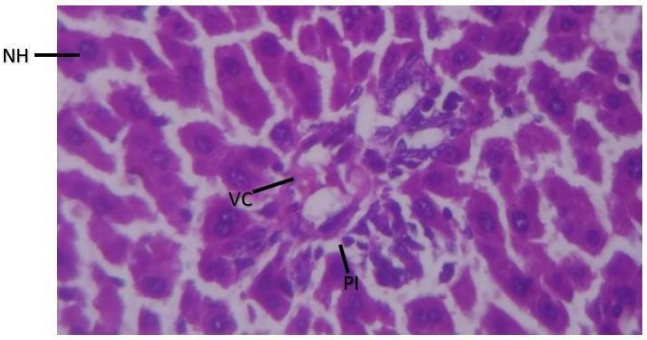

Plate 10: Rat liver given 10ml Caffeine show: normal hepatocytes (NH), vascular congestion (VC) and mild periportal infiltrates of inflammatory cells (PI): H&E 400 X

4. Discussion

This study evaluated the effects of energy drinks and caffeine on hematological and hepatic parameters in Sprague-Dawley rats.

4.1 Hematological Effects

In this study, there was no statistically significant difference in lymphocytes (LYM), mid-sized cells (MID), granulocytes (GRAN), hematocrit (HCT), mean corpuscular hemoglobin (MCH), red cell distribution width (RDW-SD and RDW-CV), platelet count (PLT), and plateletcrit (PCT) across treatment groups compared to controls.

There was however a significant decrease in total white blood cells (WBC), MID, red blood cells (RBC), hemoglobin (HGB), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), mean platelet volume (MPV), and platelet-large cell ratio (P-LCR), especially in the high-dose caffeine (10 ml) and energy drink groups. These reductions indicate a possible dose-dependent hematopoietic suppression, which could be affecting the immune response and hematopoiesis. A group researcher linked similar leukopenic effects to high caffeine doses, while other researcher described caffeine-induced bone marrow suppression (Deldicque et al., 2008; Nawrot et al., 2003).

Reports recorded contrasts with our study as they reported a significant increase in WBC, RBC and haemoglobin levels after regular energy drink intake, and linked their findings to possible erythropoietic stimulation or immune activation (Jabbar and Al-Hakkak, 2024). However, findings from this current study were consistent with the report from who reported reduction in red blood cell indices and platelet activation (Pallangyo et al., 2023). This study observed a reduction in MPV and P-LCR which may point towards alteration thrombopoiesis and increased platelet activation. A study by linked chronic consumption of energy drink with disruptions of the body;s clotting mechanisms, suggesting a potential for long term hematological disruptions with chronic energy drink or caffeine consumption (Pallangyo et al., 2023).

4.2 Hepatic Effects

Results from this study showed that liver enzymes in Sprague Dawley rat's models were significantly altered by the consumption of energy drinks and their components. However, when total and conjugated bilirubin levels across the experimental groups and the control group were compared, there was no statistically significant difference. Our finding aligns with the work of who recorded no significant changes in direct or total bilirubin following the intake of 250 ml of Wild Tiger beverage in human subjects (Salim, 2018). Conversely, it contradicts the findings of who reported a significant increase in total bilirubin levels after prolonged energy drink consumption (Mihaiescu et al., 2024). The disparities in these results can be associated with the duration of the studies. There was also no statistically significant difference in total and conjugated bilirubin suggesting that the liver maintained its ability to metabolize hemoglobin and conjugate bilirubin with glucuronic acid, showing normal hepatic function.

In addition, there were also no statistically significant differences in Alkaline Phosphatase (ALP) levels between any of the experimental groups and the control group. This result is consistent with studies by who reported no change in ALP activity following oral administration of 100 mg/kg of caffeine, and also observed similar results after long-term caffeine administration (Bassey et al., 2017; Moneim et al., 2009). However, a group researcher found a significant increase in ALP levels in rats administered two doses of a high-energy drink (Bukhar et al., 2012). ALP is a class of isoenzymes found in the cytosol of liver cells, the fact that the ALP levels in this study were not increased, suggest that the rats did not experience acute liver damage or dysfunction (Lowe et al., 2023).

Similarly, there was no statistically significant difference in aspartate transaminase (AST) levels across the groups compared with the control. This report agrees with whose study showed no significant difference in AST after long term caffeine administration in a rat model (Moneim et al., 2009). However, this result is in contrast to the work of which recorded a significant decrease in AST after administering Hype energy drink (Adibsaber et al., 2023). Also, some researcher observed an increase in AST after just two doses of high energy drink (Bukhar et al., 2012). After several weeks of energy drink administration also recorded a significant increase in AST (Elbendary et al., 2023). The normal levels of AST observed in our study suggest the absence of acute liver injury or dysfunction and this may be attributed to the duration of the study and concentrations of the various constituents of the EDs.

There were no statistically significant differences in levels of Alanine

Transaminase (ALT) when experimental groups were compared with control group. This is in agreement with both of whom reported no significant changes in ALT following prolonged caffeine or energy drink administration (Moneim et al., 2009; Elbendary et al., 2023). However, this finding contradicts who reported a significant increase in ALT, the absence of significant ALT alterations observed in this study suggests stable liver function without acute damage (Bukhar et al., 2012).

For total protein levels, a statistically significant decrease was noted in the 5 ml and 10 ml caffeine groups compared to the control, while the energy drink groups showed no significant differences. This aligns with findings by who reported no significant changes in total protein after oral caffeine or energy, drink administration (Bassey et al., 2017; Moneim et al., 2009; Bassey et al., 2017). The decrease in total protein levels in the caffeine treated groups could be a sign of slow decline in the synthetic function of the liver.

Albumin levels showed no statistically significant differences among all groups. This is consistent with reports by who observed no significant changes in albumin levels after caffeine administration (Moneim et al., 2009; Bassey et al., 2017). It also contrasts with who reported a significant decrease in serum albumin after energy drink administration (Bassey et al., 2017). The stability of albumin levels in this study suggests preserved liver function and no adverse effects on overall health.

However there was a statistically significant decrease in globulin concentrations in groups administered 5 ml and 10 ml caffeine compared to the control group, while no significant differences were seen in the energy drink groups. This findings did not aligns with studies by who which reported no changes in globulin after caffeine administration (Moneim et al., 2009; Bassey et al., 2017). It also contradicts who reported a significant decrease in globulin levels following energy drink treatment (Bassey et al., 2017). The decrease in globulin observed with caffeine may reflect impaired liver synthetic function, which could be associated with conditions such as liver disease (e.g., cirrhosis) or inflammation, given globulin's role in immune function.

Histopathological evaluation of the liver in rats treated with non-alcoholic energy drinks and caffeine showed structural changes such as congestion, vasodilatation, and periportal inflammatory infiltrates, suggesting the onset of portal hepatitis. These findings are in line with the study conducted by who observed liver damage characterized by inflammatory cell infiltration and activation of Kupffer cells following caffeine consumption (Khayyat et al., 2015). The activation of Kupffer cells signifies the liver's immune response to injury. Furthermore, the present study demonstrated a dose-dependent response, where the severity of liver damage increased with higher doses of energy drinks and caffeine. This is consistent with who also reported that higher doses of caffeine led to more significant liver inflammation (Abd El-Rahman, 2020). Similarly, a group researchers found that caffeine consumption increases liver inflammation and activates immune responses in a dose-dependent manner, reinforcing the hepatotoxic potential of prolonged or high-dose intake of caffeine and energy drinks (Kutia et al., 2020).

5. Conclusion

This comparative study concludes that while moderate consumption of energy drinks and caffeine does not significantly affect most hematological and hepatic indices, high dose administration especially of caffeine may result in bone marrow suppression and reduced hepatic protein synthesis. Decreases in WBC, RBC, HGB, MCHC, MID, MPV, and globulin levels raise concerns over potential immune compromise, anemia, and altered hemostasis. Also the presence of infiltrates of inflammatory cells in the histology slides indicates the onset of hepatocytes damage and the level of damage is dose dependent. These findings support previous reports of caffeine-related hematopoietic suppression and histological alterations; the decrease in levels of total protein and globulin levels is a pointer to the decline in the synthetic function of the liver. There is therefore need for further longitudinal studies to better assess the chronic safety profile of these commonly consumed beverages.

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