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Cardiotoxic Effects of Red Bull and Monster Energy Drinks in Developing Rats: Evidence of Dose-Dependent Myocardial Necrosis and Hemorrhage

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Abstract: Energy drinks (EDs), e.g., Red Bull and Monster, are popular among adolescents and young; however, their cardiovascular adverse effects are a matter of concern given their high content of caffeine, taurine, and sugars. The aim of the study was to examine impact of two of the most common commercial energy drinks on the histological structure of the cardiac tissue for immature male albino rats. **Methods**: Forty young albinos male rats (5–6 weeks old, 120–140 g) were randomly divided into five groups (8 each). The control group was administrated normal diet and tap water. The initial group treated (T1) received Red Bull at a dose of 3.57 ml/kg, the second (T2) was 2xT1. T3 and T4 were injected with monster at the above dosages. The beverages were offered daily for 45d orally. After experiment, animals were killed with an overdose of anesthesia, and their hearts were excised and mounted for microscopic observation by conventional histological techniques. **Results**: In the control group, the heart was healthy and normal in appearance. Slight thinning of muscle fibers and mild disorganization were noticed in T1. T2 had more severe damage was characterized by tissue disruption, hemorrhage and necrosis. T3 also demonstrated moderate damage, with most severe changes observed in T4, which received the highest level of exposure to Monster (extensive tissue damage, fiber-interstitial bleeding, and cell necrosis). **Conclusion**: Prolonged consumption of energy drinks, especially at high doses, induced severe structural damage in cardiac tissue of growing rats, raising concerns about the safety of energy drink consumption among adolescents and young adults.

Keywords: Energy drinks, Histopathology, Cardiac tissue, Immature rats, Myocardial damage.

Introduction

Energy Drinks (EDs), including Monster and Red Bull, are increasingly popular all over the world, particularly among young adults and adolescents. They were branded as physical and mental performance enhancers as a result of their high concentration of caffeine and other bioactive compounds such as ginseng, taurine, glucose, and B-vitamins (1, 2). In 2020, the global energy drink market was valued at $45.8 billion, with Red Bull holding over 50% of total revenue (3). The primary stimulant in energy drinks is caffeine. While moderate consumption can promote alertness as well as physical functioning, excessive consumption has been associated with adverse cardiovascular, metabolic, and neurological effects like tachycardia, arrhythmia, insomnia, anxiety, and hypertension (4–6). The cognitive effects of caffeine have been rigorously studied, but less rigorous study has been afforded to other ingredients like taurine and sugar-although they might also contribute to inducing adverse physiological changes (7,8). Present data in laboratory animals show evidence that long-term exposure to energy drinks (EDs) can result in histological disturbances of some organs, especially the heart, the morphological changes observed are loss of structural organization of the myocardial fibers, necrosis, cytoplasmic vacuolation, and inflammatory infiltration (9,10). The same effects are amplified when EDs are taken in developing years of life, as immature cardiomyocytes are more prone to both structural and electrophysiological alterations (11,12). Moreover, preclinical studies indicate that heightened calcium level in the cardiomyocytes, secondary to caffeine and other stimulants, results in calcium toxicity within the myocardium, causing arrhythmias and myocardial injury (13,14). In humans, however, clinical cases report on cardiac complications of extreme ED consumption such as ventricular tachycardia and cardiac arrest—especially when coupled with alcohol/ stress (15–17). This emerging evidence has raised concerns to public health,

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particularly regarding the high prevalence of consumption by young people (18,19). Clinical adverse effects of energy drinks including tachycardia, hypertension, and insomnia have been previously described, but the majority of studies are based on signs or symptoms that do not necessarily prove a particular pathophysiological pathway. There is limited histopathological data, especially in immature cardiac tissue which is more susceptible to exogenous insults. This study has therefore been designed to address this lack of knowledge by describing the detailed histological changes on myocardium and by comparing the dose-dependent structural cardiac effects of two most commonly used energy drinks (Red Bull & Monster).

Materials and Methods

Ethical approval

All experimental procedures involving laboratory animals in this study, were conducted in full compliance with institutional ethical standards. The study received prior approval from the Institutional Research Ethics Committee at the College of Education, University of Al-Qadisiyah, Iraq, (Approval No. 13- 19/1/2025). Animal care and handling followed established guidelines to ensure humane treatment, minimize discomfort, and uphold the integrity of the research process.

Experimental Animals

The study was conducted using forty immature male albino rats of 120–140 g body weight and 5–6 weeks of age. The animals were obtained from the College of Education, University of Al-Qadisiyah, animal house, Biology Department. Animals were maintained in controlled laboratory conditions (temperature 25 ± 2°C, photoperiod of 12 hours) and fed with a standard laboratory chow with free access to water during the experiment.

Experimental Design

In this study, immature male albino rats of 5–6 weeks old with weights ranging between 120–140 g were employed. The rats were randomly divided into 5 groups (8 animals per group), based upon their matched body weight and age to achieve homogeneity among the groups, to limit the bias, and to adjust variability as follows:

- **Group C (Control):** Received only standard food and tap water.
- **Group T1:** Received Red Bull orally at a dose of 3.57 ml/kg body weight.
- **Group T2:** Received a double dose of Red Bull (7.14 ml/kg body weight).
- **Group T3:** Received Monster energy drink at a dose of 3.57 ml/kg body weight.
- **Group T4:** Received a double dose of Monster (7.14 ml/kg body weight).

The drinks were administered daily for 45 consecutive days orally via gastric tube. The dosage was based on previously established protocols concerning human equivalent doses and studies on energy drink poisoning (1,9).

Dose Determination

The selected dose of 3.57 ml/kg for the T1 group was calculated based on a standard human equivalent consumption. A typical energy drink can (250 ml) is commonly consumed by an average adult weighing approximately 70 kg. Thus, the human intake per body weight is approximately 3.57 ml/kg (250 ml ÷ 70 kg). This value was directly translated to rats by adjusting for body weight, without applying a correction factor, as the goal was to simulate real-world human consumption levels in a comparable manner. This approach aligns with previous toxicological studies using volume-per-body-weight scaling for liquid substances in rodents (1,9).

Comparison of Red Bull Vs. Monster Energy Drink Contents

The composition difference between Red Bull and Monster in energy drinks is summarized in Table 1, which can explain the mode differences from the aspect of composition in the toxic effects on the heart. The comparison is made between the caffeine, sugar, additional stimulants, and other formulation components that might have an impact on the myocardial response (6).

Table 1. Red Bull vs Monster Energy Drink Composition, and Scientific Relevance

Component	Red Bull (250 ml)	Monster (250 ml)	Scientific Relevance
Caffeine	80 mg	~85 mg	Similar levels; Monster may contain slightly more depending on batch.
Taurine	1000 mg	1000 mg	Identical concentration.
Sugar	27 g	27 g	Equal sugar content; may contribute to oxidative stress.
Carbohydrates	27 g	29 g	Slightly higher in Monster.
Guarana	Absent	Present	Additional source of caffeine in Monster.
Ginseng	Absent	Present	Herbal stimulant; may enhance physiological

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			effects.
L-carnitine	Absent	Present	Implicated in metabolic stimulation.
B Vitamins	B3, B5, B6, B12	B2, B3, B6, B12	Red Bull includes B5; Monster includes B2.
Flavor Profile	Single standard flavor	Multi-flavored variants	Monster's variety may promote overconsumption, especially in youth.

Sample Collection and Histological Preparation

At the end of experimental time, all the animals were anesthetized and euthanized humanely by inhalation of chloroform under the guidelines established by the institution for the use and care of laboratory animals. Hearts were excised immediately, washed with normal saline, and fixed in 10% neutral buffered formalin for 48 hours. Fixed tissues were then processed by routine histological procedure: dehydration in rising grades of ethanol, clearing in xylene, and embedding in paraffin wax. 5 µm thick sections were sectioned on a rotary microtome and stained with hematoxylin and eosin (H&E) for microscopy (20, 21).

Microscopic Examination

Histological slides were observed by light microscope (Olympus, Japan) at different magnifications (10x, 40x, 100x). Structural changes such as alterations in the orientation of myocardial fibers, nuclear morphology, hemorrhage, and necrosis were analyzed using descriptive approach. Observations were qualitatively displayed in a comparative table 1 to indicate the extent of tissue damage in all groups.

Microscopic Examination of Cardiac Tissue

Histological investigation of the hematoxylin and eosin (H&E) stained sections of cardiac tissues indicated dose-related changes in the myocardial architecture among the tested rats.

Control Group (C)

Control group samples showed normal histological structure of the cardiac tissue. At low power (Figure 1A), the myocardial fibers were well oriented in regular, parallel fashion, which were striated with preserved structural integrity. At greater magnification (Figure 2), cardiomyocyte nuclei were seen to be elongated and peripheral to the cells, as would be expected of normal myocardium. The specimen did not show degeneration, hemorrhage, or necrosis. These values are for comparison with the treated ones (treated). Signs are indicated by arrows in Figures 1 and 2. Arrowheads in Figure 1 indicate the alignment of muscular fibers and organization of general tissue, and in Figure 2 are used to indicate the elongated peripheral nuclei - illustrating no pathological changes.

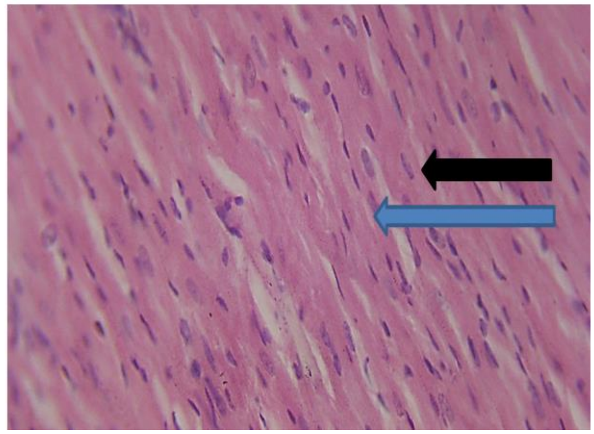

Figure 1: Histological section of heart tissue in the control group showing normal cardiac muscle fibers with regular alignment and peripheral nuclei. (H&E stain, low magnification)

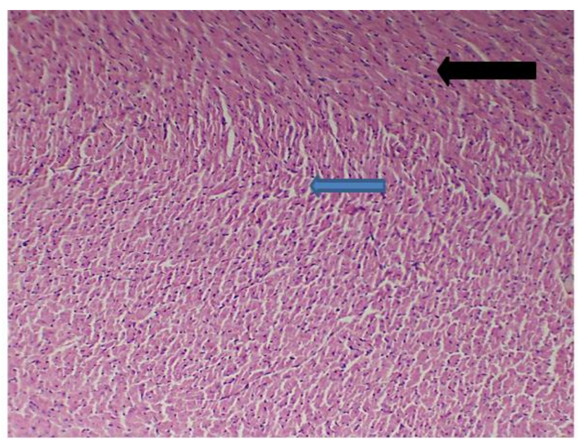

Figure 2: Higher magnification of heart tissue in the control group confirming intact myocardial architecture and absence of pathological changes. (H&E stain, high magnification)

Group T1 (Red Bull 3.57 ml/kg)

Cardiac specimens of the T1 group, which were treated with a low dose of Red Bull (3.57 ml/kg), showed early histological changes with respect to the control group. At a lower magnification (Figure 3), the myocardial fibers exhibited slight loss of architectural alignment with the presence of atrophy and rounding of the fiber profiles. Interfibrillar spaces were moderately widened, indicating tissue stress at early stages.

At greater magnification (Figure 4), subtle degenerative changes were more apparent. The cardiac muscle fibres showed decreased diameter and partial disarrangement.

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From Nuclea nuclei appeared shrunken and concentrated (pyknotic), indicating early nuclear condensation, which is a characteristic of cells under stress. Of note, no bleeding or necrosis occurred at this stage.

Arrows in Figures 3 and 4 help in pointing out major pathological findings. The disordered distribution and degenerative muscle fibers are shown in figure 3 with arrows. Pyknotic nuclei and disarray between fibers (arrows) reveal early, yet non-lethal myocardial injury in Figure 4.

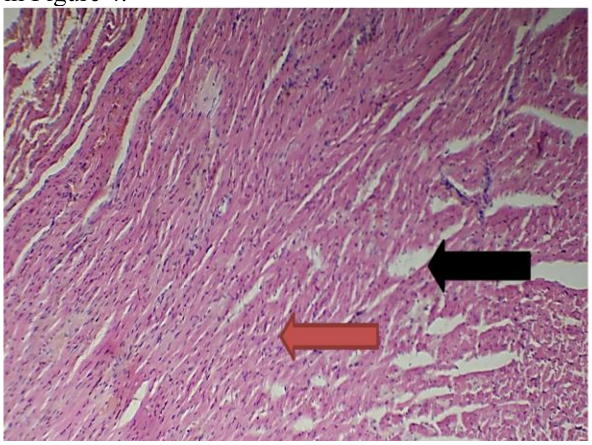

Figure 3: Heart tissue from group T1 (Red Bull 3.57 ml/kg) showing disorganized and atrophied cardiac fibers with spherical nuclei and widened inter-fiber spaces. (H&E stain, low magnification)

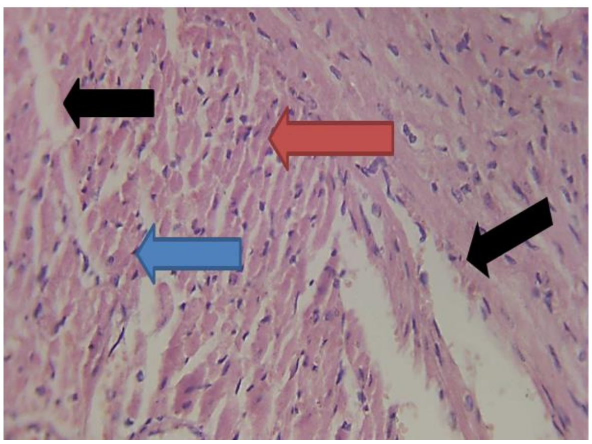

Figure 4: High magnification of group T1 cardiac tissue demonstrating fiber shrinkage and nuclear condensation without necrosis. (H&E stain, high magnification)

Group T2 (Red Bull 7.14 ml/kg)

The cardiac tissue of the T2 group (high dose of Red Bull; 7.14 ml/kg) demonstrated markedly worse histopathological changes than those of the control and T1 groups. At low power (Figure 5), myocardial fibers were severely disorganized and fragmented. Dilated interstitial spaces were visible, and the presence of inter-fiber hemorrhagic foci was apparent, suggesting vascular insufficiency and early tissue damage. In higher power (Figure 6), the myocardial destruction seemed extensive. Muscle fibers were disrupted and roved apart in large measure, with extensive nuclear clumping and pyknosis. Multiple foci of necrosis were observed, and there was loss of cell architecture and nuclear breakdown. There was also obvious diffuse hemorrhage between the injured fibers .Arrowheads in Figs 5 and 6 indicate significant degenerative changes. Arrowheads indicate the areas with partially damaged muscle fibers and few muscle cell debris and intact but edematous area of skeletal muscle, respectively in Figure 5. Arrows in Figure 6 refer to areas of necrosis, fragmented cardiomyocytes and condensed or absent nuclei, all in all confirming irreversible myocardial injury following high-dose Red Bull intake.

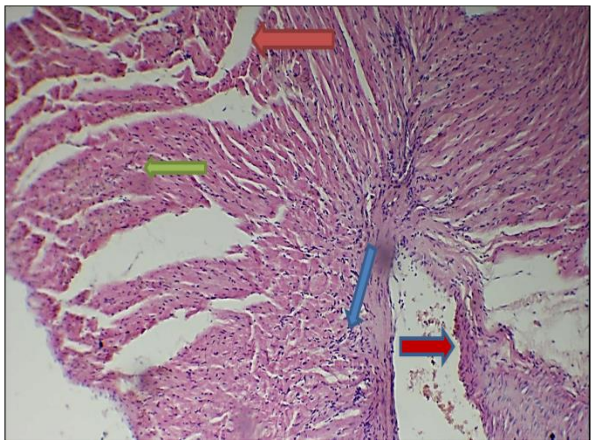

Figure 5: Myocardial section from group T2 (Red Bull 7.14 ml/kg) revealing disrupted fiber structure, interstitial hemorrhage, and early necrotic signs. (H&E stain, low magnification)

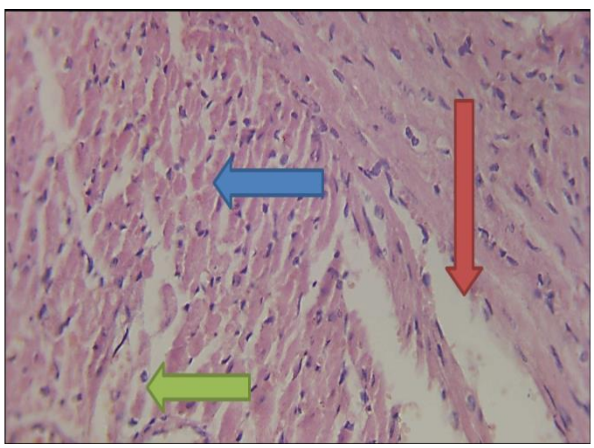

Figure 6: High magnification of group T2 showing fragmented fibers, nuclear degradation, and diffuse hemorrhage. (H&E stain, high magnification)

Group T3 (Monster 3.57 ml/kg)

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Cardiac sections in T3 (Monster energy drink, high dose 3.57 ml/kg) group showed moderate histopathological changes compared to control and T1. At the low magnification (Figure 7), the myocardial fibers were disarrayed, atrophic and rounded. Inter-fiber distance was increased, and a focally vacuolated myocardium was observed, indicative of architectural strain and early degenerative alterations. At greater magnification (Figure 8), disorganization of the cardiomyocytes was more marked. The shape of the fibers was irregular and the amount of cytoplasm was decreased. Nucleus were round and more condensed as the early stages of nuclear damage. No widespread necrosis was observed, however, these results indicate an ongoing degeneration. Arrow heads in Fig. 7 and Fig. 8 indicate dramatic histological changes. The rounded, atrophied muscle fibers and spaces of vacuolation are indicated by arrows in Fig. The arrows in Figure 8 point to condensed nuclei and disarrayed fiber alignment, which indicate that the middle dose of Monster group may have caused moderate myocardial injury.

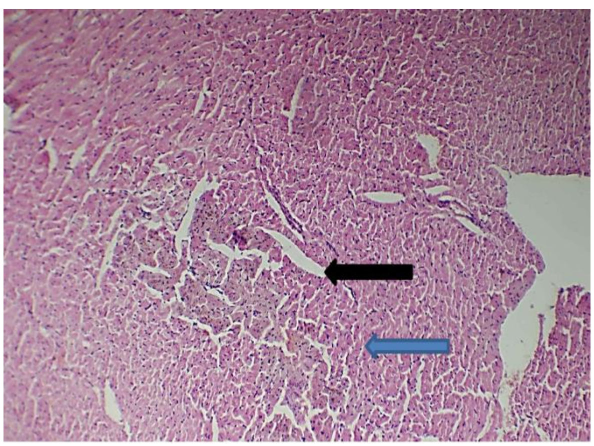

Figure 7: Heart tissue from group T3 (Monster 3.57 ml/kg) showing rounded and atrophied fibers with increased inter-fiber spacing. (H&E stain, low magnification)

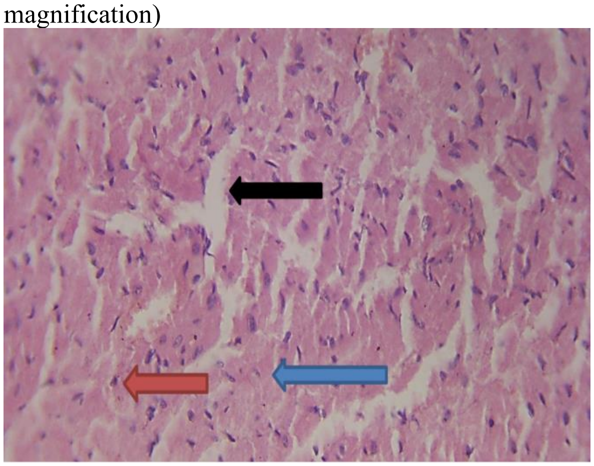

Figure 8: High magnification of group T3 myocardial fibers exhibiting degeneration, nuclear condensation, and fiber disarray. (H&E stain, high magnification)

Group T4 (Monster 7.14 ml/kg)

The cardiac tissue from the T4 group treated with a high dose of Monster energy drink had the most severe crush-like myocardial dystrophy compared to the rest of the experimental groups. On a low magnification scale, the myocardial fibers underwent extensive disintegration; they do not retain the correct location and orientation parallel to each other. Large hemorrhagic areas were noted between the muscle bundles, and the entire tissue looks metabolically catastrophic. On a higher magnification, pathology is even more apparent. The muscle fibers are fragmented, and at least some of them are necrotic with a complete loss of the cytoplasm. Nuclei are either not observed at all, or they are represented by residual nuclear debris. Diffuse hemorrhage is cloudy throughout the field due to significant vascular injury and most likely irreversible myocardial degeneration. Pathological features are marked with arrows in Figures 9 and 10. The arrows in Figure 9 indicate an area with the most pronounced fiber cut and accompanying hemorrhage. In Figure 10, arrows mark a large necrotic area between the muscle fibers, the loss of nuclei, and fragmentation of the cardiomyocytes. The two figures support the conclusion that the Monster has a pronounced cardiotoxic effect when taken in large quantities.

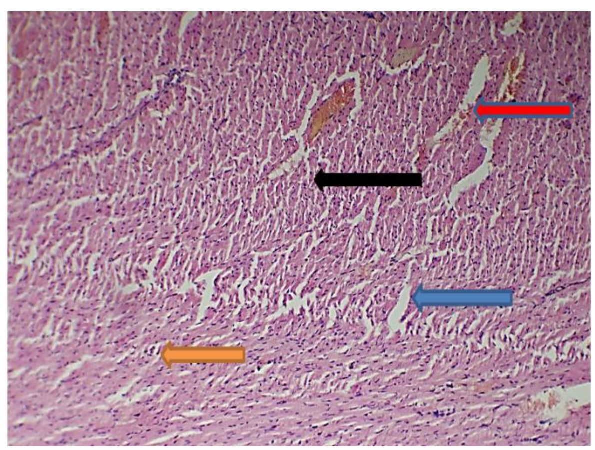

Figure 9: Cardiac section from group T4 (Monster 7.14 ml/kg) showing extensive fiber disruption and hemorrhagic areas. (H&E stain, low magnification)

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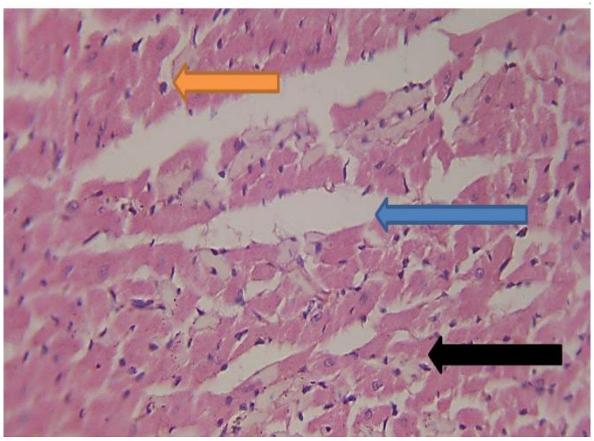

Figure 10: High magnification image of group T4 illustrating necrotic cardiac tissue with diffuse hemorrhage and loss of structural integrity. (H&E stain, high magnification)

Descriptive and semi-quantitative analysis of histological changes in cardiac tissue among the experimental groups are shown in Table ٢. The following four criteria were evaluated: structure integrity, nuclear shape, hemorrhagic and necrotic condition. All were scored on a scale of 0 to 3 (0 = optimal, 1 = mild, 2 = moderate, 3 = severe/extensive) to indicate the degree of pathologic alteration. This method gives a more positive comparison of cardiotoxic effects by different levels and types of energy drinks.

Table ٢. The semi-quantitative analysis of the histological alterations in the cardiac tissues

Group	Structural Integrity	Nuclear Morphology	Hemorrhage	Necrosis	Structural Score	Nuclear Score	Hemorrhage Score	Necrosis Score
Control (C)	Normal	Centrally elongated	None	None	0	0	0	0.0
T1 (Red Bull 3.57 ml/kg)	Mild loss of structural organization	Condensed spherical	Absent	Absent	1	1	0	0.0
T2 (Red Bull 7.14 ml/kg)	Severe disruption	Clumped/pyknotic	Present	Present	2	2	2	2.0
T3 (Monster 3.57 ml/kg)	Moderate disruption	Rounded condensed	Mild	Mild	2	2	1	1.0
T4 (Monster 7.14 ml/kg)	Extensive damage	Lost/fragmented	Diffuse	Extensive	3	3	3	٣

Discussion

The present histological investigation provides robust evidence that chronic consumption of energy drinks, namely Red Bull and Monster, results in significant and progressive structural damage to cardiac tissue in immature male rats. This damage intensifies with increasing dosage, highlighting a clear dose-dependent cardiotoxic effect.In the control group, cardiac fibers exhibited regular arrangement, intact striations, and peripheral nuclei-hallmarks of healthy myocardial tissue (9). In contrast, rats receiving low doses of Red Bull or Monster (T1 and T3) demonstrated mild histopathological changes, including fiber atrophy, nuclear condensation, and loss of alignment (22, 23). These changes correspond with early signs of oxidative stress and are supported by reports indicating that even moderate intake of caffeine and taurine can destabilize calcium homeostasis and mitochondrial function (13, 23,14). High-dose groups (T2 and T4) showed widespread, severe myocardial damage with contraction band necrosis, interstation hemorrhage, diffuse necrosis, and total disruption of tissue architecture. These results parallel those of Romero-Herrera et al. (11), who showed extensive fiber degeneration, and by Xiao et al. (24), who described swelling of mitochondria and disruption of cellular integrity after high doses of the stimulant. The diffuse bleeding is suggestive, and adding to the complexity of the situation is capillarorrhagia, probably related to sustained hypertensive episodes and sympathetic over activity secondary to excessive caffeine use (17, 25, 26). The pathways that mediate these changes are known to

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involve intracellular calcium overload, reactive oxygen species (ROS) generation, and catecholamine-induced ischemia, actions which are well documented in caffeine toxicosis (13,15, 23). Taurine, although partially protective in acute doses, has been found to exacerbate calcium influx and oxidative stress when co-administered with caffeine on a chronic basis (12, 27). The fiber disarray and nuclear pyknosis observed in T2 and T4 are histopathologic changes characteristic of necrotic cell death, which is in line with the results of Nadeem et al. (16) and El-Rahman et al. (10), who described energy-drink-induced cardiomyocyte apoptosis and tissue necrosis. Moreover, the vascular injury and hemorrhage (T4 group in particular) are consistent with the findings of Hakim et al. (22) and Chami & Di Primio (17), demonstrating that energy drinks can cause endothelial injury as well as increase blood pressure.Notably, the amount of damage appears to be higher for the Monster double dose group (T4) relative to the Red Bull equivalent treatment (T2). Such a response could be due to formulation differences such as increased sugar, herbal stimulants, or ratios of caffeine: taurine (25,8). The additive effects of sugar-induced insulin resistance and additional oxidative stress have been reported for energy drink models (23). The histological damage was more remarkable in rats that were treated with Monster than with Red Bull, particularly at high doses. This discrepancy could be related to the different compositions of the two energy drinks. Monster not only has more caffeine and sugar than your average energy drink, but extra stimulants like guarana, ginseng and L-carnitine, according to the company's website, as well as the addition of the carbohydrate maltodextrin. These compounds can work together to cause synergistic enhancement of oxidative stress, calcium dysregulation, and metabolic burden on cardiomyocytes, while Red Bull, in comparison has fewer active stimulants, and in less complex a formula. The additive stimulant burden from Monster may be responsible for the heightened myocardial perturbation noted in this group. These observations are consistent with earlier accounts indicating that multi-ingredient energy drinks are more likely to impair cardiotoxicity as compared with single-ingredient preparations (6).This study also supports the results from Romero-Herrera et al. (11), who showed that exogenous toxicants exposed to immature tissues of the young rats are particularly toxic as a result of less developed antioxidant systems and increased metabolic needs. While it is the skeletal muscle, which was targeted for their study, there was systemic vulnerability that is compatible with the cardiac tissue susceptibility reported here. This is further confirmed by Buscariollo et al. (28), who found that maternal caffeine consumption during gestation led to a sustained decrease in offspring and grand-offspring left ventricular function and caused dilated cardiomyopathy in the first generation (F1) and hypertrophic cardiomyopathy in the following generations. These data indicate that fetal caffeine exposure could interfere with normal heart development and lead to increased susceptibility for heart dysfunction later in life. Similar to one conducted by Weng et al. (29), which reported that maternal consumption of caffeine during pregnancy was related to a higher risk of miscarriage, suggesting possibly adverse effects on fetal growth and, thus, on the IRC, considering the heart is one of the organs affected by in utero exposure to caffeine. James (30) also researched caffeine use in pregnancy and suspected its role in the growth and development of the fetus, including myocardial development. Taken together, these findings confirm the hypothesis that perinatal caffeine exposure exerts detrimental effects on myocardial development and confers susceptibility to myocardial damage. Taken together, the histological results of the present work reveal structural damage of the heart following the chronic consumption of energy drinks, and to a greater extent at supra-therapeutic doses. While their specific roles were not investigated in the present study, previous work suggested that oxidative stress, calcium dysregulation or metabolic changes indeed participate in the mechanisms that cause the observed defects of the myocardial degeneration (6, 13). These processes result in visible damage at the tissue level in terms of mild atrophy and nuclear condensation in low doses to full tissue necrosis and hemorrhage in high doses. The high prevalence of energy drink consumption in the general population, particularly among adolescents and young adults, raises concern regarding the public health impact. As noted by Nadeem et al. (16) and Hanafi et al. (19), Cardiac complications related to energy drink consumption – including arrhythmia, increased blood pressure, and sudden cardiac death – are on the rise, with young people, often with no underlying health issues, accounting for a significant proportion of the increase. The consequences associated with this are alarming in light of the large amount of unregulated consumption of these products. The histopathological changes seen in this study such as disarray of myocardial fibers, condensation of the nucleus, and necrosis, might potentially represent a structural injury which, if present in humans as well, would compromise cardiac contractility, and electrical stability. These alterations may have potential implications for sustained remodeling, arrhythmogenesis, and eventually cardiac function. In the context of physiological frailty in adolescence and young adulthood, serious consideration should be given to the translation of such findings to the clinic. As highlighted by Li et al. (٣١), prevention strategies are now required to be integrated to counteract the cardiovascular risk inherited by youth over-consumption of energy drinks.

Conclusion

This research offered clear histological proof that early chronic treatment with commercial energy drinks (Red Bull and Monster) exerted progressive dose-dependent structural damage in the myocardium of immature male rats. The changes they observed were variable, including slight myocardial fiber atrophy and nuclear condensation in the normal dose group and more wide spread fiber fragmentation, hemorrhage and necrosis in the high dose groups. Monster, when administered in higher doses, produced slightly more pronounced cardiac disturbance compared to Red Bull, indicating formulation reliant toxicity. These observations emphasise the importance of considering such cardiotoxic risks of excessive energy drink consumption, especially during developmental periods, and draw attention to the necessity of both regulation and further public health guidance for the unregulated use of energy drinks in adolescents.

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Conflict of interest

No conflict of interest is disclosed by the authors.

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