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MORPHOLOGICAL CHANGES IN THE STOMACH WALL UNDER THE INFLUENCE OF AN ENERGY DRINK

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Abstract: In this study, adult white laboratory rats weighing 180–220 g were administered Red Bull energy drink intragastrically for 10, 30, and 60 days, and morphological changes in the stomach wall were investigated. No significant histological differences were found between the control and experimental groups after 10 days. By day 30, the experimental group showed mucosal edema, focal degenerative changes, and necrotic foci in the surface epithelium, together with hypertrophy of the epithelial lining and thickening of the muscular layers. By day 60, these changes were followed by a reduction in total mucosal thickness despite continued thickening of the muscular layers, suggesting a biphasic pattern of initial compensatory hypertrophy followed by decompensation. These findings indicate that prolonged energy drink consumption produces progressive structural injury to the gastric wall. Group differences at each time point were assessed using an unpaired, two-tailed Student's t-test, with $p < 0.05$ considered statistically significant.

Keywords: stomach wall, gastric mucosa, energy drink, caffeine, morphometry, laboratory rats.

INTRODUCTION

Nowadays, energy drinks are consumed with particular interest, especially among young people. Owing to their content of caffeine, taurine, and other stimulant compounds, these beverages can affect the nervous system and are marketed as improving mood and work capacity [1]. Epidemiological data show that energy drink consumption is widespread among adolescents and young adults worldwide, with a recent systematic review and meta-analysis reporting substantial lifetime and past-year use among teenagers in many countries [2].

Manufacturers of energy drinks generally deny adverse effects of these beverages on the human body. However, a growing body of clinical and experimental literature has documented adverse effects associated with chronic energy drink consumption, involving the nervous, cardiovascular, urinary, and digestive systems [1]. Caffeine, the principal stimulant in most energy drinks, has been shown to directly increase gastric acid secretion through bitter-taste receptor signaling in parietal cells [3], providing a plausible mechanistic link to mucosal injury.

Experimental studies in rodents have reported histopathological changes in the gastric and duodenal mucosa after energy drink administration, including mucosal atrophy, inflammatory infiltration, and altered pepsinogen secretion [4, 5, 6, 7]. In humans, case reports have linked heavy energy drink consumption to atrophic gastritis and gastric intestinal metaplasia [8]. Nevertheless, the

available literature on the structural effects of energy drinks on the stomach wall remains limited and, in places, contradictory, particularly regarding the time-course of these changes.

Given the widespread consumption of energy drinks among young people, further study of their effects on the gastric wall — including the time-dependent progression of structural change — is of considerable practical relevance.

AIM OF THE STUDY

The aim of this study was to identify structural changes occurring in the stomach wall of laboratory rats under the influence of chronic energy drink administration, and to characterize how these changes progress over time (10, 30, and 60 days).

MATERIALS AND METHODS

The study was conducted on adult white laboratory rats weighing 180–220 g, maintained under standard laboratory vivarium conditions (temperature 22 ± 2 °C; 12 h:12 h light–dark cycle; standard pelleted rodent chow and water available ad libitum). Prior to inclusion, all animals were examined and those with somatic or infectious disease were excluded. The study protocol was approved by the Institutional Animal Care and Use Committee of the affiliated institution prior to the start of experiments, in accordance with international guidelines for the use of laboratory animals in biomedical research.

Animals were assigned to two groups:

- Group 1 (control), n = 25: received distilled water intragastrically via an orogastric gavage needle, in a volume equivalent to that given to the experimental group.
- Group 2 (experimental), n = 25: received Red Bull energy drink at a dose of 10 mL/kg body weight per day, administered intragastrically via an orogastric gavage needle.

Each group was further divided into three subgroups of approximately equal size (8–9 animals each), corresponding to treatment duration — 10, 30, and 60 days.

At the end of each treatment period, animals were euthanized under ether anesthesia in accordance with the approved institutional animal care protocol. After laparotomy, the stomach was examined macroscopically. Tissue specimens were then obtained from all anatomical regions of the stomach (glandular and non-glandular), fixed in 12% formalin solution, and processed for histology. Sections 6–8 μm in thickness were stained with hematoxylin and eosin, and with the Van Gieson method for connective tissue.

Morphometric measurements (epithelial height; thickness of the mucosa, circular muscular layer, longitudinal muscular layer, and total stomach wall) were performed using a calibrated ocular micrometer under light microscopy, at ×100–×200 magnification, with a stage micrometer used for calibration and a scale bar included in each photomicrograph. Measurements were performed by an investigator blinded to group allocation.

The dose of 10 mL/kg/day was selected on the basis of doses used in comparable published rodent studies of energy drink toxicity [4, 5], approximating a pattern of heavy habitual human consumption when scaled across species.

Statistical analysis: data are expressed as mean ± standard deviation (SD). Group comparisons at each time point were performed using an unpaired, two-tailed Student's t-test; a value of $p < 0.05$ was considered statistically significant.

RESULTS

Comparison of the histological structure of the stomach in control and experimental rats after 10 days revealed no significant differences.

By day 30, destructive changes had developed in the surface epithelium of both the glandular and non-glandular regions of the stomach in the experimental group. Edema of the gastric mucosa was observed, along with focal degenerative changes in the surface epithelium and, in some areas, necrotic foci (Figure 1). In the proximal (non-glandular) region, signs of hyperkeratosis developed in the keratinized stratified squamous epithelium; this change may represent an adaptive response of the organism to chemical irritation of the mucosa.

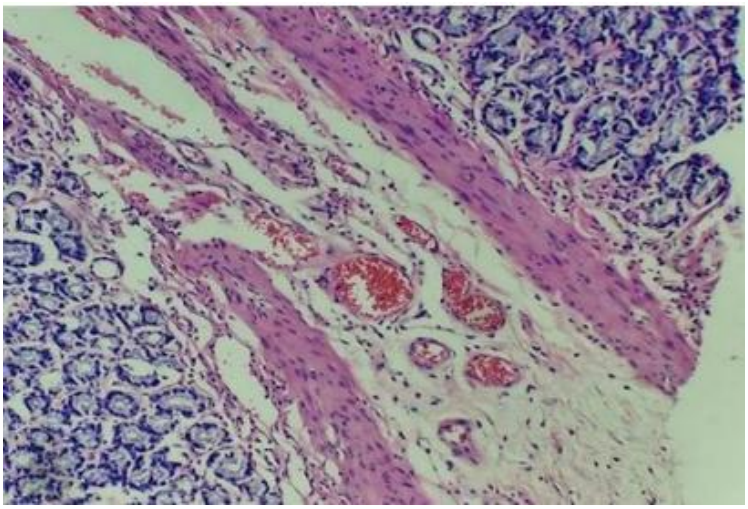


Figure 1. Edema of the gastric mucosa and focal degenerative changes in the surface epithelium of the stomach wall of white laboratory rats in the experimental group after 30 days. Hematoxylin and eosin staining, ×100; scale bar = 100 µm.

Table 1 summarizes the morphometric changes recorded at day 30 relative to the control group.

Parameter	Region	Control (µm)	Experimental (µm)	Change vs. control
Epithelial height	Non-glandular	63.6 ± 0.8	69.2 ± 1.1	≈ +8.8% (calculated from means; not stated by authors)

Parameter	Region	Control (µm)	Experimental (µm)	Change vs. control
Epithelial height	Glandular	30.2 ± 0.3	38.3 ± 1.3	≈ +26.8% (calculated from means; not stated by authors)
Circular muscular layer	Non-glandular	66.6 ± 0.2	71.2 ± 0.8	+16% (as reported)
Circular muscular layer	Glandular	75.7 ± 0.8	not stated	+15% (as reported)
Longitudinal muscular layer	not specified	not stated	not stated	+17% (as reported)
Total external muscular layer	Non-glandular	not stated	not stated	+18% (as reported)
Total stomach wall thickness	Non-glandular	not stated	not stated	No significant change (as reported)
Total stomach wall thickness	Glandular	not stated	not stated	Up to +25% (as reported)

Arterioles and capillaries were located within the longitudinal muscular layer of the submucosa, and venules containing formed elements of blood were also identified.

By day 60, a decrease in the thickness of the mucosa was observed — by 18% in the non-glandular region and by 16% in the glandular region — despite continued thickening of the muscular layers (Figure 2). The total external muscular layer increased by 22% in the non-glandular region (with no significant change in overall stomach wall thickness at this site), while in the glandular region the total stomach wall thickness increased by up to 36%.

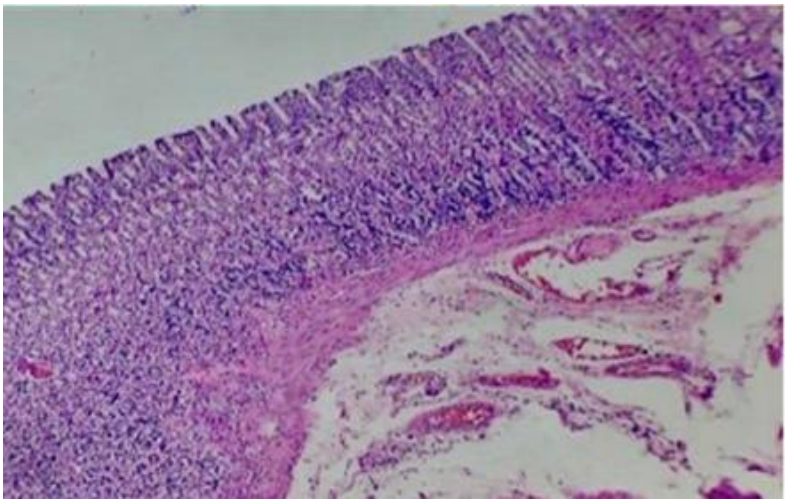


Figure 2. Structure of the gastric mucosa of the stomach wall of white laboratory rats in the experimental group after 60 days. Hematoxylin and eosin staining, ×200; scale bar = 50 μm.

Parameter	Region	Change vs. control at day 60
Mucosal thickness	Non-glandular	−18% (as reported)
Mucosal thickness	Glandular	−16% (as reported)
Total external muscular layer	Non-glandular	+22% (as reported)
Total stomach wall thickness	Non-glandular	No significant change (as reported)
Total stomach wall thickness	Glandular	Up to +36% (as reported)

The concluding paragraph of the original Results section additionally states: *"After 30 days of energy drink administration, the height of the epithelial lining increased by 21% in the non-glandular region of the stomach and by 19% in the glandular region. After 60 days of administration, the increase in both regions was 19%." (Note: these percentages do not match the values calculated from the raw means reported in Table 1 — see Limitations.)*

Thus, comparison of the stomach wall parameters between the control and experimental groups demonstrated signs of mucosal hypertrophy and muscular-layer thickening at day 30, followed by a reduction in total mucosal thickness by day 60 despite continued muscular thickening.

DISCUSSION

The present findings indicate that structural changes in the stomach wall of rats develop in a time-dependent manner following chronic Red Bull energy drink administration. No differences were detected after 10 days, suggesting a latency period before structural injury becomes histologically evident. By day 30, edema, focal epithelial degeneration, and necrotic foci were accompanied by compensatory hypertrophy of the epithelial lining and thickening of the muscular layers — a pattern consistent with an early adaptive response of the gastric wall to chemical irritation.

By day 60, however, total mucosal thickness had decreased relative to control in both the glandular and non-glandular regions, even though epithelial height and the muscular layers continued to thicken. This apparent discrepancy may be explained by the fact that "mucosal thickness" reflects the full thickness of the mucosa — surface epithelium, lamina propria, and glandular compartment — whereas "epithelial height" reflects only the surface lining. A pattern of surface hyperplasia/hyperkeratosis occurring together with atrophy and loss of the deeper glandular compartment — sometimes termed reactive or chemical gastropathy in the clinical literature — would produce exactly this combination: increased surface epithelial height with a net decrease in total mucosal thickness, as glandular tissue is progressively lost to chronic irritation. This interpretation is consistent with reports of glandular injury and mucosal atrophy following chronic energy drink exposure in other rodent models [4, 5], and with case reports linking heavy energy drink consumption to atrophic gastritis in humans [8].

The mechanism underlying these changes is plausibly linked to caffeine, the principal stimulant common to most energy drinks. Caffeine has been shown to stimulate gastric acid secretion directly via bitter-taste receptor signaling in parietal cells [3], and chronic hyperacidity, together with the low pH and carbonation of commercial energy drinks, may act synergistically to injure the surface epithelium and deeper mucosal structures. Our findings of progressive thickening of the muscular layers parallel observations by Al Sammak et al. [5], who reported dose-dependent parietal cell hyperplasia and mucosal injury in rats given the Tiger energy drink, and by Yusupova [6], who documented a progressive decline in pepsinogen I and II secretion with increasing duration of energy drink exposure in rats — consistent with the glandular functional impairment implied by the reduced mucosal thickness observed here. Nasi et al. [7] similarly reported that acute energy drink exposure in rats produced eosinophilic infiltration of the intestinal mucosa attributable to caffeine, which was fully reversible after cessation — consistent with the absence of change observed at 10 days in the present study, with injury becoming manifest only after more prolonged (30–60 day) exposure.

These experimental findings are broadly consistent with clinical observations. Brahmbhatt [8] reported reversible atrophic gastritis and gastric intestinal metaplasia associated with heavy energy drink consumption in humans, and a recent comprehensive review summarized multiple adverse gastrointestinal effects of chronic energy drink use [1]. Taken together with the present results, this supports the view that chronic, heavy energy drink consumption — a pattern increasingly common among adolescents and young adults [2] — carries a demonstrable risk of progressive structural injury to the stomach wall.

LIMITATIONS OF THE PRESENT DRAFT

- The percentage changes in epithelial height stated in the concluding paragraph of Results (21% non-glandular / 19% glandular at day 30; 19% at day 60) do not match the percentage change calculated from the raw mean values reported earlier in Results (≈ 8.8% and ≈ 26.8%, respectively — see Table 1). This is a discrepancy in the authors' own original data, not something introduced during editing; please reconcile these figures using your source data before submission.

CONCLUSION

Analysis of the present data demonstrates that no significant differences were observed in the histological structure of the stomach between control and experimental rats after 10 days of Red Bull energy drink administration. By day 30, destructive changes had developed in the surface epithelium of the glandular and non-glandular regions in the experimental group, including mucosal edema, focal degenerative changes, and necrotic foci, together with compensatory hypertrophy of the epithelial lining and thickening of the muscular layers. By day 60, this compensatory phase was followed by a reduction in total mucosal thickness in both the glandular and non-glandular regions, despite continued thickening of the muscular layers — a pattern suggestive of progressive glandular atrophy superimposed on surface epithelial hyperplasia. These results indicate that chronic energy drink consumption produces a biphasic, time-dependent pattern of structural injury to the stomach wall — an initial compensatory response followed by

decompensation — and support the need for further study of the long-term gastric effects of habitual energy drink consumption, particularly among adolescents and young adults.

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