



Histopathological Effects of Repeated Low-Dose Aspirin Administration on the Stomach and Duodenum of Male Albino Rats

Mohammed K. Hassani*

Department of Biology, College of Science, University of Misan, Maysan, Iraq.

Article's Information	Abstract
Received: 14.11.2025 Accepted: 12.07.2026 Published: 15.09.2026	Aspirin is a widely used non-steroidal anti-inflammatory drug with analgesic, antipyretic, and antiplatelet properties. Despite its mounted healing blessings, repeated exposure may additionally impair gastrointestinal mucosal integrity and increase the threat of gastric and intestinal damage. The present study aims to investigate the histopathological results of repeated oral administration of aspirin on the stomach and duodenum of twelve adult male of albino rats. The control group acquired no aspirin, while the treatment group acquired aspirin at a dose of 13.2 mg/kg/day by way of orogastric gavage for 14 consecutive days. After experiments, animals were euthanized underneath anesthesia, and stomach and duodenal tissues were amassed, fixed in 10% neutral buffered formalin, and stained with hematoxylin and eosin. Histopathological changes had been evaluated in both organs using lesion scoring. At baseline, there was no significant difference in body weight between control and aspirin-treated groups (221.6 ± 13.29 , 225.0 ± 12.24 g, respectively; $P = 0.66$). After 14 days, the control group showed an increase in body weight to 233.3 ± 15.05 g, whereas Aspirin-treated group showed a decrease to 215.8 ± 9.70 g, with a significant differences ($P = 0.03$) between the groups. The histopathological examination of these animals revealed gastric epithelial degeneration, mucosal abrasion and ulcerative/wound repair changes, inflammatory cell infiltration, vasoconstriction, and hemorrhagic changes. In the duodenum, epithelial degeneration, villous damage, inflammatory cell infiltration, edema, and congestive and hemorrhagic changes were observed. Overall, lesion severity was greater in the aspirin-treated animals than in the control animals across the histopathological parameters evaluated. Repeated oral administration of aspirin up to 13.2 mg/kg/day for 14 days induced marked histopathological changes within the gastric and duodenal mucosa of adult male albino rats, accompanied by a reduction in body weight. The findings provide experimental evidence of gastrointestinal mucosal injury after repeated aspirin administration. Further studies using larger model sizes, two dose scores, quantitative morphometry, and molecular biomarkers to elucidate dose-response timelines and underlying mechanisms.
Keywords: Aspirin, Stomach, Duodenum, Histopathology, Albino rats.	
	http://doi.org/10.22401/ANJS.29.3.07 *Corresponding author: Mohamedkamel@uomisan.edu.iq
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1. Introduction

Gastric ulcers, which are chronic lesions on the lining of the stomach, represent a major global health issue. The emergence of these ulcers is mainly linked to an imbalance between the stomach's protective mucosal barrier and harmful influences like stress, tobacco use, alcohol consumption, and various medications. Overproduction of stomach acid, often caused by extended use of non-steroidal anti-inflammatory medications or infection by *Helicobacter pylori*, markedly contributes to ulcer formation. These elements activate distinct cellular and molecular processes that can result in ulcer development in either the stomach or the duodenum. Common clinical signs include anorexia, nausea, vomiting, bloating, gastrointestinal pain, and acid reflux.

Gastric ulcers impact approximately 8% to 10% of the global population, with occurrences of 40% in developed nations and 80% in developing countries [1, 2]. The most common clinical condition in our environment is a gastric ulcer, which affects people of all ages and genders and has a large global influence on health economics and patient quality of life, the ulcer of stomach are complex by perforation, bleeding, and corrosion of the mucosa of stomach [3]. The most significant negative effects consist of gastric ulcers, internal bleeding in the stomach, and aggravated asthma. Due to an increased risk of internal bleeding in older adults, alcohol consumers, those using other nonsteroidal anti-inflammatory drugs, or those on anticoagulants, the use of aspirin is not recommended during the later stages of pregnancy and is generally discouraged for children with viral infections. This is because it poses a risk for developing Reye's syndrome, and high amounts may result in tinnitus. Non-steroidal anti-inflammatory medications, known as NSAIDs, are characterized by their straightforward mechanism of action and minimal negative side effects, making them suitable for various mild to moderate medical conditions. They are regarded as a reliable option for situations that necessitate repeated use of pain relief drugs, such as in the case of arthritis. Aspirin, classified as a mild acid, carries a heightened risk of causing irritation in the upper gastrointestinal tract, primarily affecting the stomach with prolonged usage. Due to its chemical properties, aspirin can result in damage to the mucosal membrane and may lead to the onset of peptic ulcer disease; if complications arise, it can result in perforation and localized bleeding. Research shows that approximately 25% of individuals receiving long-term NSAID therapy might develop peptic ulcers, while only around 4% of these cases are likely to experience severe complications such as bleeding or perforation, additional studies have indicated that low-dose aspirin along with other NSAIDs are key contributors to upper gastrointestinal bleeding globally. Low-dose aspirin is commonly prescribed for preventing heart disease, yet even at lower amounts such as 75mg per day, it can double the chances of gastric ulcers occurring [4]. Aspirin (acetylsalicylic acid) is a type of non-steroidal anti-inflammatory medication (NSAID) that has anti-inflammatory, antipyretic, and pain-relieving properties, aspirin has a chemical formula of $C_9H_8O_4$ and a molecular weight of 180 Dalton, one of the most often used medications worldwide is aspirin, having saved the lives of billions of people from ailments like strokes, fever, rheumatism aches, heart attacks and ischaemia in terms of the desired activity, it is still considered a better treatment than alternatives such as the anticoagulant warfarin [5]. Aspirin is included in the essential medicine list by the World Health Organization. In the United States, aspirin ranked as the 42nd most commonly prescribed drug in 2017, with more than 17 million prescriptions issued. Additionally, aspirin is utilized on a long-term basis to assist in reducing the likelihood of heart attacks, strokes, and blood clots among individuals who are at elevated risk, [6]. Although aspirin is commonly utilized, the precise ways it operates remain unclear. It is thought that its fundamental actions relate to the suppression of prostaglandin production within the body. Aspirin acts as a non-selective inhibitor of the COX enzyme, and its effectiveness in alleviating pain stems from its blockade of the COX-1 and COX-2 enzymes in central nervous system cells, as well as its rapid distribution in cerebrospinal fluid [7]. The purpose of this research is to observe the development of illness indicators in animals who consume aspirin, even though it is commonly utilized in many parts of the globe. However, research related to the adverse effects of this medication is limited and focuses on a small scope. Thus, the present study aimed to monitor the negative effects of aspirin, particularly concerning the gastrointestinal tract. This will help in understanding the effect on human.

2. Materials and Methods

2.1 Experimental animals and ethical approval

Twelve adult male albino rats (*Rattus norvegicus*), aged 12–16 weeks, and weighing two hundred–250 g, were obtained from the Animal House of the College of Science, University of Misan Ethical approval was modified to receive from the Ethics Committee of the University of Misan (Approval No. 197/10/2025). Animals are housed in clean plastic cages with suitable bedding, with a soft/12 h dark cycle at 12 h under managed environmental conditions of 20–23°C. Animals have access to standard laboratory food and consumed water for the duration of the experimental period. The animals were allowed to acclimate to the experimental environment for one week before the start of the experiment.

2.2 Experimental Design

The animals were randomly allocated into two experimental groups with six animals in every group: Control group (n = 6): untreated animals. Aspirin-treated group (n = 6): animals receiving aspirin at 13.2 mg/kg/day for

14 consecutive days by using orogastric gavage. Body weight become recorded at the start of the experiment and again on the quit of the 14-day treatment length.

2.3 Aspirin Preparation and Administration

A commercially available enteric-lined aspirin formula (Aspirin Protect, one hundred mg; Bayer Bitterfeld GmbH, Germany) was used due to the fact the supply of acetylsalicylic acid [9]. Aspirin changed into administered at 13.2 mg/kg/day with the aid of orogastric gavage for 14 consecutive days. Aspirin tablets containing 100 mg of acetylsalicylic acid were finely ground and mixed in 0.5% carboxymethyl cellulose (CMC) to acquire a uniform suspension. This mixture was made fresh prior to each dose and was constantly stirred during administration through the mouth using gavage method at a dosage of 13.2 mg/kg of body weight, with a dosing volume of 5 mL/kg ; therefore, the final concentration of aspirin was modified to 2.64 mg/mL. The specific dose for each rat was determined based on its weight through the following formula:

$$\text{Dose (mg)} = 13.2 \times \text{body weight (kg)}.$$

The 13.2 mg/kg dosage was derived from a conversion based on body surface area, transitioning from the appropriate human dose to the equivalent dose for rats, utilizing standard Km values of 37 for adult human and 6 for rats, following this conversion approach, the equivalent dose for rats was evaluated as follow:

$$\text{Rat-equivalent dose} = \text{Human dose} \times (37/6), \text{ yielding approximately } 13.2 \text{ mg/kg in rats.}$$

2.4 Body-Weight

Assessment Body weight was measured for each animal immediately before treatment and on the end of the 14-day experimental period. The alternate in body weight was calculated as:

$$\text{Change in body weight (g)} = \text{final body weight} - \text{baseline body weight}.$$

2.5 Anesthesia, Euthanasia, and Tissue Collection

At the end of the 14-day experimental period, animals have been anesthetized the usage of ketamine/xylazine in accordance with the institutionally approved animal protocol and subsequently euthanized. The stomach and duodenum were carefully removed immediately after euthanasia and amassed for histopathological exam.

2.6 Histological Processing and Hematoxylin and Eosin Staining

Collected stomach and duodenal tissues have been fixed in 10% neutral buffered formalin. Following fixation, tissues were processed the usage of recurring histological approaches, along with dehydration, clearing, and paraffin embedding. Paraffin sections had been prepared and stained with hematoxylin and eosin (H&E) consistent with the method described by means of Suvarna et al. [8].

2.7 Histopathological Assessment

Histopathological alterations have been evaluated inside the stomach and duodenum of control and aspirin-treated animals. The assessed gastric parameters included: epithelial degeneration; mucosal erosion/ulcerative; inflammatory-cell infiltration;congestion/ hemorrhagic ; and edema. The assessed duodenal parameters covered: epithelial degeneration; inflammatory-mobile infiltration; congestion/hemorrhagic; villous harm; and edema. The lesion rankings suggested in table 2 have been used for comparison between experimental groups.

2.8 Statistical analysis

Statistical analysis was performed using IBM SPSS, version 21.0. Continuous variables were assessed for normality using the Shapiro–Wilk test. Body-weight data are presented as mean $\pm$ standard deviation (SD). For compare between two independent-sample t-test was used when the data met the assumption of normality; otherwise, the non-parametric Mann-Whitney U test was applied. Because histopathological lesion scores represent ordinal severity data and the sample size was small ($n = 6/\text{group}$), the Mann-Whitney U test was used to compare lesion scores between the control and aspirin-treated groups. All statistical tests were two-tailed, and $P < 0.05$ was considered statistically significant.

3.Results

3.1 Effect of Aspirin Administration on Body Weight

At baseline, there was no statistically significant difference in body weight between the control and aspirin-treated groups (221.6 ± 13.29 and 225.0 ± 12.24 g, respectively; $P = 0.66$). After 14 days, the mean body weight increase to 233.3 ± 15.05 g in the control group, while the aspirin-treated group showed a decrease in mean body weight to 215.8 ± 9.70 g. The difference in body weight between the two groups on the end of the experimental period was statistically significant ($P = 0.03$) (Table 1) that presents Body weight of control and aspirin-treated rats before and after the 14-day experimental period

Table 1. Body weight of control and aspirin-treated rats before and after the 14-day experimental period

Parameter	Control	Aspirin-treated	P-value
Initial body weight (g)	221.6 ± 13.29	225.0 ± 12.24	0.66
Final body weight (g)	233.3 ± 15.05	215.8 ± 9.70	0.03*

* $P < 0.05$ indicates statistical significance.

3.2 Histopathological Findings inside the Stomach

Histological examination of the stomach in control rats demonstrated the stomach wall is made up of four layered structures that are arranged concentrically: mucosa, submucosa, muscularis externa, and serosa (Figure (A)). The mucosa is noticeable beneath it, the submucosa comprises well-supplied vascular connective tissue (Figure 1 (B)). Gastric mucosa showing short gastric depressions on the exterior connect to elongated, tube-like stomach glands which reach via isthmus, neck, and base layer of smooth muscle muscularis mucosae (Figure 1 (C)). Part of gastric mucosa showing isthmus and neck and superior base of stomach glands are observed, prominent parietal cells, dark -stained mucous neck cells in the isthmus, columnar chief cells (Figure 1 (D)). Gastric pits showing simple columnar epithelium covers the luminal surface of pits, the base of every cell contains a round shaped nucleus. The cytoplasm at the apical surface does not take up much stain due to the inadequate preservation of mucus in standard slides. Lamina propria consists of highly cellular loose connective tissue. A single stomach pit is cut at an angle, showing the connection of its interior space together with the gastric interior space (Figure 1 (E)). The inferior section of a stomach gland located in the fundic region exhibits sizable, rounded parietal cells arranged either individually or in clusters, intermixed with chief cells that smaller basophilic. Every parietal cell displays a distinct eosinophilic stain and contains a centrally positioned, spherical nucleus. Along the base of certain glands, the majority of the cells lining the glandular lumen consist of chief cells; parietal cells are found in greater abundance in the upper sections of the mucosal layer (Figure 1 (F)).

3.3 Histopathological changes in the stomach following aspirin administration

The stomach demonstrating that shed dead cells are visible within the lumen, more extensive ulceration with the beginning of necrosis, localized cell death of the epithelium exhibiting disrupted cell membrane, compromised cytoplasm and nuclei undergoing karyolysis, along with significant clustering of lymphocytic inflammatory cells (Figure 2 (A)). The stomach showed destruction of connective tissues accompanied by the clustering of inflammatory cells within the lamina propria and muscularis mucosa and regions of necrosis in the submucosa (Figure 2 (B)). The stomach showing cytoplasm that is vacuolated or has a slight stain, alongside pyknotic nuclei, dilatation of the glandular luminae and mucosal hemorrhagic lesions, mucosa ulceration, infiltration of inflammatory cell, congestion blood vessels, bleeding in some areas (Figure 2 (C)). The fundic mucosa showing shedding of the top layer of epithelial cells and infiltration of leucocytic (Figure 2 (D)). The fundic mucosa showing shedding of the outer epithelial layer, certain glands exhibit altered structural design with enlargement of their central section (Figure 2 (E)). The fundic mucosa showing certain oxyntic cells appear to be diminished in size with a condensed nucleus while others are vacuolated, there is also widening of gastric glands (Figure 2 (F)). The fundic mucosa showing oxyntic cells possess a cytoplasm that is acid-loving and have nuclei that are round in shape. A small number of cells exhibit vacuolation and pyknotic nuclei. Mucous neck cells appear to be normal (Figure 2G). The results demonstrate significant alteration of the typical structure of the gastric mucosa after the continuous use of aspirin the corresponding histopathological lesion scores are presented in (Table 2) that presents histopathological lesion scores in the stomach and duodenum of control and aspirin-treated rats

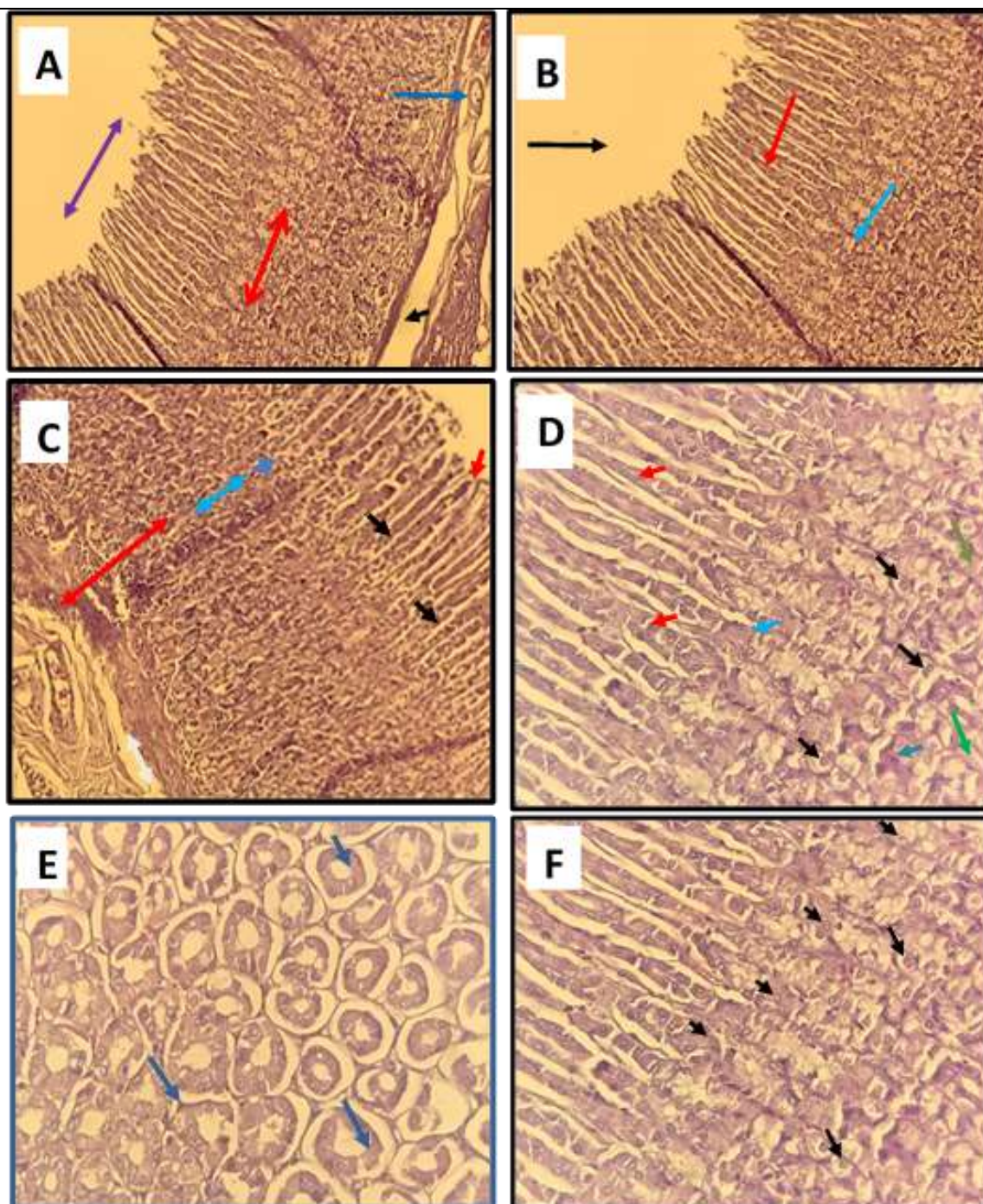


Figure 1. Representative H&E-stained sections of the stomach of control rats. (A) General organization of the gastric wall showing mucosa, submucosa, muscularis externa, and serosa. (B) The mucosa is noticeable beneath it, the submucosa comprises well-supplied vascular connective tissue. (C) Gastric mucosa showing short gastric depressions on the exterior connect to elongated, tube-like stomach glands which reach via isthmus, neck, and base layer of smooth muscle muscularis mucosae. (D) Part of gastric mucosa showing isthmus and neck and superior base of stomach glands are observed, prominent parietal cells, dark-stained mucous neck cells in the isthmus, columnar chief cells. (E) Gastric pits showing simple columnar epithelium covers the luminal surface of pits, the base of every cell contains a round-shaped nucleus. (F) The inferior section of a stomach gland located in the fundic region exhibits sizable, rounded parietal cells arranged either individually or in clusters, intermixed with chief cells that are smaller and basophilic.

Table 2. Histopathological lesion scores in the stomach and duodenum of control and aspirin-treated rats

Organ	Histopathological parameter	Control	Aspirin-treated
Stomach	Epithelial degeneration	0.00 ± 0.00 ^a	2.33 ± 0.51 ^b
Stomach	Mucosal erosion/ Ulcerative changes	0.00 ± 0.00 ^a	2.33 ± 0.51 ^b
Stomach	Inflammatory-cell infiltration	0.00 ± 0.00 ^a	2.50 ± 0.54 ^b
Stomach	Congestion/hemorrhagic changes	0.00 ± 0.00 ^a	1.33 ± 0.51 ^b
Stomach	Edema	0.00 ± 0.00 ^a	0.00 ± 0.00 ^a
Duodenum	Epithelial degeneration	0.00 ± 0.00 ^a	2.16 ± 0.75 ^b
Duodenum	Inflammatory-cell infiltration	0.00 ± 0.00 ^a	1.50 ± 0.54 ^b
Duodenum	Congestion/hemorrhagic changes	0.00 ± 0.00 ^a	1.50 ± 0.54 ^b
Duodenum	Villous damage	0.00 ± 0.00 ^a	2.00 ± 0.63 ^b
Duodenum	Edema	0.00 ± 0.00 ^a	1.66 ± 0.51 ^b

3.4 Histological features of the normal duodenum

Duodenum showing a plica circularis. Plicae are crescent-shaped folds composed of a core of submucosal connective tissue that is overlain by mucosa. The mucosa contains numerous densely packed villi that extend into the lumen, while the muscularis externa is made up of two layers of smooth muscle (Figure 3 (A)). The mucosa and submucosa of Duodenum showing acini that secretory of mucosal brunner gland penetrate muscularis mucosae to stabilize deep within the submucosa, minor ducts from the gland empty into the bases of intestinal crypts. Villi are projections of the mucosa covered by simple columnar epithelium and brunner glands (Figure 3 (B)).

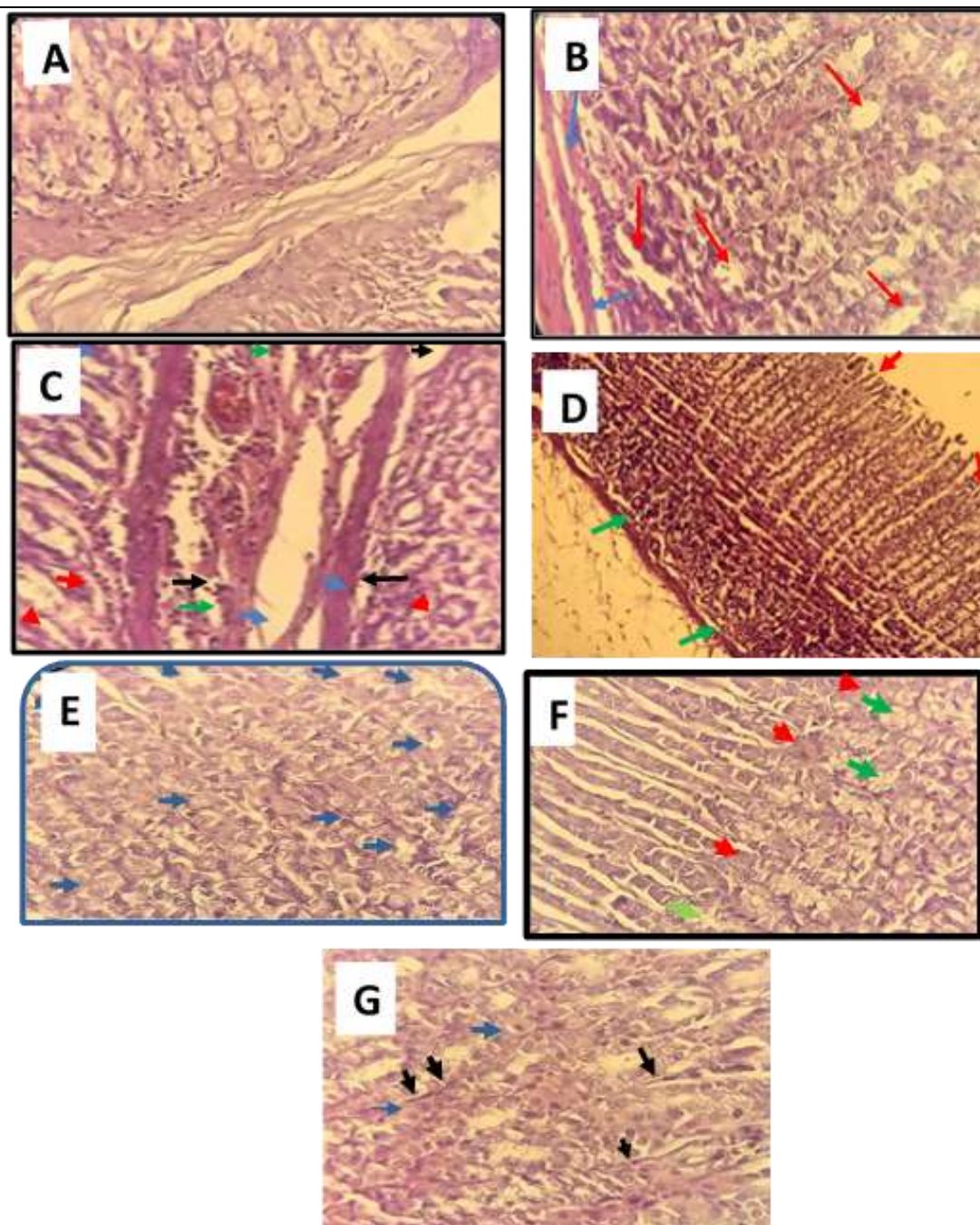


Figure 2. Representative H&E-stained sections of the stomach of aspirin-treated rats showing histopathological alterations. (A) The stomach demonstrating that shed dead cells cells, more extensive ulceration with the beginning of necrosis. (B) The stomach showed destruction of connective tissues accompanied by the clustering of inflammatory cells within the lamina propria and regions of necrosis in the submucosa. (C) The stomach showing cytoplasm that is vacuolated, alongside pyknotic nuclei, mucosal hemorrhagic lesions, mucosa ulceration, infiltration of inflammatory cell, congestion blood vessels, bleeding in some areas. (D) The fundic mucosa showing shedding of the top layer of epithelial cells and infiltration of leucocytic. (E) The fundic mucosa showing shedding of the outer epithelial layer, certain glands exhibit altered structural design with enlargement of their central section. (F) The fundic mucosa showing certain oxyntic cells appear to be diminished in size with a condensed nucleus while others are vacuolated, there is also widening of gastric glands. (G) The fundic mucosa showing various cellular changes and inflammatory infiltration.

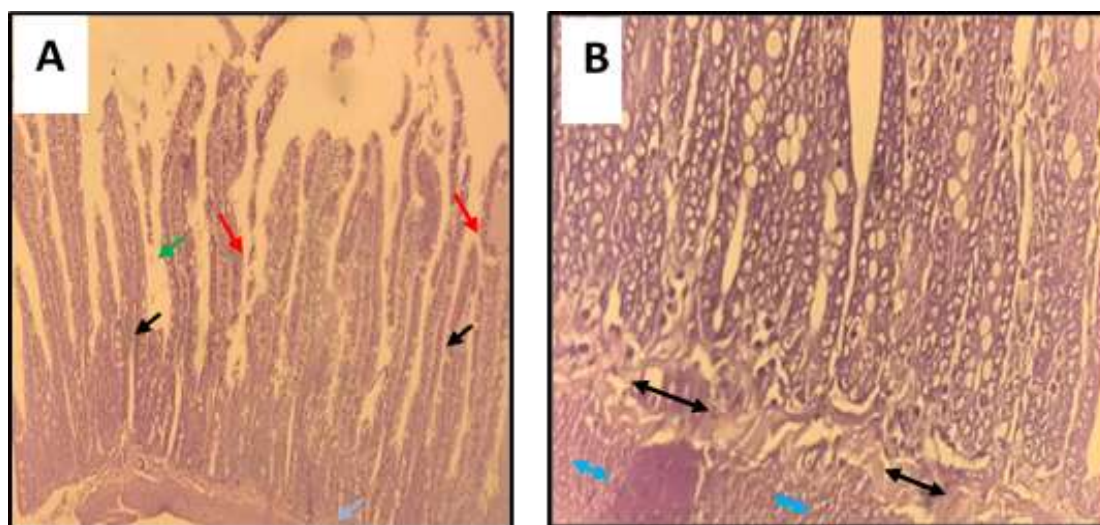


Figure 3. Representative H&E-stained sections of the duodenum of control rats. (A) Duodenum showing a plica circularis . Plicae are crescent-shaped folds composed of a core of submucosal connective tissue, that is overlain by mucosa. The mucosa contains numerous densely packed villi that extend into the lumen, while the muscularis externa is made up of two layers of smooth muscle . (B) The mucosa and submucosa of Duodenum showing acini that secretory of mucosal brunner gland penetrate muscularis mucosae to stabilize deep within the submucosa, minor ducts from the gland empty into the bases of intestinal crypts. Villi are projections of the mucosa covered by simple columnar epithelium and brunner glands .

3.5 Histopathological changes in the duodenum following aspirin administration

Duodenum demonstrating destruction epithelial cells, vacuolations in the large number of cells in mucosa, thicker aggregation of inflammatory cells near the basal line of mucosa, blood congestion, dispersed of connective tissue fibers in submucosal layers, exfoliated epithelial cells degeneration (Figure 4 (A)). Duodenum showing missing tips and shedding of villi in the mucosal epithelial layer “underlying severe ulceration”, deteriorated regions containing cell debris and the space between villi (Figure 4 (B)). Duodenum displaying significant vacuolation in epithelial cells, numerous mononuclear cell infiltrates present in lamina propria (Figure 4 (C)). Duodenum demonstrating significant vacuolations in epithelial cells, deterioration regions including cell debris and observed oedematous in lamina propria with raise in infiltrates of mononuclear cell (Figure 4 (D)). Duodenum showing many vacuolations in epithelial cells .Inflammation cells infiltration in lamina prppria and submucosal oedema (Figure 4 (E)). Collectively, these findings reveal marked epithelial and stromal changes in the duodenum following repeated aspirin administration. The corresponding lesion scores are summarized in Table 2.

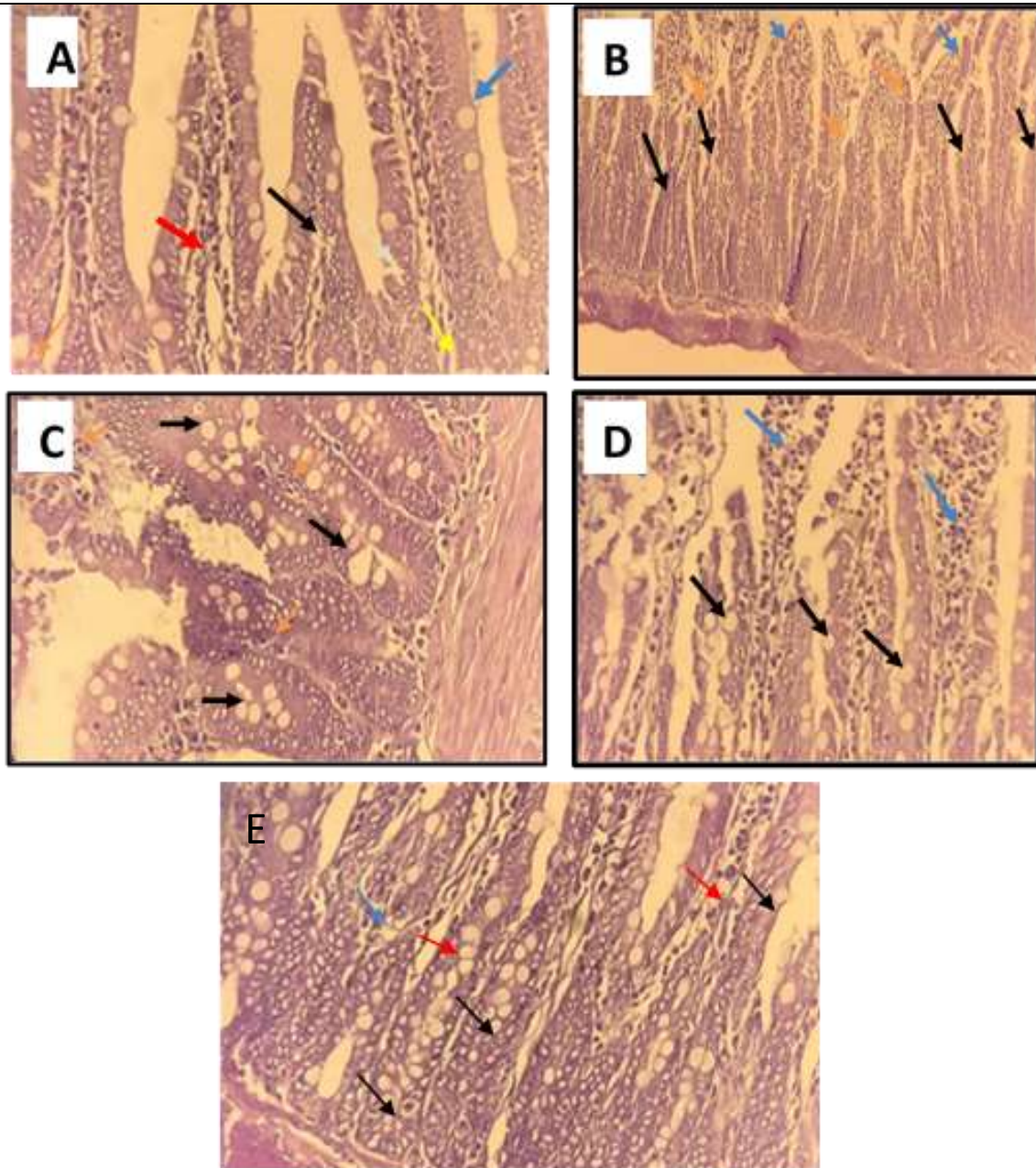


Figure 4. Representative H&E-stained sections of the duodenum of aspirin-treated rats showing histopathological alterations. (A) Duodenum demonstrating destruction epithelial cells, vacuolations in the large number of cells in mucosa, thicker aggregation of inflammatory cells near the basal line of mucosa.(B) Duodenum showing missing tips and shedding of villi in the mucosal epithelial layer.(C) Duodenum displaying significant vacuolation in epithelial cells , numerous mononuclear cell infiltrates present in lamina propria. (D) Duodenum demonstrating significant vacuolations in epithelial cells, deterioration regions including cell debris and observed oedematous in lamina propria with raise in infiltrates of mononuclear cell. (E) Duodenum showing Many vacuolations in epithelial cells .Inflammation cells infiltration in lamina prppria and submucosal oedema .

4. Discussion

4.1 Stomach Histopathological Alterations

Histologically observation on section of stomach from untreated rats group (control) showed normal structure of The stomach's structure consists of four layered sections: mucosa, submucosa, muscularis externa, and serosa, these results agreement with Mukaddes et al. [10] who reported the stomach consists of the mucosa, submucosa muscularis (muscularis externa). Moreover in recent study the results on stomach from group that treated by aspirin showed different histologist changes, Aspirin is commonly utilized as a pain-relieving anti-inflammatory medication and for the prevention of heart-related incidents. Significant digestive system adverse reactions, particularly stomach ulcers and internal bleeding, significantly restrict its medical use. Gastric ulcer was induced through the oral intake of aspirin over a period of 14 days. This condition was demonstrated by the shedding of the surface epithelial layer, the presence of exfoliated cells, and alterations in the architecture of fundic glands, along with the enlargement of several gastric glands. These findings align with another investigation by Mohammed et al. [14] that indicated the presence of surface erosions on the stomach mucosa, rest of gastric glands visible within lumen, and superficial cells of mucous exhibiting softly stained cytoplasmic features and swollen nuclei. Another study by Saeed et al., [15] who histopathological finding revealed that single oral dose of Aspirin 100mg/kg in early ulcer group made ulceration and sloughing of epithelial cells of mucosa, severe congestion and edema in the submucosa as well as coagulative necrosis and edema in the gastric glands. The processes through which NSAIDs lead to the shedding of the superficial epithelium were detailed via Ittiyavirah and Paul [16], they indicated that the localized activity of these drugs can destroy epithelial cells directly, a phenomenon linked to their suppression of prostaglandin E2 and prostaglandin I2 in the stomach, which are crucial in suppressing gastric acid production. Additionally, they cause osmotic lysis, which occurs when charged NSAIDs become trapped, resulting in cell dying attributed to the disruption of oxidative phosphorylation. Earlier research indicated that non-steroidal anti-inflammatory drugs could hinder the healing of epithelial tissue by diminishing the function of epidermal growth factor signaling, while the current study did not evaluate EGF, this process might help to clarify the histopathological changes seen in the gastric lining [17]. Also the enlarged stomach glands observed in this study may result from the deterioration of the cells that border these gastric glands, leading to the impression of a broad lumen [18]. Furthermore, the group with ulcers exhibited substantial vacuolation and enlargement of parietal cells, whereas others seemed to be contracted and had pyknotic nuclei, this observations are consistent for a study by Seleem et al. [19] that revealed degeneration characteristics in the oxyntic cells of the ulcer group. The nuclei of these cells were reduced in size with an irregular nuclear membrane and an abundance of heterochromatin, along with noticeable vacuolations in the cytoplasm. This vacuolation may be connected to the heightened development of the secretory canalicular membrane caused by elevated gastric acid production attributed to the diminished suppression influence for prostaglandins in oxyntic cells [20]. Gastric ulcers form within the stomach, impact a large number of individuals globally, and indicate a breach in the layer of the stomach mucosa that extends past the muscularis mucosa, as inflammatory mediators, neutrophils play a significant role and can produce strong reactive oxygen species such as superoxide, hydrogen peroxide, and oxidants from myeloperoxidase, thereby facilitating lipid peroxidation; these reactive oxygen species are extremely toxic to cells and can lead to tissue injury. Additionally, free radicals generated by neutrophils that infiltrate ulcerated gastric tissues hinder the healing process of gastric ulcers in rats [21, 22]. Moreover prior research has shown that when medications cause inflammation in the stomach mucosa, there is a corresponding rise in the production of tumor necrosis factor- α (TNF- α), which increases the creation of superoxide produced from neutrophils and stimulates the production of interleukin-1 (IL-1), resulting in accumulations of neutrophil [23]. Interrupted gastric epithelium, was found in previous studies and the gastric ulcer may be either surface or deep enough to touch the gastric gland base. Disruption epithelial layer, known as mucosal erosion, is frequently seen in cases of severe gastritis, if the damage is significant enough to go through the muscularis mucosa and affect the submucosa, it is classified as an ulcer. In contrast, it has been noted that peptic ulcers represent zones of deterioration and tissue death within the gastrointestinal mucosa that have been subjected to acid-peptic secretions [24, 25]. According to their experiment of some researchers, giving aspirin for two weeks caused the stomach pits to widen and the mucosal cells to desquamate, additionally giving aspirin for four weeks caused more widespread lesions [26]. Certain authors observed several deterioration changes of the peptic and oxyntic cells that can be clarified by the fact that the origin of these modifications stems from the production of reactive oxygen species (ROS) which leads to oxidative harm in the cell membrane and ultimately cell rupture. An alternative interpretation was provided by another source, which linked these alterations to heightened permeability of mitochondria, mitochondrial dysfunction, and the movement of mitochondrial proteins

(specifically apoptosis-inducing factor) [26, 27]. The peptic cells could show greater resistance compared to the mucous columnar and oxyntic cells, this phenomenon might be attributed to their positioning, which causes them to face a higher level of damage from aspirin in comparison to peptic cells that are found deeper within the gland, Researchers indicated that superficial mucous cells are located along the anterior space and the stomach pit, mucous neck cells are found in the necks of the glands, parietal cells are distributed between the mucous neck cells and throughout the deeper sections of the gland, whereas peptic cells are primarily located in lower areas of the stomach glands [28].

4.2 Duodenal Histopathological Alterations

Observations on section of duodenum from untreated rats group (control) demonstrated the villi's typical histological structure, with normal mucosal layers and overlaying mucosal epithelium state free from any injuries that were indicated by simple columnar epithelium in the villi of the duodenum, goblet cells were observed interspersed among those epithelial cells, the lamina propria of the duodenal mucosa was also noted in a normal state made up of loose connective tissue with no irregularities detected, these observations agreement with Călămar et al. [11] who reported the wall of small intestine in all species of mammalian composed of the mucosa, sub-mucosa, muscularis. In addition other researcher mention that the tissues structures of the stomach and intestine were consist of four layers which are (mucosa, submucosa, muscularis, and serosa) [12, 13]. Histopathological investigation of the sections from rats duodenum treated with aspirin in the current investigation revealed a loss of typical architecture, destruction epithelial cells, vacuolations in the large number of cells in mucosa, thicker aggregation of inflammatory cells near the basal line of mucosa, blood congestion, dispersed of connective tissue fibers in submucosal layers, exfoliated epithelial cells degeneration, this may be due to aspirin administration has been known to cause acute and chronic ulcers and gastrointestinal bleeding, this findings agree with Garcia Rodriguez et al. [29] who recorded results in a study similar to those in the current study. Histological observation shows mucosa and submucosa inflammation accompanied by ulceration, erosion of epithelia tissues and hemorrhage within the stomach and duodenum as observed in Wistar rat treated with aspirin [9]. Another study by Goldstein et al. [30] that mentioned Aspirin use has been related to a two-fold increased risk of severe gastrointestinal events. Gastrointestinal ulcers and stomach bleeding are amongst the main adverse effects of aspirin following oral administration [31]. Olayemi et al. [9] who indicated in your research that the use of Aspirin led to damage of the epithelial lining and mucosal layer of the duodenum, this finding was additionally supported by histomorphometric evaluation, which demonstrated a reduction in the thickness of the duodenal mucosa in rats treated with aspirin, along with a decline in the height of the villi after the administration of aspirin. Free radicals produced as a result of oxidative stress raise inflammatory mediators and damage intestinal mucosa [32]. Similar results have been reported by Brzozowski et al. [33], NSAID-induced damage to the gastric mucosa may occur due to several causes: inflammatory cell infiltration, mucosal blood flow, cytokines, free radicals, and gastric acid production. Another study by Mahmoud and Abd El-Ghffar [34] findings suggest that Aspirin administration results in both acute and chronic gastric ulceration, with the development of ulcerative lesions and hemorrhagic areas attributed to multiple pathogenic mechanisms responsible for gastric mucosal damage, consistent with previous research.

4.3 Body-Weight Changes

The aspirin-treated group showed a significant reduction in body weight after the 14-day experimental period compared with the control group. In contrast, the control animals showed an increase in body weight for the same period. The reduction in body weight can be associated with reduced food consumption, gastrointestinal irritation, impaired nutrient usage, or other systemic effects associated with repeated aspirin exposure. However, food consumption and associated metabolic parameters were not assessed in the present study. Therefore, the mechanism responsible for the observed weight loss can't be determined from the current data. Future experiments should monitor food and water consumption throughout the experimental period to determine whether or not body-weight changes are primarily related to altered nutritional intake or to different systemic effects of repeated aspirin administration [9].

4.4 Overall Interpretation

Taken together, the histopathological findings indicate that repeated aspirin exposure at the investigated dose was associated with injury to both gastric and duodenal mucosa. The gastric lesions were characterized predominantly by using epithelial degeneration, mucosal erosion/ulcerative modifications, inflammatory-cell

infiltration, and congestion/hemorrhagic modifications, while duodenal injury was characterized by epithelial degeneration, villous damage, irritation, edema, and vascular changes. The findings support the concept that gastrointestinal toxicity is an important unfavourable effect related to repeated aspirin exposure. Nevertheless, the present study is primarily histopathological and does not establish the molecular pathways chargeable for the observed tissue damage.

4.5 Limitations of the Study

Several barriers must be taken into consideration whilst deciphering the findings. First, the sample size was relatively small, with six animals per group, which can also limit statistical strength. Second, only one aspirin dose and one treatment duration were evaluated; therefore, dose-response and time-based results could not be established. Third, the observe became constrained in the main to histopathological assessment and did no longer include quantitative morphometric measurements or biochemical and molecular markers of oxidative stress, inflammation, apoptosis, or mucosal defense. Fourth, only male rats were included, and therefore the findings may not be generalizable to female animals. Future studies ought to comprise larger pattern sizes, multiple aspirin doses and treatment intervals, quantitative morphometric analysis, and molecular biomarkers to similarly characterize aspirin-induced gastrointestinal damage.

5. Conclusions

The present study demonstrates that repeated oral administration of aspirin at 13.2 mg/kg/day for 14 days is associated with histopathological damage in the stomach and duodenum of adult male albino rats. Gastric changes included epithelial degeneration, mucosal erosion/ulcerative modifications, inflammatory-cell infiltration, and congestion/hemorrhagic modifications, whereas duodenal alterations covered epithelial degeneration, villous damage, inflammatory infiltration, edema, and congestion/hemorrhagic modifications. Aspirin-treated animals also showed a significant reduction in body weight compared with control animals on the quit of the experimental length. These findings provide experimental proof of gastrointestinal mucosal damage associated with repeated aspirin exposure. Further research the use of larger sample sizes, a couple of doses, quantitative morphometry, and molecular and biochemical biomarkers are warranted to decide dose-response relationships and clarify the mechanisms underlying aspirin-induced gastrointestinal injury.

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Conflict of Interest: The author declares that there is no conflict of interest related to this study.

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