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Histological Effect of ginger on the stomach wall in white albino rabbit

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I. Abstract:

Ginger (*Zingiber officinale* Roscoe) has been widely used for its medicinal properties, including anti-inflammatory and digestive benefits. This study investigated the histological effects of ginger on rabbit stomachs over different exposure periods. Twenty-four adult albino rabbits were divided into four groups: two control groups (euthanized at 45 and 60 days) and two treated groups (administered 400 mg/kg ginger extract orally, euthanized at 45 and 60 days). Stomach samples were processed for histological analysis using H&E, PAS-AB (pH 2.5), and Masson trichrome staining. Results indicated that ginger supplementation induced significant changes in gastric wall histological structure, including mucosal hyperplasia, increased mucus production and number of parietal cell in fundus region at 45 days, and parietal and chief cell hyperplasia with mucus depletion at 60 days. These findings suggest that ginger influences gastric mucosal activity in a time-dependent manner, potentially due to its bioactive compounds.

Keywords: ginger, rabbit stomach, histology, gastric mucosa, Zingiber officinale

II. Introduction:

Rabbits were used as experimental model by researchers especially in Iraq (Al-Eqabi et al., 2021, Kalef et al., 2024, Shwaish et al., 2024)

Ginger (Zingiber officinale Roscoe), a popular herbaceous plant, has been generally used as a flavoring agent and herbal medicine for centuries. The main components of ginger rhizome are carbohydrates, lipids, essential oils, terpenes, and phenol compounds such as shogaol and gingerol (AL-Bayaty, 2006, Akinyemi et al., 2015).

Herbal medicines are the dominant requirement in both developed and developing countries as a source of primary health care owing to their quality, broad biological and medicinal activities, high safety margins, and lower costs. Ginger contains fresh or dried roots of Zingiber officinale. The English botanist William Roscoe gave the plant Zingiber officinale in an 1807 publication (Almalki et al., 2017).

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The Chinese have used ginger for at least 2500 years for digestive support, antinausea remedies, bleeding disorders, and rheumatism (Nafia, 2012). It was also used to treat alopecia, toothache, snakebite, and respiratory conditions. In Traditional Chinese Medicine, ginger is a pungent, dry, warming, yang herb for diseases activated by cold, damp weather (Akinyemi et al., 2016).

Ginger is used extensively in Ayurveda, the traditional medicine of India, to block excessive clotting (heart disease), hepatoprotective (Mustafa & Jawad, 2024), reduce cholesterol and fight arthritis and control diabetes (Hameed & Mahmood, 2024). In Arabian medicine, ginger is considered a stimulant. Some Africans believe that eating ginger regularly will help repel mosquitos (Mahmood, 2024). The Greeks wrapped ginger in bread and ate it after meals for digestive support. Subsequently, ginger was included directly into bread and confections such as gingerbread. The Spanish valued ginger, so they established ginger plantations in Jamaica in the 1600s. The Eclectic physicians of the 19th century depended on ginger to induce sweating, raise hunger, cure nausea, and as a topical ointment (Dongre et al., 2015).

Recently, ginger has been extensively cultivated from Asia to Africa and the Caribbean and is used universally as a nausea remedy, as an anti-spasmodic, and to promote warming in case of chills. Ginger is also extensively consumed as a flavoring agent; it is approximate that in India, the individual average daily consumption is 8-10 gm of fresh ginger root. The German commission E has also approved the use of ginger root as a treatment for indigestion and prophylactic against motion sickness (Atef et al., 2013). Ginger is believed to be a plant with properties to rebalance symptoms of osteoarthritis. Ginger has been taken internally and used externally in China, frequent as a compress, patch or in combination with moxibustion (Funk et al., 2016). Also, some researcher used to enhance health of carp fish (Ajeel & Al-Faragi, 2013).

The rabbit's stomach holds approximately 15% of the volume of the entire gastrointestinal tract (O'Malley, 2005). It is thin walled, J-shaped, and lies to the left of the midline (Ghoshal & Bal, 1989). The well-developed cardiac sphincter is lined with non glandular stratified squamous epithelium and prevents vomiting. The fundus contains parietal cells that secrete acid and intrinsic factors and chief cells that secrete pepsinogen. The pylorus has a well-developed, muscled sphincter (Ghoshal & Bal, 1989). When comparing the rabbit's stomach with the man, the division of layers of the gastric wall mucosa (with various concentrations of villi as gastric regions), submucosa, proper, and serosa lamina (Oliveira et al., 2001).

This experiment aimed to study the effects of ginger on rabbit's stomach Histology at different periods.

III. Materials and Methods:

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1.Plant preparation:

The ginger will cut into small pieces and air-dried for 5 to 6 days. The dried ginger will ground to a fine powder using an electronic grinder. Spread the ginger on a plate and dry in the hot sun or in a dehydrator. Once completely dry, grind the dried ginger in a blender or food processor until it becomes a fine powder. Sieve the powder and return any chunks to the food processor to grind into a finer powder (Reddy et al., 2014).

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2. Animals:

Twenty four adult albino rabbits were used in this study. These rabbits were divide into 4 groups:
G1 control animals (4 rabbits) were be euthanized after 45 days of experiment.
G2 control animals (4 rabbits) were be euthanized after 60 days of experiment.
G3 treated animals (8 rabbits) were euthanized after 45 days of ginger intake at a dose of 400 mg/kg oral watery extract.
G4 treated animals (8 rabbits) were euthanized after 60 days of ginger intake at a dose of 400 mg/kg oral watery extract.

Histological samples:

Stomachs were taken from all animals at the 2 different stages of experiment. These samples were conduct to staining with (H&E, PAS-AB(PH-2.5), Masson trichrome) for checking

- Thickness of Mucosa
- Thickness of submucosa
- Thickness of muscularis
- Length of gastric gland

Stomach samples were cut out and washed with normal saline and then by 10% formalin fixed for 72 hrs. Next to fixation, specimens were dehydrated through ascending series of ethyl alcohol (70%, 80%, 90% and 100%) each for 2 hrs , then cleared with xylene for ½ hr. Specimens were infiltrated with paraffin wax (58 – 60ºC) then embedded with paraffin wax to obtain blocks of paraffin. Paraffin sections of six microns were obtained by using rotary microtome. General and special stains

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were used to stains the tissue sections such as hematoxyline-eosin (H&E), Masson Trichrome (MTC), Periodic acid schiff (PAS) (Rabie and Haibat, 2020).

IV. Results

The histological changes figures of stomach showed that gastric wall comprised of an ideal tunica mucosa, tunica submucosa, tunica muscularis and tunica serosa (fig.1 A). At the cardiac and fundus regions of stomach, the tunica mucosa comprised of marked tall epithelial folds that lined by simple columnar epithelium while that the thick layer of the lamina propria had occupied by simple tubular glands (Gastric glands), and the muscularis mucosa has build-up by thin of 3-4 layers of smooth muscle fibers (fig.1B). The gastric glands at the level of neck part of gastric glands were building by mucous secreting cells that revealed abundant of mucous secretion (fig.1C), and the body of gastric glands was builds-up mostly by parietal (Oxyphilic) cells that chowed polygonal shape, had eosinophilic cytoplasm and contained large spherical nucleus, the chief cells were small size has basophilic cytoplasm increase in number in fundus region, while the funds of gastric gland mostly comprised of chief cells (fig.!D). The tunica submucosa was comprised of vascular loose connective tissue (fig.1D). The tunica muscularis was comprised of two layers of smooth muscle fibers: inner circular layer and outer longitudinal layer of tunica muscularis, the outer layer was slightly thin while the outer layer was thicker (fig.1D). The stomach (antrum) from rabbits in 45 days group shows hyperactivity of mucosal cell, increases mucus production and hyperplasia of gastric mucosa and Parietal cells (Figure 11). While, at 60 days group shows hyperplasia of Parietal cells and Chief cells, with depletion of mucus production (Figure 12).

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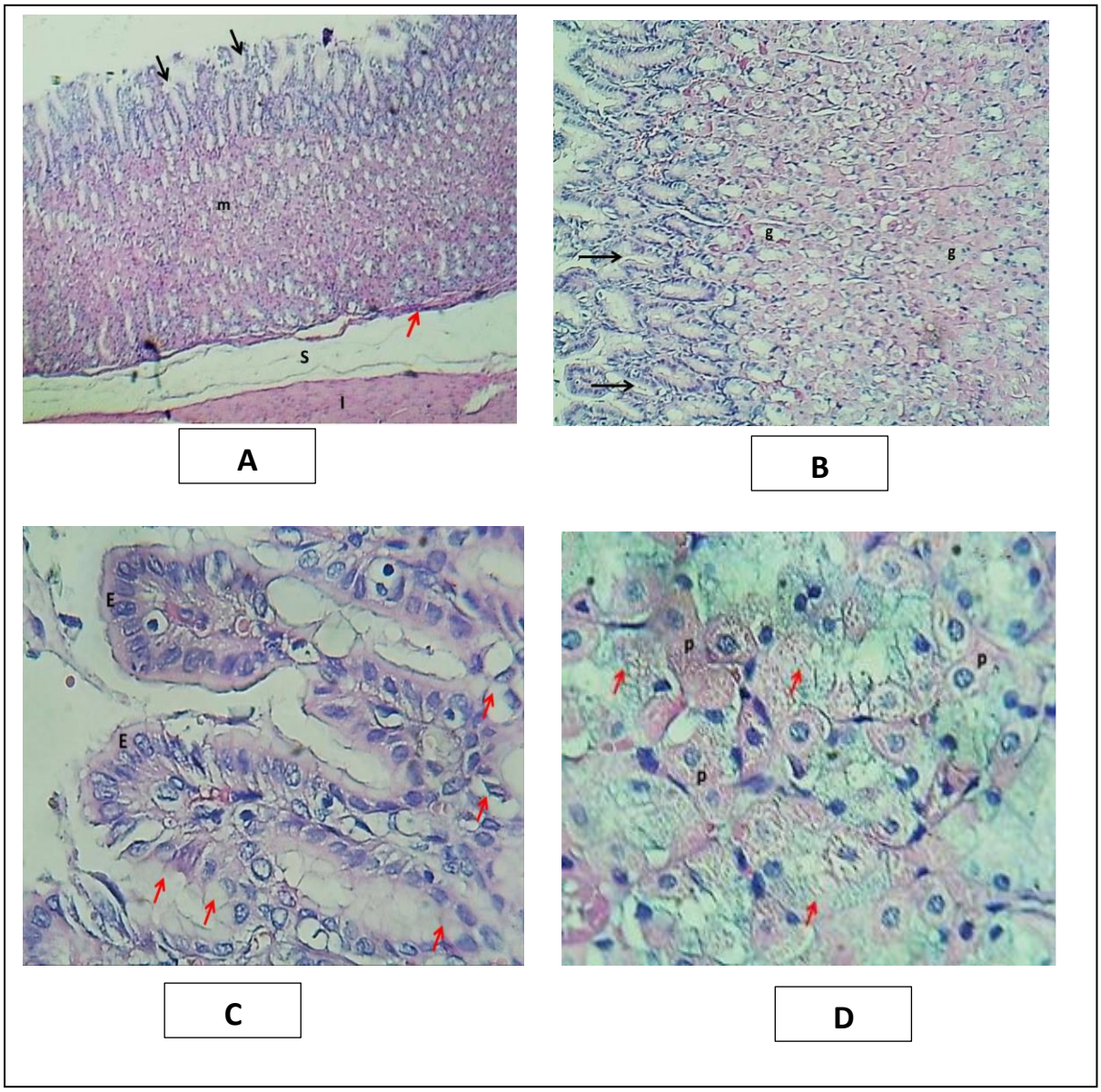

Figure 1: A. section of gastric wall - cardiac region (control) shows mucosa (m), submucosa (S), inner layer (I) of tunica muscularis, epithelial folds –faveoli (Black arrows), muscularis mucosa (Red arrow). B. epithelial folds- faveoli (Black arrows), simple tubular glands (gastric glands) (g). C. shows epithelium (E), & mucous secreting cells (arrows), D. shows mucous secreting cells (arrows) . H&E.40x

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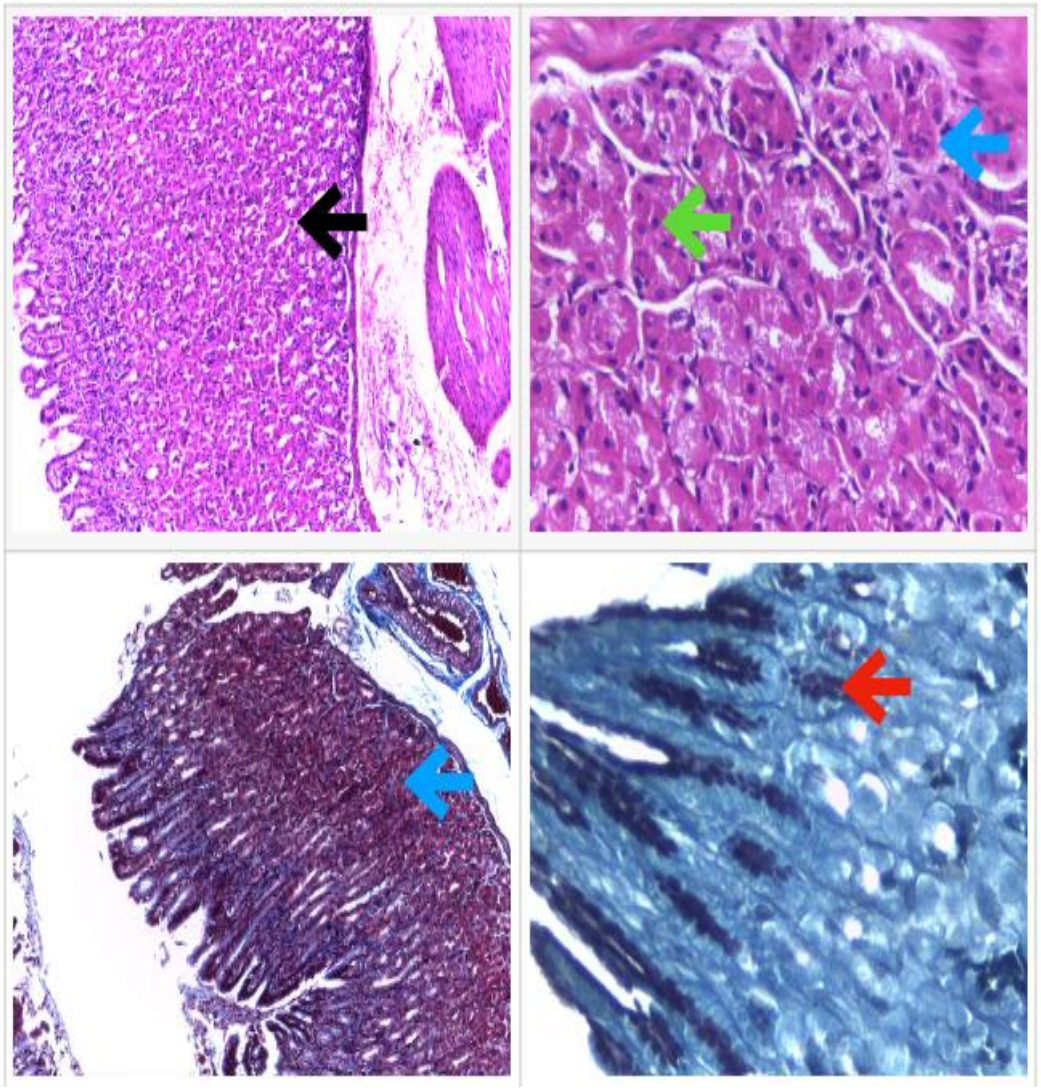

Figure 2. Histophotomicrographs of stomach (antrum) from rabbits in 45 days group shows hyperactivity of mucosal cell (black arrow), increases mucus production (red arrow) and hyperplasia of gastric mucosa (blue arrow)and Parietal cells (green arrow). A&B, H&E X40,,H&E X4, C, Masson X40, D , Alcian blue X40 .

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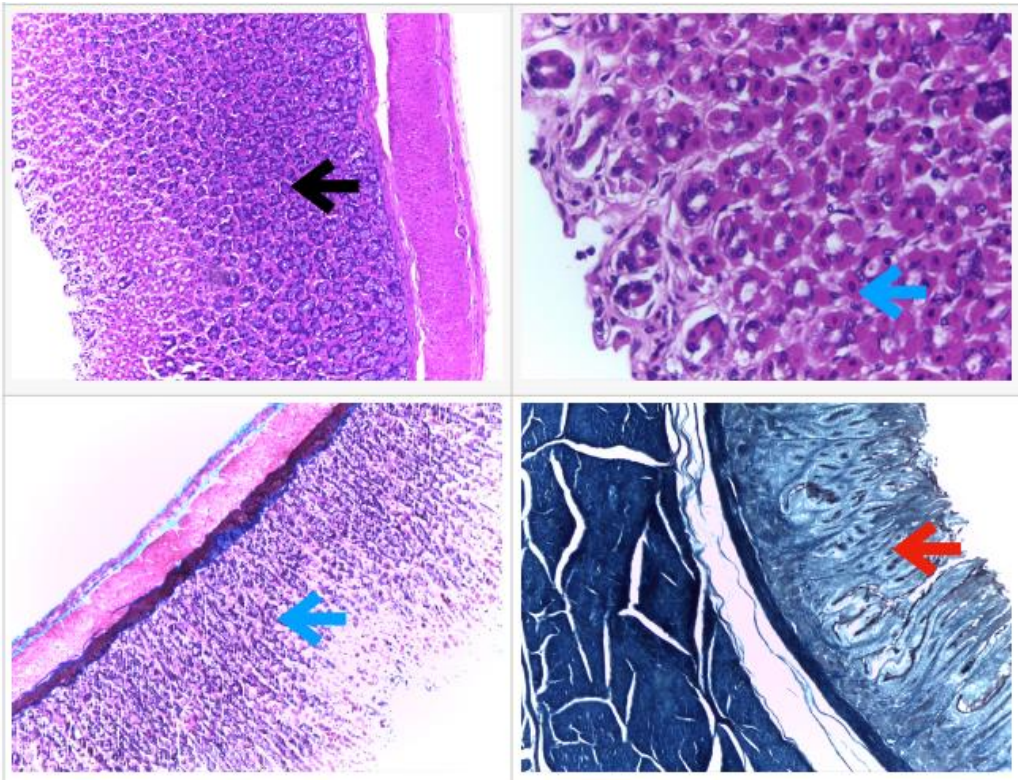

Figure 3. Histophotomicrographs of stomach (antrum) from rabbits in 60 days group shows hyperplasia of Parietal cells and Chief cells (blue arrow), with depletion of mucus production (red arrow). A, H&E X40,B,H&E X40, C, Masson X4, D, Alcian blue X10.

V. Discussion:

The present study investigated the histological effects of ginger (*Zingiber officinale* Roscoe) on rabbit stomachs over different exposure periods (45 and 60 days). The findings revealed significant time-dependent alterations in gastric mucosal structure, glandular activity, and mucus secretion. These changes suggest that ginger exerts both protective and modulatory effects on gastric physiology, which may be attributed to its bioactive compounds, including gingerols, shogaols, and phenolic constituents (Akinyemi et al., 2015; Almalki et al., 2017).

At the 45-day mark, ginger supplementation resulted in hyperactivity of mucosal cells, increased mucus production, and hyperplasia of the gastric mucosa and parietal cells. This aligns with previous research indicating that ginger enhances gastric mucus secretion, which serves as a protective barrier against acid-induced damage (Dongre et al., 2015). Mucus plays a crucial role in preventing ulceration by neutralizing gastric acid and shielding the epithelial lining from erosive factors (Atef et al., 2013). The observed increase in mucus secretion may be mediated by ginger's ability to

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stimulate prostaglandin E2 (PGE2) synthesis, a key factor in mucosal defense mechanisms (Funk et al., 2016).

Additionally, the hyperplasia of parietal cells suggests that ginger may influence gastric acid secretion. While acute ginger intake has been reported to suppress excessive acid production (Reddy et al., 2014), prolonged exposure (as seen in this study) could lead to adaptive cellular proliferation to maintain gastric homeostasis. This finding is consistent with traditional uses of ginger in Ayurvedic and Chinese medicine, where it is employed to manage dyspepsia and gastric irritation (Almalki et al., 2017).

By the 60-day period, histological examination revealed hyperplasia of both parietal and chief cells, accompanied by a reduction in mucus secretion. This shift suggests a transition from a protective to a secretory-dominant state in the gastric mucosa. The depletion of mucus could indicate either due to Downregulation of mucus production due to prolonged ginger exposure, or Compensatory glandular hypertrophy to maintain digestive efficiency.

The increase in chief cells (which secrete pepsinogen) implies enhanced proteolytic activity, possibly improving protein digestion. However, the decrease in mucus raises concerns about potential mucosal vulnerability if ginger is consumed excessively over long periods. Previous studies have reported similar biphasic effects, where ginger initially enhances mucosal protection but may lead to adaptive changes with chronic use (Oliveira et al., 2001).

The study also noted thickening of the muscularis mucosa, particularly in the pyloric region, where smooth muscle layers exhibited increased density. This finding supports ginger's known prokinetic effects, which may enhance gastric motility and emptying (Ghoshal & Bal, 1989). Such an effect aligns with ginger's traditional use in alleviating gastroparesis and indigestion (Funk et al., 2016).

For instance, Atef et al. (2013) found that ginger extract reduced ethanol-induced gastric ulcers in rats by enhancing mucus secretion. Dongre et al. (2015) reported that ginger juice protected against aspirin-induced gastric damage, similar to our 45-day findings. Funk et al. (2016) suggested that chronic ginger intake could influence gastric acid regulation, consistent with our 60-day observations.

However, some discrepancies exist, particularly regarding long-term effects. While some studies suggest sustained benefits (Akinyemi et al., 2015), others indicate potential adaptations or desensitization (Oliveira et al., 2001). These variations may stem from differences in dosage, administration route, or species-specific responses.

Conclusion

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This study demonstrates that ginger induces time-dependent histological changes in the rabbit stomach, with early-phase mucosal protection (increased mucus, parietal cell activity) transitioning to later-phase glandular adaptation (chief cell hyperplasia, reduced mucus). While ginger appears beneficial for short-term gastric health, prolonged use may alter secretory dynamics, warranting further investigation.

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