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Curcumin versus omeprazole against the effect of deferasirox on fundic gastric mucosa of adult male albino rat: immunohistochemical and scanning electron microscopic study

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ABSTRACT

Despite deferasirox (DFX) efficacy in hemochromatosis treatment, it has many gastrointestinal side effects. Omeprazole and other proton pump inhibitors are prescribed for patients complaining from these side effects. Curcumin has anti-inflammatory and antioxidant effects. The study aims to determine the influence of DFX on the histological structure of fundic gastric mucosa of adult male albino rats and to establish the possible beneficial effect of curcumin versus omeprazole. Thirty-two adult male albino rats were split into four groups; control group, group II were treated by DFX (100 mg/kg), group III and group IV received curcumin (100 mg/kg) and omeprazole (20 mg/kg), respectively one hour before administration of DFX. All treatments were given orally once daily for 4 weeks. Samples from the fundus of stomach were subjected to light, immunohistochemical and scanning electron microscopic studies. DFX treated group revealed variable degrees of mucosal lesions by light microscope and were confirmed by scanning electron microscope (SEM). a significant reduction in periodic acid-Schiff stain reaction and a significant increase in cleaved caspase-3 immunohistochemical expression were recorded. The histological structure of fundic mucosa was preserved in both curcumin and omeprazole treated groups, but it was better in curcumin treated group. Curcumin is more effective than omeprazole in preserving changes caused by the administration of DFX on the histological structure of the fundic mucosa of the stomach. So, it is recommended for patients who treated by DFX for long time to protect the gastric mucosa.

Key words: Deferasirox, Curcumin, Omeprazole, SEM, periodic acid-Schiff stain, Fundus, Stomach

1. Introduction

Iron is a necessary element that is vital to many bodily metabolic functions, such as energy production, immunological response, and oxygen transport. The body may accumulate too much iron in some disease states that is called iron overload (McDowell et al., 2024). Iron overload is linked with multiorgan damage and causes serious adverse effects, including hemosiderosis, impotence, infertility, liver cirrhosis, liver cancer, hepatitis, cardiac dysfunctions, and metabolism problems (Entezari et al., 2022). Currently, three main medications are available to remove excess iron for hemochromatosis treatment, ferrioxamine administered parenterally and oral chelators such as deferiprone and deferasirox (DFX) (Salem et al., 2023). DFX is a cornerstone drug in chelating overloaded iron brought on by repeated blood

transfusions now because of its effectiveness and simplicity of administration. Despite DFX having a generally good safety profile, many investigations revealed several incidences of serious organ toxicity following its prolonged administration (Gottwald et al., 2020). Additionally, many gastrointestinal (GIT) symptoms were reported by patients who were using DFX such as nausea, vomiting, stomach pain or even GIT hemorrhage (Muzamil et al., 2015). Omeprazole and other proton pump inhibitors (PPIs) are extensively utilized to manage the GIT complication of DFX as erosive esophagitis, peptic ulcers, and gastroesophageal reflux. However, the high possibility of drug-drug interactions between omeprazole and other co-medication must be taken into consideration (Bauters et al., 2010; Yadlapati and Kahrilas, 2017). Omeprazole has been shown to have anti-inflammatory and antioxidant impact on the mucosa of the stomach (Chanchal et al., 2016). However, its prolonged usage may rise the opportunity of damage of renal tissue, decreases vitamin B_{12} absorption and raises the risk of heart attacks due to reduction of blood magnesium levels (Katz et al., 2013; Hussein et al., 2023). Curcumin is a polyphenolic substance that is utilized in conventional medicine and is thought to be a source of food enhancer or nutritional pigment. Its consumption could be beneficial with a number of chronic conditions, including diabetes, hypertension, and obesity (Pattanayak et al., 2016; Shabbir et al., 2021). Disorders associated with inflammation and oxidative stress are treated with curcumin. Additionally, curcumin has been used to treat GIT conditions such diarrhea, flatulence, dyspepsia, and even gastric and duodenal ulcers (Kwiecien et al., 2019). So, the purpose of this work was to ascertain the impact of DFX on the histological structure of gastric fundic mucosa of adult male albino rat and establish the potential protective role of curcumin versus omeprazole.

2. Materials and methods

Drugs

Deferasirox (Generic name: Exjade) is in the form of 500 mg tablets, Novartis, Egypt. Curcumin was bought as a bottle containing 10 grams of yellow powder (Cat. No. C1386) from Sigma chemical company, Egypt. Omeprazole (Generic name: Pepzol) is in the form of 20 mg capsule, Hikma pharma company, Egypt.

Animals

Thirty-two adult male albino rats, weighing 180-200 grams each and 12 weeks old were used. The animal use and care committee at Tanta University, Faculty of Medicine, Egypt agreed to all the procedures of this experiment with approval code 36264PR651/4/24.

Experimental design

Following their adaptation, the rats were randomly divided into four groups (8 rats each) as follows: control group (G1): was divided into two equal subgroups: subgroup 1: rats were maintained without any treatment. Subgroup 2: rats received 0.5 ml of distilled water (the diluting vehicle of DFX, curcumin and omeprazole) orally daily for 4 weeks. DFX treated group (G II): each rat received DFX (100 mg/kg) dissolved in distilled water once daily orally for 4 weeks (Adel et al., 2021) DFX and curcumin treated group (G III): each animal received an aqueous suspension of curcumin (100 mg/kg) once daily orally for 4 weeks (Lubbad et al., 2009) one hour before administration of DFX by the same dose, route and time of administration as in group II . DFX and Omeprazole treated group (G IV): each rat received omeprazole (20 mg/kg) dissolved in distilled water once daily orally for 4 weeks (Elkerdasy et al., 2021) one hour before administration of DFX by the same dose, route and time of administration as in G II.

At the end of the fourth week, all animals were put under anesthesia with an intraperitoneal injection of sodium pentobarbital at a dose of 50 mg/kg (Ghasi et al., 2020). Specimens from the funds of the stomach were excised and prepared for light and scanning electron microscopic studies.

Light microscopic study

Fatty gastric fundic samples were fixed, dehydrated, and cleared. After embedding, sections of 5 microns were stained with Hematoxylin and Eosin (H&E) (Bancroft and Layton, 2019) and Periodic acid-Schiff stain (PAS) (Layton and Bancroft, 2019).

Immunohistochemical staining

Five micrometer (5μm) thick sections of the fundus were deparaffinized, rehydrated, rinsed, incubated with the primary antibody diluted 1:100 (cleaved caspase 3 to demonstrate cell apoptosis) (Lab Vision Thermo Fisher Scientific, USA, catalog number RB-1197-R7). Thereafter, they were co-incubated with biotinylated secondary antibody (Dako North America, Inc., CA, USA). Immunohistochemical activity was visualized by 3, 3′-diaminobenzidine chromogens. Mayer's hematoxylin was added as a counter stain. Saline was used as a substitute for the primary antibody to provide negative control. The positive control for caspase 3 was tonsil tissue. Positive reactions appeared as brown cytoplasmic or nuclear **(**Sanderson et al., 2019).

Scanning electron microscopic study

Small pieces of stomach were immersed in phosphate buffered glutaraldehyde 2.5% for fixation and post-fixed in phosphate buffered 1% Osmium tetra oxide. The samples were dehydrated, dried using liquid CO_2 then fixed to the stubs and coated with particles of gold (El-Tantawi, 2007; Zhou et al., 2007). Finally, the specimens were inspected and photographed using JEOL, JSM- 5200 LV scanning electron microscope at Electron Microscope Unit, Faculty of Medicine, Tanta University.

Morphometric study

For morphometric analysis, the software "Image J" (version 1.48v National Institute of Health, Bethesda, Maryland, USA) was used. Non-overlapping 10 fields from each group at a magnification of 400X for PAS and 200X for caspase-3 stained sections were used to quantitatively evaluate the followings:

1. Mean area percentage of PAS positive reaction.

2. Mean area percentage of caspase-3 positive cells in caspase-3 immunostained sections. The prepared slides for light microscopic and morphometric studies were inspected and captured using an Olympus light microscope with a built-in camera in the Histology and Cell Biology department, Faculty of Medicine, Tanta University.

Statistical analysis

We One-way analysis-of-variance (ANOVA) and the post hoc Tukey test were utilized to compare quantitative data that were shown as means and standard deviations (SD). *p*-values less than 0.05 denoted statistical significance (Emsley et al., 2010).

3. Results

Light microscopic, hematoxylin and eosin results

Microscopic examination of the fundic gastric mucosa` sections from GI (control) depicted the normal histological construction of the gastric fundic mucosa. The epithelium that lined the surface and extended to the narrow gastric pits was a simple columnar mucous secretory epithelium, with oval pale basal nuclei. Mucous appeared foamy forming a coat over the surface epithelium and extending to the narrow gastric pits. The gastric glands appeared narrow, straight and filling the lamina propria. Each gland consisted of an isthmus, neck and base (Figs. 1 and 2). The lower part of the glands was occupied by parietal cells with many chief cells in between. The parietal cells appeared large polyhedral or triangular with central spherical nuclei and eosinophilic cytoplasm. The base of the fundic glands showed predominance of chief cells. They appeared low columnar with basal spherical nuclei and basal darkly basophilic cytoplasm (Fig. 3). Regarding DFX treated group (G II), uneven degrees of mucosal lesions were observed. Some sections showed erosion of the surface mucosa or even exfoliated cells in the lumen.

The surface lining columnar cells appeared with dark stained or irregular nuclei. Extravasated RBCs were observed in between the glands (Figs. 4 and 5). Wide, irregular and discontinuous gastric glands were also seen. Cystic dilatation of some glands with sloughing of the lining epithelium in the lumen was detected. Parietal cells appeared with dark stained nuclei and marked vacuolation of the cytoplasm. Decreases in the density of the chief cells which were detected with dark pyknotic nuclei and decreased cytoplasmic basophilia were found (Figs. 6 and 7). Noteworthy, examination of G III (curcumin treated group) depicted apparently normal lining epithelial cells and regular arrangement of the fundic gastric glands which appeared straight, crowded (Fig. 8).

The surface epithelium and the gastric pits were lined by simple columnar mucous secretory cells with basal pale oval nuclei. The majority of parietal cells appeared with eosinophilic cytoplasm and central rounded nuclei except few cells appeared with dark stained nuclei. Closely packed chief cells with basal rounded nuclei and basal basophilic cytoplasm were detected. (Figs. 9 and 10). Omeprazole treated group (G IV) depicted nearly regular mucosal structure with focal detached surface epithelium and few columnar cells with dark stained nuclei. (Figs. 11 and 12). A few parietal cells appeared with vacuolated cytoplasm and some chief cells showed darkly stained nuclei (Fig. 13). Dilated congested blood vessels within the lamina propria were also detected (Fig. 13).

Periodic acid Schiff reaction (PAS)

The control group showed the characteristic magenta red color of PAS positive reaction for mucin film mainly on the surface epithelium and the gastric pits (Fig. 14). The PAS reaction was depleted, interrupted and revealed a highly significant decrease in DFX treated group (p<0.001) versus the control group (Fig. 15). Nevertheless, sections from curcumin and omeprazole treated groups (G III and GIV) respectively depicted a nearly normal PAS-positive reaction with an insignificant difference versus the control (p>0.05) but it was a highly significant increase versus G II (DFX group) (p<0.001) (Table 1, Histogram 1). (Figs. 16 and 17).

Immunohistochemical results

The control group showed faint cytoplasmic caspase-3 expression in few cells of the gastric glands (Fig. 18). DFX treated group showed massive positive expression with a highly significant increase of cleaved caspase-3 immunoreactivity in many cells in all regions of the gastric glands versus the control (p<0.001) (Fig. 19). Moderate expression of cleaved caspase-3 was found in curcumin and omeprazole treated groups, respectively, distributed all over the mucosa and a highly significant decrease versus the DFX treated one (p<0.001) was detected. Omeprazole treated group showed a highly significant increase versus the control group (p<0.001) while the curcumin treated group showed just a significant decrease (p<0.01) versus the control (Table 1, Histogram 1, Figs 20 and 21).

Scanning electron microscope results

Examination of the control group revealed surface mucous epithelial cells which were dome shaped, separated by well demarcated boundaries and surrounding the aperture of the gastric pits. Mucous over the epithelial surface was also detected (Fig. 22). DFX treated group examination showed disturbed architecture of the surface epithelial cells which appeared with rough eroded surfaces, as well as loss of its dome shaped appearance and the boundaries between cells with disturbed wide gastric pits (Fig. 23). As regards the curcumin treated group, most of the surface epithelial cells appeared with dome shaped surface and intact cellular boundaries covered by mucous, surrounding the gastric pits. Few cells appeared with rough surface. Swollen detached epithelial cell was also noticed (Fig. 24). While the omeprazole treated group revealed dome shaped surface epithelial cells surrounding the gastric pits. Other surface cells still appeared with rough eroded surface (Fig. 25).

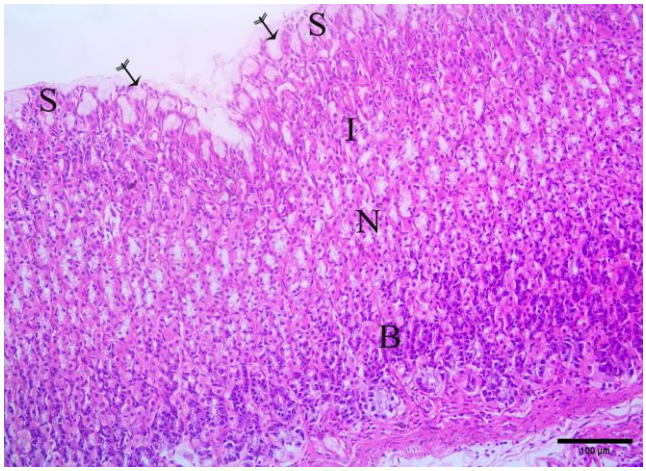


Fig. 1. Fundic mucosa of control group (G I) shows the gastric mucosa with surface lining columnar cells (S) extending to narrow gastric pits (feathery arrows). The lamina propria is occupied with the fundic glands which are divided into isthmus (I), neck (N) and base (B) (H&E x 200, scale bar =100µ).

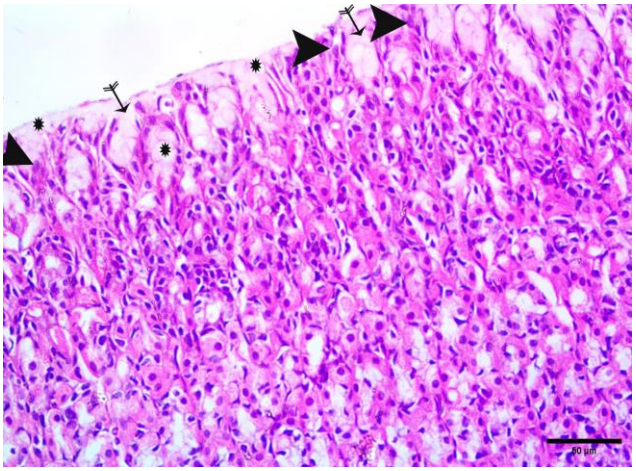


Fig. 2. The upper part of the fundic mucosa from the control group shows the surface lining columnar mucous secretory cells with basal oval pale nuclei (arrow heads) which extending to the narrow gastric pits (feathery arrows) and covered by the cloudy appearance of mucous (stars) (H&E x 400, scale bar=50µ).

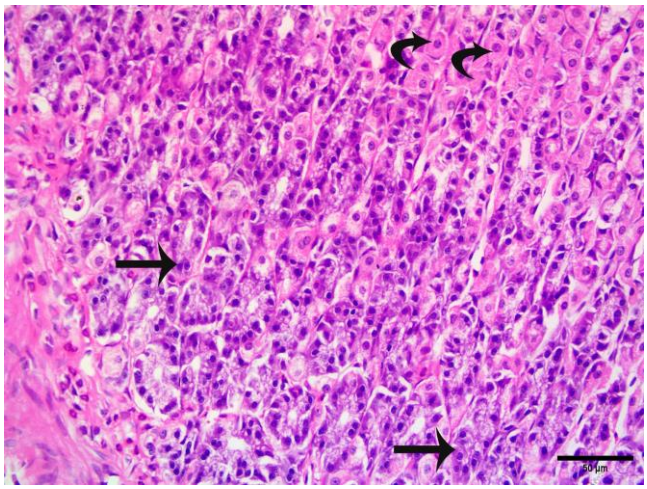


Fig. 3. The basal part of the fundic mucosa from the control group shows parietal cells with eosinophilic cytoplasm and central spherical nuclei (curved arrows). The chief cells are massively distributed in the basal part with basal rounded nuclei and basal dark basophilic cytoplasm (arrows) (H&E x 400, scale bar=50µ).

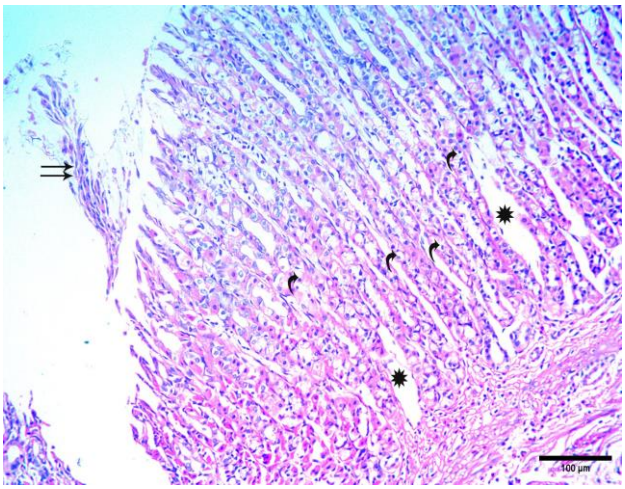


Fig. 4. Fundic mucosa from group II (DFX treated group) shows sloughed surface epithelium (double arrows). Many parietal cells appear with dark stained nuclei and vacuolated cytoplasm (curved arrows). Wide spaces in between the fundic gastric glands are also noticed (stars) (H&E x200, scale bar=100µ).

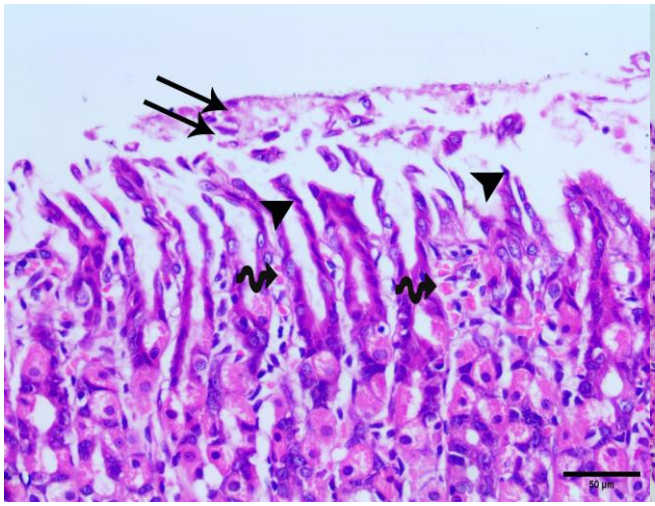


Fig. 5. The upper part of the fundic mucosa from DFX treated group shows exfoliated surface epithelium (double arrows). Some epithelial cells appear with dark stained irregular nuclei (arrow heads). Notice extravasated RBCs (wavy arrows) (H&E x400, scale bar=50µ).

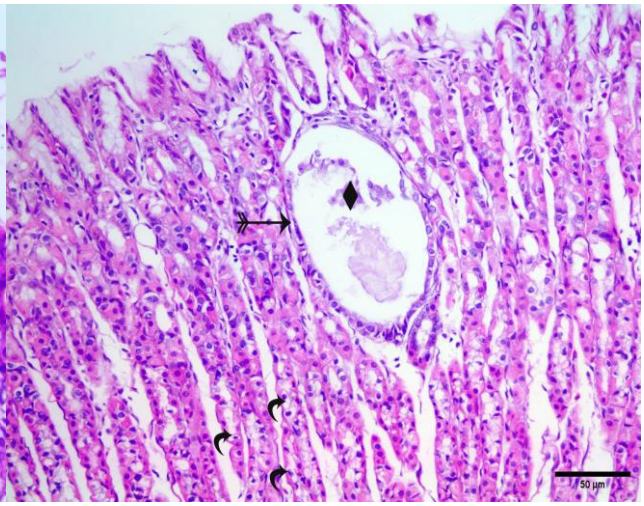


Fig. 6. The upper part of the fundic mucosa from DFX treated group shows cystic dilatation of the gland (feathery arrow) with detached epithelium (diamond) in its lumen. Parietal cells appear with vacuolated cytoplasm and darkly stained nuclei (curved arrows) (H&E x400, scale bar =50µ).

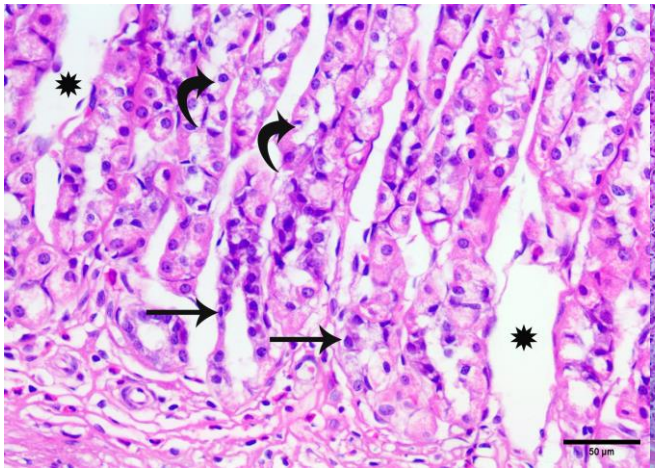


Fig. 7. The basal part of the fundic glands from DFX treated group shows wide separation (stars) at the base of the glands. Apparent decrease in the density of the cheif cells which appear with dark stained nuclei and decreased cytoplasmic basophilia (arrows). Notice parietal cells appear with vacuolated cytoplasm and darkly stained nuclei (curved arrows) (H&E x400, scalebar =50µ).

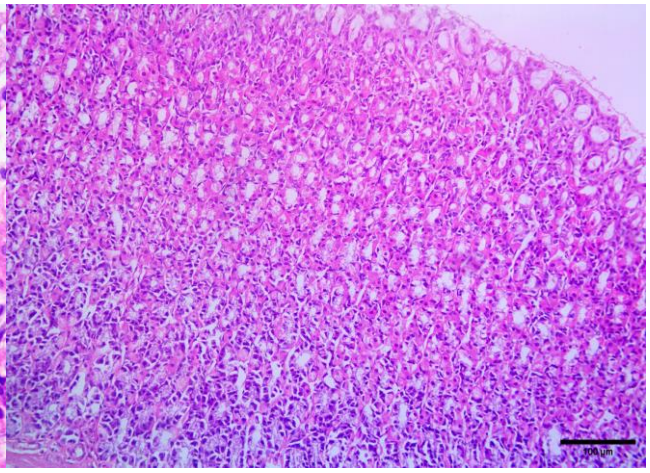


Fig. 8. Fundic mucosa from group III (curcumin treated group) shows straight and crowded fundic glands (H&E x200, scale bar =100µ).

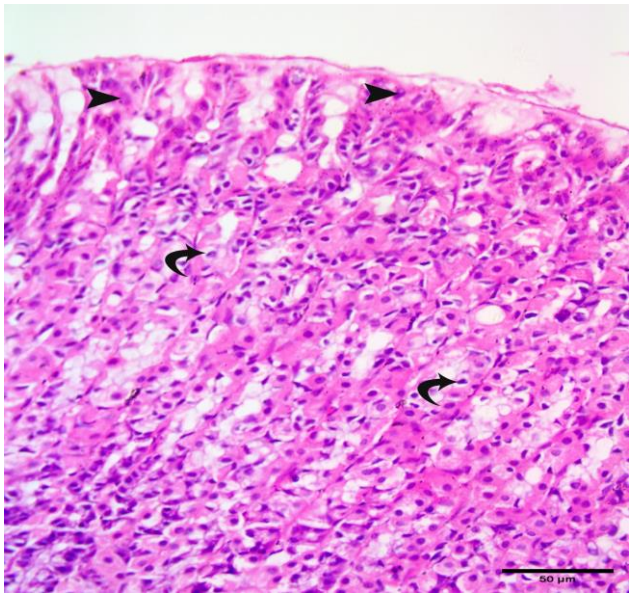


Fig. 9. The upper part of the fundic mucosa from the curcumin treated group shows the surface columnar epithelial cells with basal oval pale nuclei (arrow heads). Some parietal cells appear with dark stained nuclei and vacuolated cytoplasm (curved arrows) (H&E x400, scale bar=50µ).

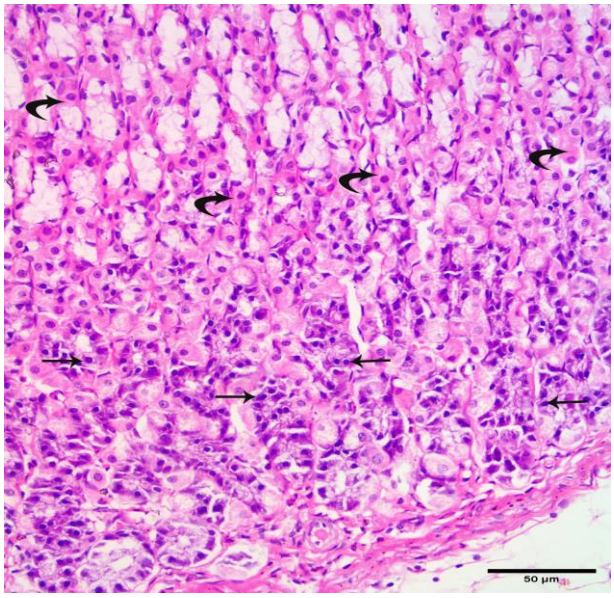


Fig. 10. The basal part of the fundic glands from curcumin group shows closely packed chief cells with basal rounded nuclei and basal cytoplasmic basophilia (arrows). Notice many parietal cells appear with eosinophilic cytoplasm and central spherical nuclei (curved arrows) (H&E x400, scale bar=50µ).

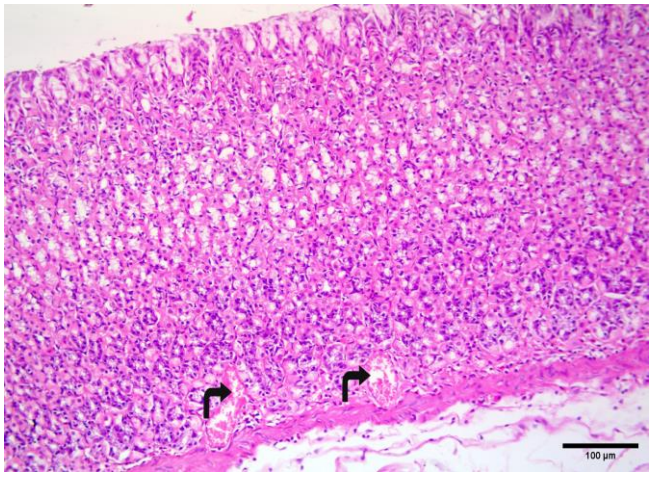


Fig. 11. Fundic mucosa from G IV (omeprazole treated group) shows the regular arrangement of the gastric glands. Notice the dilated congested blood vessels in the lamina propria (angled arrows) (H&E x200, scale bar=100µ).

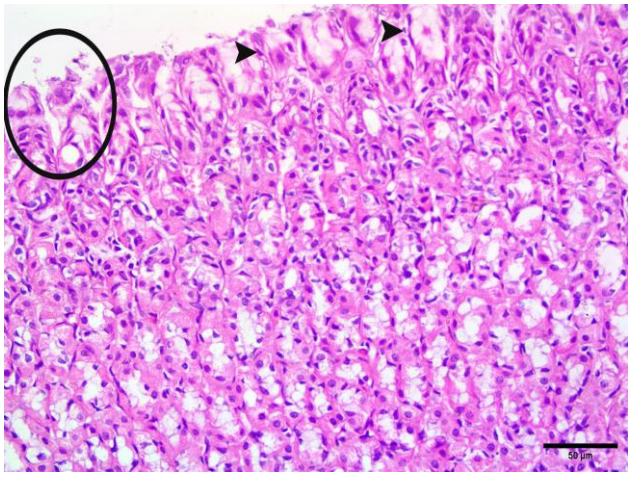


Fig. 12. The upper part of the fundic mucosa from omeprazole group shows focal detached epithelium (circle) and some surface epithelial cells with darkly stained irregular nuclei (arrow heads) (H&E x400, scale bar=50µ).

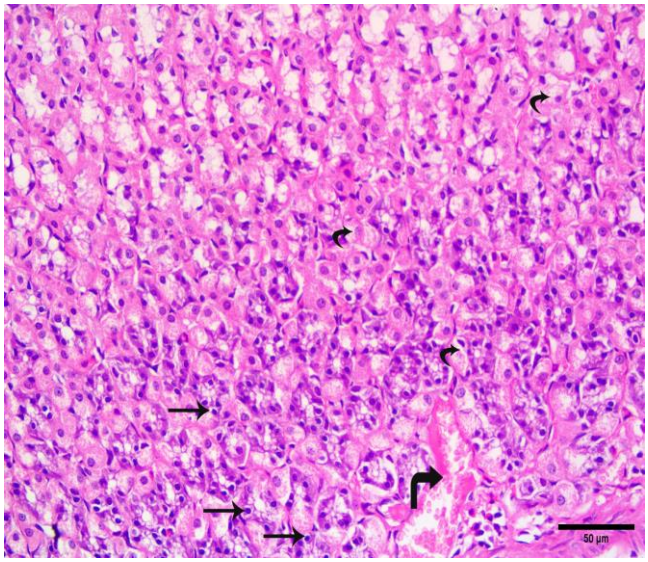


Fig. 13. The basal part of the fundic glands from omeprazole treated group shows some chief cells with dark stained nuclei (arrows) and few parietal cells with vacuolated cytoplasm (curved arrows). Notice the dilated congested blood vessel within the lamina propria (angled arrow) (H&E x400, scale bar=50µ)

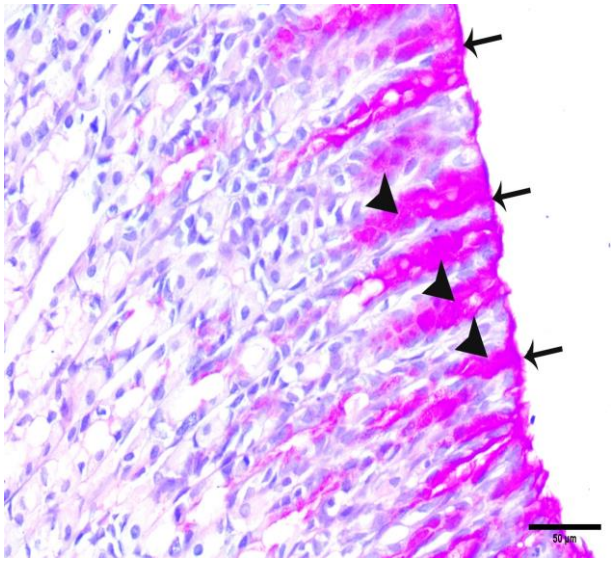


Fig. 14. Control group shows strong magenta red color of PAS on the surface (arrows) extending to the gastric pits (arrow heads) (PAS x400, scale bar=50µ)

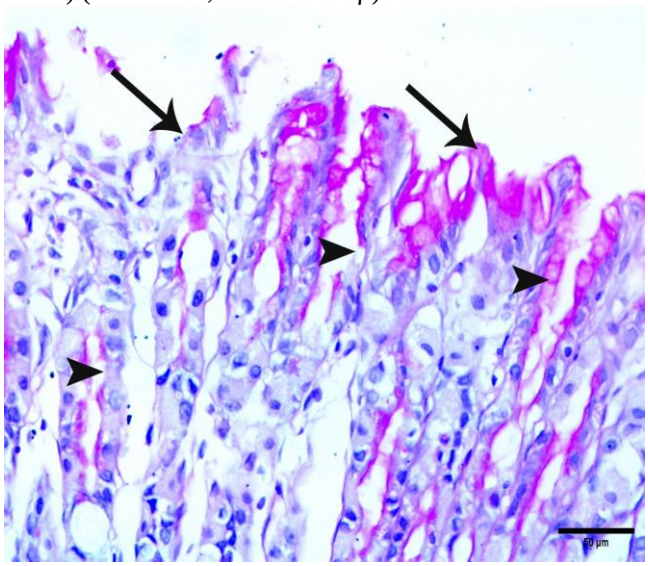


Fig. 15. A section from DFX treated group shows interrupted and depleted PAS reaction in the surface (arrows) and within the pits (arrow heads) (PAS x400, scale bar=50µ).

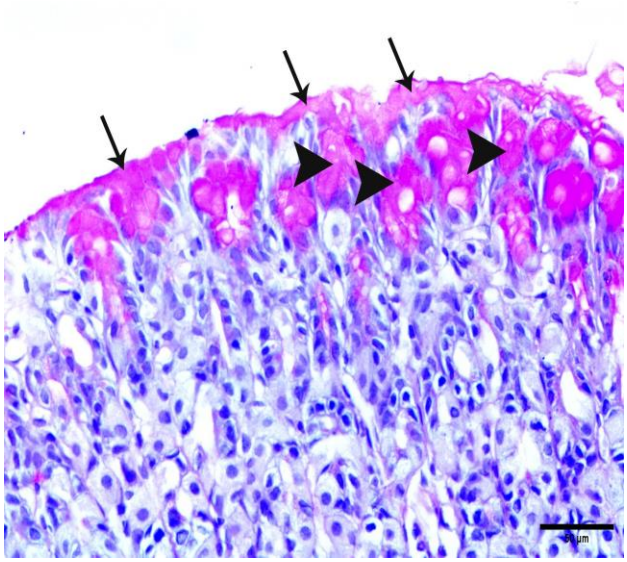


Fig. 16. A section from curcumin treated groups shows strong magenta red color of PAS in the surface (arrows) and gastric pits (arrow heads). (PAS x400, scale bar=50µ)

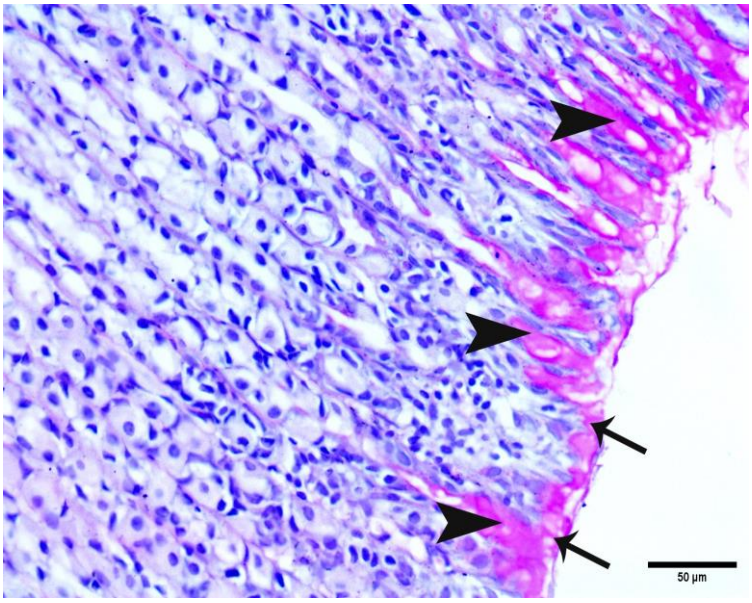
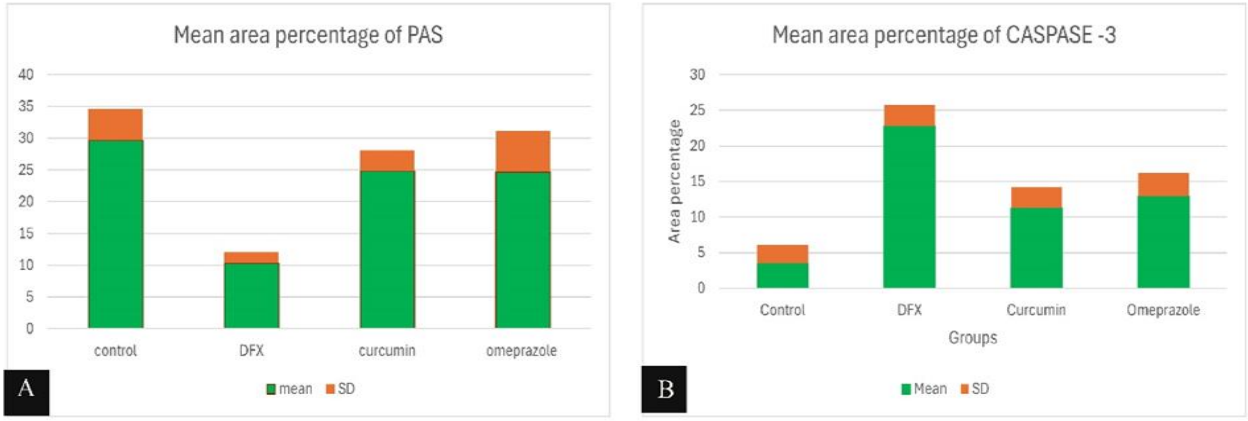


Fig.17. A section from omeprazole treated groups shows strong magenta red color of PAS in the surface (arrows) and gastric pits (arrow heads)(PAS x400, scale bar=50µ)

Table 1. Comparison between the studied groups

	Control	**DFX group**	**Curcumin group**	**Omeprazole group**
PAS reaction (%)	29.67±4.96	10.34±1.68***	24.79±3.28	24.71±6.47
Caspase-3 immunoreaction (%)	3.49±2.63	22.76±2.96 ***	11.32±2.87**	12.92±3.26***

Data are represented as mean ±SD, ** Significant as compared to control group ($p<0.01$), *** Highly significant as compared to control group ($p<0.001$).



Histogram. 1. A. Mean ±SD of the mean area percentage of PAS positive reaction in different groups and B. Mean ±SD of the mean area percentage of cleaved caspase-3 immunohistochemical reaction in different groups.

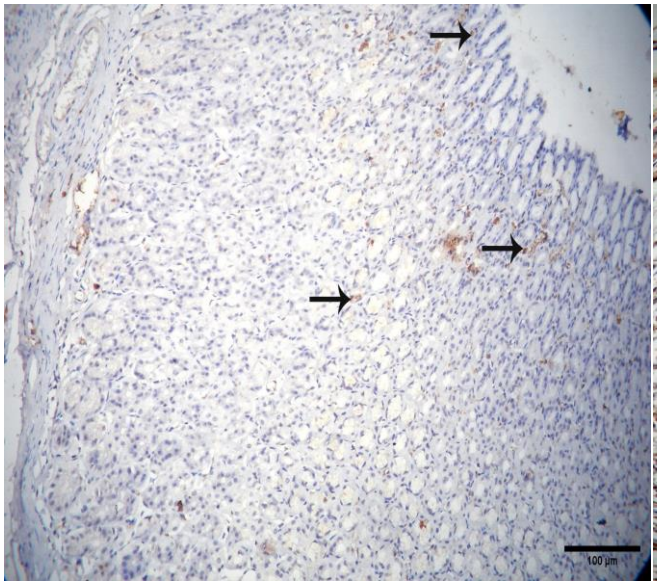


Fig. 18. A photomicrograph of immunohistochemical cleaved caspase 3 stained section from the control group showing faint positive immunoreaction in a few cells of the fundic glands (arrows) (cleaved Caspase 3, x200, scale bar=100µ).

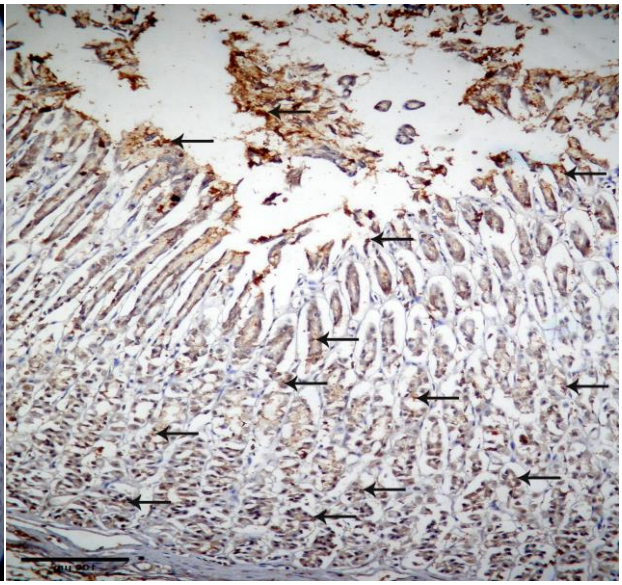


Fig. 19. A photomicrograph of immunohistochemical cleaved caspase 3 stained section from DFX treated group shows strong marked immunoreaction in many cells of all parts of the fundic glands (arrows) (cleaved caspase 3 x200, scale bar=100µ)

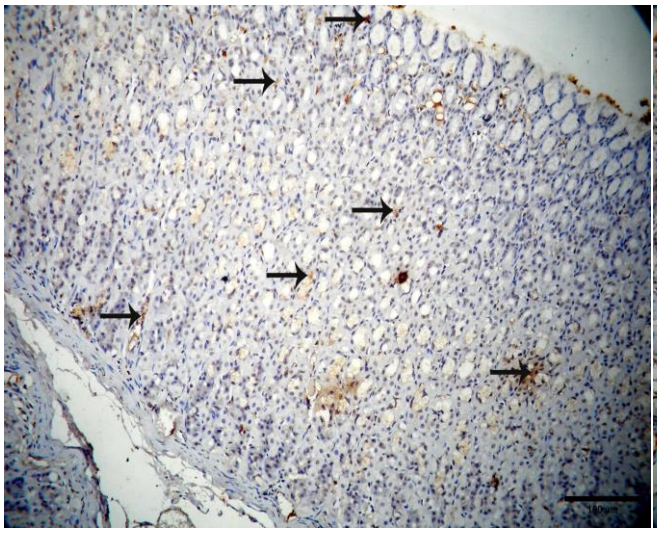


Fig. 20. A photomicrograph of immunohistochemical cleaved caspase 3 stained section from curcumin treated group shows moderate immunoreaction in some cells of the fundic glands (arrows) (cleaved caspase3 x200, scale bar=100µ).

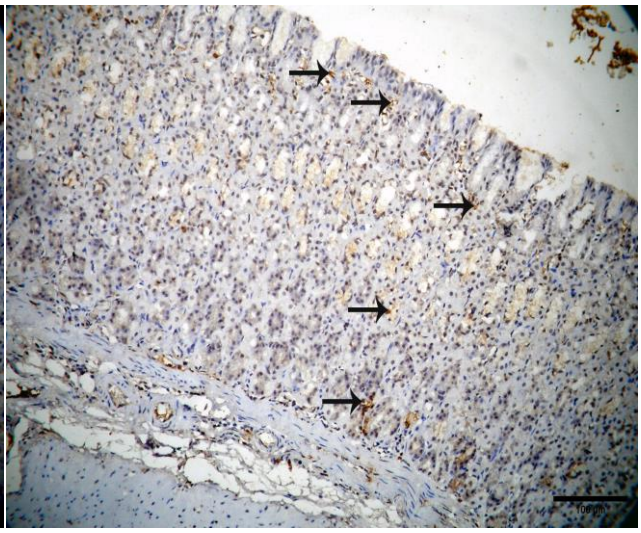


Fig. 21. A photomicrograph of immunohistochemical caspase 3 stained section from omeprazole treated group shows moderate immunoreaction in some cells of the fundic glands (arrows) (caspase3 x200, scale bar=100µ).

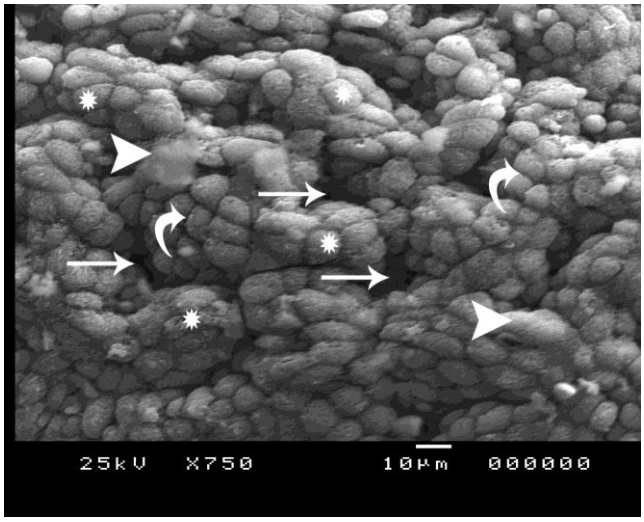


Fig. 22. A scanning electron micrograph of control group shows the gastric pits (arrows) are surrounded by dome shaped surface mucous epithelial cells (stars) with well demarcated boundaries (curved arrows). Notice mucous (arrowhead) over the epithelial surface is also present (SEM, x750, scale bar 10µ).

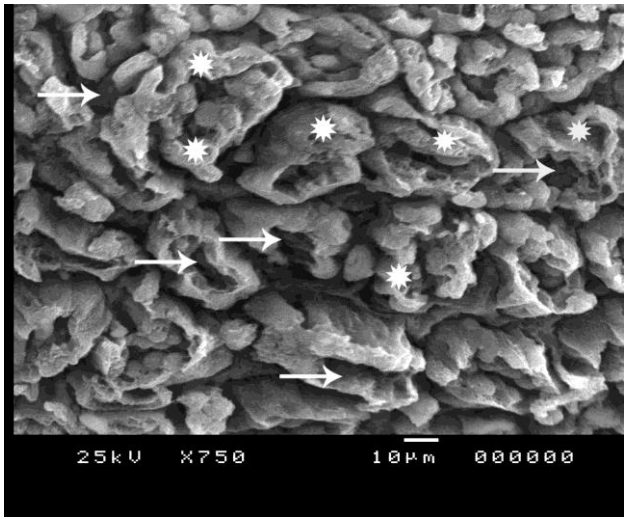


Fig. 23. A section from DFX treated group shows disturbed architecture of surface mucous epithelial cells which appear with rough eroded surfaces and loss of cell boundaries (stars). Wide disturbed gastric pits are also present (arrows) (SEM, x750, scale bar 10µ).

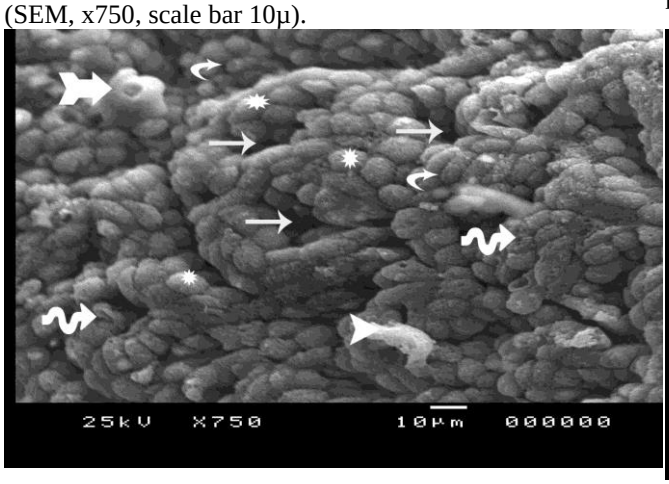


Fig. 24. A section from the curcumin treated group shows dome shaped surface epithelial cells (stars) with intact cell boundaries (curved arrow) surrounding the gastric pits (arrows). Few epithelial cells appear with rough surface (wavy arrow). Swollen detached epithelial cell is also noticed (bifid arrow). Notice mucous over cells (arrowhead) (SEM, x750, scale bar 10µ)

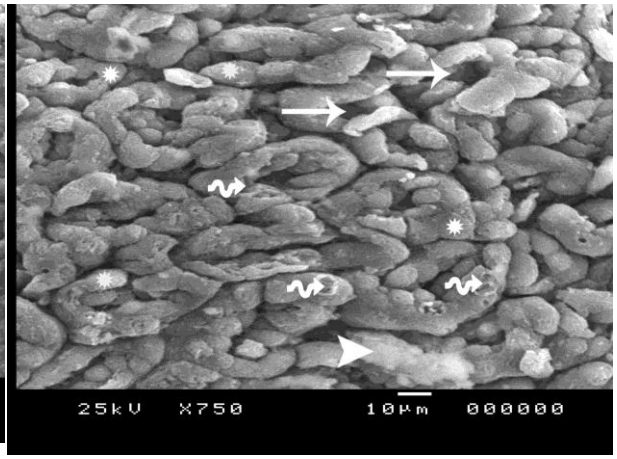


Fig. 25. A section from the omeprazole treated group shows dome shaped surface epithelial cells (stars) surrounding the wide gastric pits (arrows). Other surface cells still appear with rough eroded surface (wavy arrows) (SEM, x750, scale bar 10µ).

4. Discussion

DFX is an iron-chelating medication which is considered the first drug of choice for treating high iron levels in patients needing long term blood transfusions (Rahdar et al., 2021). Digestive problems such as abdominal pain, nausea, vomiting and diarrhea are common with DFX intake (Jencks et al., 2017). Preventing and controlling the adverse effects that could result in dosage decrease, stoppage, or termination are crucial tactics for improving DFX therapy (Kattamis et al., 2018). Thus, the aim of this study was to inspect the potential hazards of DFX on the histological structure of the fundic gastric mucosa and to evaluate the potential protective role of curcumin versus omeprazole. In this work, DFX caused erosion of the epithelial lining of the fundic glands with exfoliation of some cells. The glands were wide, distorted and discontinuous. In addition,

many of the nuclei of the lining columnar cells were irregular and pyknotic. There was noticeable cytoplasmic vacuolation in parietal and chief cells. The previous changes could be related to the oxidative stress resulted from DFX in the cells of the fundic glands (Fereydouni et al., 2020; Cordiano et al., 2023). On the other hand, iron diminution directs DFX-induced Bcl-xL downregulation and cell death (Badeli et al., 2019). In this work, many parietal cells and chief cells showed vacuoles in their cytoplasm in the DFX treated group. This finding could be explained by Gottwald et al. (2020) who proved that DFX has a toxic action on mitochondria. Also, DFX induces severe mitochondrial swelling as it has an elusive impact on the inner mitochondrial membrane permeability, which causes an inflow of water into the matrix and vacuolation of the cytoplasm of the cells. Sections from DFX treated group stained by PAS stain showed a faint reaction on the surface epithelium and the gastric pit with diminished neutral mucus secretion. These findings might be related to the direct toxicity of DFX that can occur in the lining cells of the GIT, one of the major excretion pathways for the drug (Díaz-García et al., 2014).

Scanning electron microscopic examination of sections from DFX treated group revealed loss of dome shape of the epithelial cells with surface erosion, and lack of intercellular demarcation between cells and wide gastric pits. Previous researches have recorded the high incidences of stomach ulcers in individuals on long-term oral DFX therapy, which could confirm these results (Bauters et al., 2010; Yadav et al., 2013). Moreover, the acute mitochondrial swelling caused by DFX may seriously result in inflammation and damage to the organs. It was recognized that mitochondrial damage strikes in diverse crucial diseases such as ischemic-perfusion injury so, usage of DFX may increase the risk of bowel inflammation and perforation (Chauhan et al., 2021).

Cleaved caspase-3 belongs to the family of proteolytic enzymes called caspases, which are well-known for their vital functions in regulating inflammation, apoptosis, and continuously activated death enzymes (Hussar, 2022; Zakariah et al., 2022). Additionally, cleaved caspase-3 is the main factor in both the extrinsic and the intrinsic (mitochondria-dependent) apoptotic pathways (Gomez et al., 2020). In the present work, there was a significant rise in the mean area percentage of caspase-3 expression in DFX-treated group. Earlier in-vitro studies have indicated that DFX prompted apoptosis in proximal tubules cells of the kidney, probably through its harmful effect on mitochondria function (Sanchez et al., 2011; Martin et al., 2017). The current study found that administration of curcumin for four weeks, one hour prior to DFX intake, had a protective impact on the histological structure of the mucosa of the fundus. Similarly, Ibrahim et al. (2019) who linked the curative effects of curcumin on gastric mucosa to its antioxidant effect via its ability to inhibit lipid peroxidation and DNA damage by stimulating of antioxidants enzymes like superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX). Curcumin also incites cytoprotective enzymes, such as heme oxygenase, glutamate-cysteine ligase, and quinone oxidoreductase (Ismail and El-Meligy, 2022). Furthermore, it was reported that curcumin-induced gastroprotection through reduction in the formation of free nitrogen radicals and decline of pro-inflammatory mediator expression. Besides, curcumin increases the mucosal epithelium's resistance through increased gastric mucosa cell proliferation and apoptosis inhibition (Kwiecien et al., 2019).

In this work, curcumin significantly reduced apoptosis in the cells of the fundic mucosa. It was mentioned that curcumin prevents apoptosis (Tuorkey and Karolin, 2009). In addition, a study suggested that curcumin is sustaining TERT-related (telomerase reverse transcriptase) anti-apoptotic function (Guo et al., 2020). On the level of scanning electron microscopic, curcumin almost preserved the dome-shaped surface of the epithelial cells, the boundaries between cells and mucous secretion. El Beshbishy et al. (2010) reported the same outcomes and hypothesized that curcumin preserves the mucus covering of

stomach mucosa. They added that mucus is crucial in the prevention of bacterial settlement and translocation as well as mechanical damage to the epithelium by creating a microenvironment that promotes quick repair. In the current work, omeprazole exerted some preservation on the structure of the gastric mucosa and showed some improvement of the apoptosis that was induced in gastric mucosa by DFX. Similar studies showed the defensive effect against gastric ulcer of omeprazole (Morjan et al., 2013). Omeprazole was found to alleviate inflammatory, dysplastic, edematous, hemorrhagic, and congested histopathological alterations (ElKalawy et al., 2018). Taking tougher, DFX oral treatment induced histological changes in the fundic mucosa of the stomach of albino rats. Curcumin is better than omeprazole in preserving these changes. Therefore, patients who are treated with DFX can benefit from curcumin in minimizing its gastric complications. Besides, curcumin is preferred than omeprazole as it lacks long term complication of omeprazole. Further human clinical research is required to validate the beneficial function of curcumin on the stomach mucosa.

Conflict of interest

No conflict of interest

5. Reference

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