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RESEARCH ARTICLE

Anti-ulcer and Gastro Protective Effects of Dexlansoprazole in Experimentally Induced Gastric Ulcer in Rats

Mohamed E.M. Mohamed[1], Mohamed A. Kamel[2], and Haitham S. Abd el Wahab[2*]

[1] Zoonoses Department, Faculty of Veterinary Medicine, Zagazig University, 44511, Egypt.
[2]Pharmacology Department, Faculty of Veterinary Medicine, Zagazig University, 44511, Egypt.
*Corresponding author email: pharmalab2000@gmail.com
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Abstract

Dexlansoprazole, a proton pump inhibitor drug, is utilized for treating erosive esophagitis and non-erosive reflux diseases. This study was conducted to explore the impact of dexlansoprazole on stomach ulcers caused by piroxicam in male Albino rats. Fifty adult rats were classified into five groups of ten each. The first group was not given any medication and received only saline, serving as control negative. Groups 2,3,4, and 5 received piroxicam (PXE) 30 mg/kg b wt. once daily for three days in a row via oral route, with the second group remaining untreated and kept as a positive control. The third group of rats was given omeprazole (OMP) 0.36 mg/kg b wt., and the fourth group was given dexlansoprazole (DXL) 0.6 mg/kg b wt. The rats in the fifth group received DXL at a dose of 1.2 mg/kg b wt. For 21 days in a row, groups 3, 4, and 5 received their medications orally once daily. Finally, rats were put to sleep and their blood was taken to measure serum AST, ALT, ALP, urea, creatinine, uric acid, serum potassium, magnesium, phosphorus and calcium. The stomach was isolated and evaluated for ulcer index, ulcer score and preventive index. A part of the stomach was prepared for tissue homogenate, while another part of the stomach and liver was utilized for histopathology. Piroxicam administration resulted in marked elevation in the gastric ulcer index, ulcer score, liver function tests, and gastric Malondialdehyde were significantly increased while gastric catalase, Super oxide dismutase, and glutathione peroxidase were significantly decreased, along with histopathological alterations were found in stomach and hepatic tissues. Treatment with either OMP or DXL elicited significant improvement in the aforementioned parameters. From the obtained results, it could be concluded that both omeprazole and dexlansoprazole are potent and effective medications for treating gastric damage caused by piroxicam, with dexlansoprazole was less superior than omeprazole but with minor adverse events on serum minerals.

Key words:

Dexlansoprazole, Omeprazole, Gastric ulcer, Antioxidant activity, and Histopathology.

Introduction

Proton pump inhibitors are the preferred medications for managing acid-related disorders like gastroesophageal reflux disease and peptic ulcer disease. This is because they can efficiently suppress the secretion of gastric acid [1].

Despite the fact that PPIs have been effective in managing Gastroesophageal reflux disease and its associated complications and are widely considered the preferred approach for treating GERD, there are still outstanding needs and considerable hurdles to overcome [2].

There are several needs that have not been met in the treatment of acid reflux. These include the requirement for faster and more efficient management of heartburn after eating, enhanced relief from heartburn during sleep for individuals with erosive esophagitis and

non-erosive reflux disease, better control of acid in Barrett's esophagus patients, and a more adaptable treatment schedule that includes PPIs [3].

Dexlansoprazole, which is the seventh proton pump inhibitor (PPI) to enter the market, is currently one of six PPIs available. It has been used clinically in various formulations as a racemic mixture. The chemical structure of lansoprazole contains an asymmetric sulfinyl group with a chiral center, resulting in two enantiomers, R (+) and S (−). Dexlansoprazole is the R-enantiomer. While the R and S isomers exhibit comparable pharmacological characteristics, research conducted in laboratory settings and in living organisms has revealed that the dominant factor behind the inhibitory effects of racemic lansoprazole on the secretion of gastric acid is mainly dexlansoprazole [4].

Piroxicam, which belongs to the oxicam derivatives and is classified as a non-steroidal anti-inflammatory drug (NSAID) is frequently used worldwide due to its broad range of pharmacological effects [5,6]. Despite its popularity, Piroxicam has several detrimental outcomes, such as gastrointestinal ulceration [7], hepatoxicity [8], and nephrotoxicity [9], among others [10].

Hence, the aim of this research is to examine how dexlansoprazole can safeguard the gastric system against mucosal ulceration caused by piroxicam in male Albino rats who have been administered omeprazole, a recognized proton pump inhibitor, for comparison purposes.

Materials and methods

Drugs

Dexlansoprazole (Doxirazole) R 30 mg and 60 mg hard gelatin capsules contain enteric coated pellets was obtained from Hikma pharmaceutical industries, Egypt. Doses were adjusted to rat according to Paget and Barnes [11] to be 0.6 and 1.2 mg/kg b wt. respectively.

Omeprazole (Omez) R 20 mg hard gelatin capsules contain enteric coated pellets was purchased from Pharaonia pharmaceutical industries, Egypt. Dose was adjusted to rat according to Paget and Barnes [11] to be 0.36 mg/kg b wt.

Piroxicam **(**Feldene) R 20 mg capsules were obtained from Pfizer Egypt pharmaceutical industries, Egypt. Dose was 30 mg/kg b wt. a single dose per day for three consecutive days [12].

Animals

The research involved the utilization of fifty male albino rats, with a weight between 150 to 200 g. These rats were procured from the animal farm situated in the Faculty of Veterinary Medicine, Zagazig University. In order to ensure stabilization, a two-week quarantine period was observed for all animals prior to their usage. Throughout the course of the experiments, the rats were housed in polypropylene cages that were furnished with wood-chip bedding and placed in a temperature and humidity-controlled room with a 12-hour light/dark schedule provided with freely accessible water and food. The temperature of the testing room was maintained at 23 ± 2C.

The Ethics Committee of the Faculty of Veterinary Medicine, Zagazig University, granted approval for the study protocol and the inclusion of rats. The approval number for this authorization is ZU-IACUC/2/F/74/2022.

Experimental design

The rats were divided into five groups, each consisting of 10 rats. The initial group served as the control and was given a saline solution. In the second group, piroxicam (30 mg/Kg) was administered once a day for three consecutive days. The third group received piroxicam + omeprazole (0.36 mg/kg) once daily for 21 days in a row. The fourth group

received piroxicam + dexlansoprazole at a dose of 0.6 mg/kg once daily for 21 consecutive days. Finally, the fifth group received piroxicam + dexlansoprazole at a dose of 1.2 mg/kg once daily for 21 consecutive days.

Blood and Tissue Sampling

After the experiment was finished (24 h after giving the last dose), the rats were put down and their tail veins were used to take blood samples. The blood was collected in clean Wasserman tubes without any clot-preventing substances. To separate the serum, the blood samples were allowed to clot and then spun in a centrifuge at 3000 rpm for 15 min.

To examine the liver and stomach, all groups were subjected to immediate removal of the organs, which were subsequently perfused using ice-cold phosphate buffered saline (PBS).

Upon completion of the fixation of the stomach onto cardboard for the purpose of macroscopic examination and evaluation of the ulcer index, a specific portion of the stomach tissue was preserved by freezing it at a temperature of −80 °C. This was done to aid in the subsequent determination of the oxidative cascade. Additionally, another part of the stomach and liver was placed in 10% neutral formalin to preserve the tissue for subsequent histopathological examination.

Assessment of gastric ulcer and preventive indexes

The curvature of the stomachs was opened to examine ulceration and the resulting ulcer score (Table 1) was defined by the method outlined in Wilhelmi and Menasse'[13]. Afterward, each stomach was washed with 0.1 M PBS and secured to acorkboard .

In order to determine the ulcer index (UI), we multiplied the average ulcer score of animals treated similarly with the proportion of animals in the group that had ulcers.

Table (1): Ulcer scoring system [13]

Score	Lesions
1	One or two minute, sporadic, punctuate lesions
2	Multiple small lesions
3	One extensive lesion or multiple moderate-sized lesion
4	Multiple large lesions
5	Multiple large lesions with stomach perforation

Preventive index "P.I."

The preventive index (the preventive effect of the any antiulcer agents used against the severity of ulceration) was generated using the equation (UI of PXE ulcerated group - UI of treated group×100) / UI of PXE ulcerated group [14] as shown in Table (2).

Table 2: Effect of oral administration of omeprazole (0.36 mg/kg b wt.), dexlansoprazole (0.6 mg/kg b wt.) and dexlansoprazole (1.2 mg/kg b wt.) in piroxicam induced ulcer on the incidence of gastric ulceration, mean ulcer score, ulcer index and preventive index

*Groups	Incidence of gastric ulceration (%)	Mean ulcer score	Ulcer index	Preventive index (%)
Control	0.00	0.00^{d}	0.00	0.00
Piroxicam	100	2.5 ± 0.35^{a}	250	0.00
Piroxicam + Omeprazole	60	1.2 ± 0.23^{bc}	70	76.6
Piroxicam + dexlansoprazole 30	80	1.6 ± 0.45^{b}	120	60.0
Piroxicam + dexlansoprazole 60	60	1.0 ± 0.34^{c}	60	80.0

*n=10 rats per group. Means ±SE within the same column carrying different superscripts are significant at $P \leq 0.05$.

Serum biochemical studies

The technique described by Reitman and Frankel [20] was utilized to determine serum AST and ALT levels, while Tietz *et al*. [21] was employed to measure alkaline phosphatase. Serum creatinine levels were determined using Larsen's method [22], serum urea levels were assessed using Coulombe and Favreau's method [23], and Trivedi et al. method [24] was utilized to measure serum uric acid levels. Tsao's method [25] was used to determine serum calcium levels, Berry et al. method [26] was used to determine serum potassium levels, and serum phosphorus levels were determined using Berti *et al*.'s method [27]. Finally, serum magnesium levels were determined by utilizing Smith's method [28]. All measurements were performed using diagnostic kits procured from BioMed, Egypt.

Preparation of tissue homogenates

Following the dissection of the tissue, it underwent a rinse with a PBS solution containing heparin (0.16 mg/ml) at pH 7.4 to eliminate residual blood cells and clots. A sonic homogenizer was utilized to blend a gram of the tissue with 5 ml of cold buffer (composed of 50 mmol of potassium phosphate, 1 mmol of EDTA, and maintained at a pH of 7.5). This was followed by a 20 min centrifugation of the homogenate, using a cooling centrifuge, at 4000 rpm, and stored at −20. In order to examine the tissue's oxidative status, several methods were utilized. Aebi's method [15] was employed to measure catalase activity calorimetrically, while the method of Nishikimi *et al*. [16] assess superoxide dismutase activity. To determine the level of glutathione peroxidase, Paglia Valentine's [17] method was utilized, and the protocol outlined by Beutler *et al*. [18] was utilized to detect the quantity of reduced glutathione. Additionally, malondialdehyde activities were examined using the approach described by Satoh [19]. All diagnostic kits used for these assays were obtained from Bio Diagnostic, Egypt.

Histopathological Examination

All animals were put to death in a humane manner (At the end of experiment (24 hrs. after the last dose) rats were sacrificed and the blood samples were collected from vein of the tail into sterile Wasserman tubes without anticoagulant.) and underwent necropsy. Standardized necropsy protocols were followed, as stated in Ruehl-Fehlert *et al*. [29] and Morawietz *et al*. [30]. The stomach and liver samples were taken from all rats. To prevent the gastric mucosa from folding, the contents of the stomach were

removed, and the mucosae were cleansed using distilled water, stretched out, and fixed with pins. Fixation of the specimens was done by placing them for 48 h in a 10% neutral buffered formalin solution. After that, they were dried out using different concentrations of ethanol, then cleared using xylene, filled with material, and finally encased in paraffin wax. The samples were sliced at 5 µm thickness, stained with hematoxylin and eosin dyes as per Suvarna *et al*. [31] and examined under a microscope.

Data analysis

The gathered data was analyzed using version 16 of the computerized SPSS programme. The outcomes were reported as mean ± SE. Tamhane and Dunlop's [32] guidelines were followed, with significance determined at $P < 0.05$ using a one-way ANOVA and Duncan's test.

Results and Discussion

PPIs have been established as the favored pharmacological option for the treatment of GERD, acid-related conditions, EE, Barrett esophagus, gastrointestinal bleeding controlling while using NSAIDs, eosinophilic esophagitis, stress ulcer prophylaxis in critically ill patients, gastric ulcer disease, and other maladies [33].

Gastric ulcer, a common digestive issue, arises when there is an imbalance between the stomach's acidic secretion and its ability to protect itself through the integrity of its lining [16].

The study in hand was to shed a light on some dexlansoprazole pharmacological and histopathological actions on top of an induced gastric ulcer, comparing its effect to omeprazole as a classical PPI.

The induction of gastric ulcers in rats by NSAIDs is a common and established model for researching the pathophysiology and pharmacological treatment of such ulcers [34]. The use of PXE at a dosage of 30 mg/kg over a period of three consecutive days resulted in a significant increase in the occurrence of ulcers (100%). It also caused a large number of lesions on the gastric mucosa (2.5 ± 0.35) and a high ulcer index (250) in the glandular sections of the stomach, as mentioned in Table 1, which categorizes the severity of ulcers (Figure 1). These findings align with the studies conducted by De-Barros *et al.* [35] and Dursu *et al*. [36], who similarly concluded that non-steroidal anti-inflammatory drugs can cause various types of gastric lesions.

Treatment with OMP 20 mg, DXL 30 or 60 mg significantly ($P \leq 0.05$) reduced the induced ulceration, treatment with DXL 60 mg give the best results followed by OMP 20 mg then DXL 30 mg when compared with PXE-administered rats. Dexlansoprazole 60 mg elicited the highest PI (80%); OMP 20 mg (76.6 %) and DXL 30 mg group (60 %). Nonetheless, the data obtained from the study propose that dexlansoprazole 60 mg has the most favorable outcomes in treating gastric ulcers, as it was validated by histopathology which revealed nearly normal gastric mucosa with insignificant inflammatory cell aggregation.

Recently, Selmi *et al*. [37] conducted a study where they discovered that OMP provides significant protection to the stomach against ulcers. They used OMP as a reference to evaluate the gastroprotective effects of the aqueous extract from *Trigonella foenum graecum* seeds.

According to Ghoshal and colleagues' findings [38] dexlansoprazole was observed to have a tendency of being superior to omeprazole in its ability to suppress the secretion of gastric acid. This information aligns with the current statement being made regarding the subject's online presentation.

According to Skrzydło-Radomańska and Radwan's [39] findings, dexlansoprazole is an effective medication used in treating and maintaining the healing of gastric or duodenal ulcers, erosive and reflux esophagitis, and NSAID-induced ulcer. The drug's prolonged elimination half-life leads to a more extended period of efficacy, making it an excellent choice as an antiulcer agent.

The safety and regular role of cells or tissues relies on maintaining the equilibrium between ROS production and scavenging potential. However, a disparity among them results in oxidative stress, which disturbs this role [40].

As revealed in Table 3, administration of PXE at a dosage of 30 mg/kg b wt. for three days resulted in a significant decrease ($P \leq 0.05$) in the levels of antioxidants, including glutathione peroxidase, superoxide dismutase, catalase, and reduced glutathione activity. Additionally, there was a notable increase in the concentration of malondialdehyde, suggesting the presence of oxidative stress. These findings align with the results reported by Aleem *et al.* [41].

When compared to the Piroxicam group, treatment with omeprazole 20, dexlansoprazole 30 or 60 mg once daily for 21 consecutive days demonstrated a substantial increase ($P \leq 0.05$) in gastric GPX, SOD, CAT, and GSH activities and a significant reduction in MDA. The best outcomes were achieved with omeprazole 20 followed by dexlansoprazole 60 mg then 30 mg.

Newer therapeutic regimens have suggested the utilization of PPIs as gastro-protective agents not solely for their ability to suppress acid production, but also due to their robust anti-inflammatory and antioxidant characteristics. PPIs have the potential to decrease the generation of ROS, which enhances their ability to fight inflammation and act as antioxidants. Nonetheless, it's possible that these agents differ in their effectiveness as antioxidants [42].

According to research conducted by Swamy *et al.* [43], the potential antioxidant effects of omeprazole, rabeprazole, and lansoprazole were examined, and it was discovered that omeprazole had a stronger antioxidant potential when compared to the other two drugs. Abed *et al*. [44] explored the potential antioxidant capacities of various PPIs, such as pantoprazole, omeprazole, lansoprazole, rabeprazole and esomeprazole. They found that omeprazole and esomeprazole had the greatest capacity for scavenging free radicals. Furthermore, these two PPIs demonstrated a significant gastrointestinal protection due to their powerful antioxidant properties, which complement their primary function as acid-suppressing agents. Agnihotri *et al.* [45] conducted research to investigate the impact of lansoprazole on gastric ulcer caused by oxidative stress. The findings of the study suggest that administering lansoprazole before inducing oxidative stress on the stomach mucosa offered a protective effect. Scientists noticed a decline in oxidation drivers like MDA, and they also saw a rise in antioxidant parameters such as GSH, SOD, catalase, and GST.

As presented in Table 4, piroxicam treatment triggered a significant rise in hepatic and renal serum biomarkers, such as creatinine, urea, uric acid, ALT, AST, and Alkaline phosphatase levels, in comparison to controls ($P \leq 0.05$). These findings were consistent with earlier researches [46-48] that indicated that piroxicam caused significant rise in markers of liver and kidney activity, lowered PG-E2 concentrations and stimulated oxidative stress.

The generation of free radicals by the medication could be the cause of kidney damage and hepatotoxicity induced by piroxicam, as per the findings. This

outcome aligns with previous studies [40] and [49]. Therefore, it is believed that piroxicam's nephrotoxic and hepatotoxic effects are mainly influenced by oxidative stress. As a result, enhanced antioxidant activity resulting from co-administration with omeprazole or dexlansoprazole might be a potential explanation for the improvement observed in liver and renal function tests.

Administering omeprazole 20 mg, dexlansoprazole 30 mg and 60 mg for 21 consecutive days on top of piroxicam resulted in improving the liver and kidney function tests relative to animals intoxicated with piroxicam alone. Interestingly, treatment with omeprazole 20 mg showed significantly greater improvement in these parameters compared to dexlansoprazole at either dosage, which indicate that omeprazole is safer on liver and kidney than dexlansoprazole.

Body minerals as potassium, calcium, magnesium, and phosphorus were measured in all groups as demonstrated in Table 5. Our research revealed that the use of omeprazole 20 mg achieved marked significant decrease of calcium, potassium, magnesium, and phosphorus levels in the bloodstream compared to the control group and the piroxicam treated group, which indicates that omeprazole had a decline effect on body minerals.

Conversely, administration of dexlansoprazole at either dose produced insignificant alterations in minerals level compared to piroxicam group and control group, indicating that dexlansoprazole does not affect serum electrolytes concentration.

Hoorn *et al*. [51] reported that patients who used omeprazole long-term experienced hypomagnesemia and hypokalemia, which led to the depletion of their overall magnesium stores.

In contrast, a safety evaluation of extended PPI treatment utilizing omeprazole and esomeprazole was conducted by Attwood and colleagues [52]. They examined earlier research studies and observed that ionized calcium levels remained stable for a period of 5 years. Additionally, the investigation revealed no notable modifications in serum calcium, vitamin D or ALP levels that were clinically significant.

According to the research conducted by Hansen and colleagues [53], there were no considerable alterations in PTH, calcium and phosphorus levels in the bloodstream as they maintained their stability and normality. Furthermore, no notable changes were observed in the levels of magnesium, 25(OH)D, or 24-h urinary calcium or magnesium levels following a 26-week course of treatment with dexlansoprazole or esomeprazole.

Regarding gastric and hepatic histopathological alterations following PXE administration our results revealed extensive epithelial lining erosions in the stomach, accompanied by significant infiltration of inflammatory cells and notable congestion of the submucosal blood vessels. Similarly, Wilhelmi, and Menasse [13] clearly revealed serious bleeding ulcer spots following PXE administration in rats. Our histopathological analysis (Figure 2) revealed normal histological architectures in the mucosa, sub mucosa and the muscular coat of the stomach of the control group (Figure 2 A). Section of piroxicam group stomach showed erosive changes, superficial mucosal necrosis with presence of detached cells in the lumen of stomach, sever inflammatory changes in the mucosa and sub mucosa (Figure 2 B). C: Ulcerative lesions and sever congestion of submucosal blood vessels were also observed (Figure 2 C). D: Stomach of omeprazole (0.36 mg/kg b wt.) treated rat showed congestion of the mucosal and submucosal blood vessels (Figure 2 D) and focal mucosal inflammatory cell aggregate (Figure 2 E).

Multifocal aggregations of inflammatory cell aggregates in the stomach lining mucosa and mild vascular congestion of the mucosal blood vessels were found in the dexlansoprazole (0.6 mg/kg b wt.) treated rat (Figure 2 F and G). The stomach of dexlansoprazole (1.2 mg/kg b wt.) treated rat showed almost normal gastric mucosa except for minute inflammatory cell aggregate and eosinophilic infiltration of the lining mucosa (Figure 2 H and I).

Our findings were backed up by the liver histopathology observations. Rats treated with piroxicam showed severe congestion in the portal blood vessels, along with biliary hyperplasia and the presence of periductal fibroblasts. Furthermore, there were moderate accumulations of round cells in the interstitial spaces, with necrotic hepatocytes interspersed among them.

Badawi [49] and Darwish *et al.* [50] discovered that NSAIDs can cause severe liver damage, including death of certain liver cells and the expansion of central veins and blood sinusoids. Their findings are in line with the present study. Liver of control group showed normal histomorphological structure with preserved hepatic lobular patterns, portal triads structures vascular tree and cords arrangement **(**Figure 3A). Liver of piroxicam-treated group showed characteristic portal congestion, biliary hyperplasia with periductal fibroblast, moderate interstitial round cells accumulations with presence of necrotic hepatocytes (Figure 3 B). Normal histomorphological structures with preserved hepatic lobular patterns, portal triads structures, vascular tree and cords arrangement except for mild vascular congestion were observed in omeprazole (0.36 mg/kg b wt.) treated group (Figure 3 C). Apparently normal hepatocytes were found in the dexlansoprazole (0.6 mg/kg b wt.) treated group (Figure 3 D). However, a mild biliary proliferation and portal congestion was observed in the portal area. Liver of dexlansoprazole (1.2 mg/kg b wt.) treated group showed normal architecture of liver, portal structures, however portal congestion, and mononuclear cell infiltration (Figure 3 E).

Conclusion

Dexlansoprazole was effective in treating piroxicam-induced gastric ulcer and demonstrated an increase in the antioxidant enzymes SOD, GPX, CAT, and GSH while decreasing MDA levels. However, omeprazole exhibited superior antioxidant properties. Additionally, dexlansoprazole had no effect on body minerals

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Conflict of Interest: The authors have no conflict of interest to declare

Table 3: Effect of oral administration of piroxicam (PXC) 30 mg/kg for 3 consecutive days followed by Omeprazole(0.36 mg/kg b wt.), Dexlansoprazole (0.6 mg/kg b wt.) and Dexlansoprazole(1.2 mg/kg b wt.) for 21 days on antioxidant enzymes.

Groups*	Parameters				
	GPx (U/mg tissue)	SOD (U/mg tissue)	CAT (U/mg tissue)	GSH (µmol/mg tissue)	MDA (µmol/mg tissue)
Control	6.15 ± 0.46^{a}	53± 2.3^{a}	4.9 ±0.07^{a}	55.3 ± 1.2^{a}	0.63 ± 0.04^{e}
Piroxicam	0.99± 0.17^{d}	14.3 ± 1.7^{d}	0.7 ± 0.08^{e}	22± 2.6^{d}	7.03 ± 0.43^{a}
Omeprazole 20	3.6± 0.51^{b}	34.7 ± 2.9^{b}	3.3 ± 0.05^{b}	41.6 ± 0.9^{b}	2.9 ± 0.09^{d}
Dexlansoprazole 30	2.03 ± 0.29^{cd}	23 ± 2.02^{c}	1.9 ± 0.06^{d}	36.3 ±0.9^{c}	5.3 ± 0.14^{b}
Dexlansoprazole 60	2.5 ± 0.25^{bc}	24.3 ± 1.7^{c}	2.6 ± 0.09^{c}	35.3 ± 1.2^{c}	4.1 ± 0.07^{c}

*n=10 rats per group. Means±SE within the same column carrying different superscripts are significant at $P \leq 0.05$.

Table 4: Effect of oral administration of piroxicam 30 mg/kg for 3 consecutive days followed by omeprazole (0.36 mg/kg b wt.), dexlansoprazole (0.6 mg/kg b wt.) and dexlansoprazole (1.2 mg/kg b wt.) for 21 days on liver and kidney parameters

Groups	ALT (U/L)	AST (U/L)	ALP (U/L)	Creatinine (mg/dL)	Urea (mg/dL)	Uric acid (mg/dL)
Control	28.90 ± 0.84^{d}	76.35 ± 3.83^{d}	175.12 ± 8.05^{d}	0.51± 0.05^{d}	10.63 ± 2.03^{c}	2.28± 0.52^{d}
Piroxicam	69.64 ± 7.25^{a}	135.8 ± 8.38^{a}	289.70 ± 20.2^{a}	0.99± 0.06^{a}	26.93 ± 0.78^{a}	6.6± 0.21^{a}
Omeprazole 20	37.33 ± 2.19^{c}	99.15 ± 3.28^{c}	215.14 ± 8.96^{c}	0.55± 0.27^{cd}	11.1 ± 0.11^{c}	2.5± 0.27^{d}
Dexlansoprazole 30	42.22 ± 0.98^{bc}	116.68 ± 4.41^{bc}	258.34 ± 4.41^{b}	0.66± 0.03^{bc}	22.56 ± 1.46^{b}	3.8± 0.12^{c}
Dexlansoprazole 60	46.45 ± 2.10^{b}	120.34 ± 4.10^{b}	276.34 ± 4.10^{ab}	0.7± 0.02^{b}	24.8± 0.44^{ab}	5.4±0.28^{b}

*n=10 rats per group. Means±SE within the same column carrying different superscripts are significant at $P \leq 0.05$.

Table 5: Effect of oral administration of piroxicam (PXC) 30 mg/kg for 3 consecutive days followed by Omeprazole (0.36 mg/kg b wt.), Dexlansoprazole (0.6 mg/kg b wt.) and Dexlansoprazole(1.2 mg/kg b wt.) for 21 days on body minerals

Groups	Parameters			
	Ca (mg/dL)	Mg(mg/dL)	Ph (mg/dL)	K(mmol/L)
Control	9.4 ± 0.06^{a}	2.46 ± 0.03^{a}	4.4 ± 0.12^{a}	7.4 ± 0.06^{a}
Piroxicam	8.9 ± 0.05^{b}	2.4 ± 0.01^{ab}	4.2 ± 0.06^{ab}	7.03 ± 0.08^{b}
Omeprazole 20	7.3 ± 0.08^{c}	2 ± 0.06^{c}	3.5 ± 0.11^{c}	5.1 ± 0.06^{c}
Dexlansoprazole 30	8.9 ± 0.003^{b}	2.35 ± 0.03^{ab}	3.9 ± 0.04^{b}	7.06 ± 0.03^{b}
Dexlansoprazole 60	8.8 ± 0.08^{b}	2.3 ± 0.05^{a}	4.1 ± 0.08^{b}	6.9 ± 0.03^{b}

*n=10 rats per group. Means±SE within the same column carrying different superscripts are significant at $P \leq 0.05$.

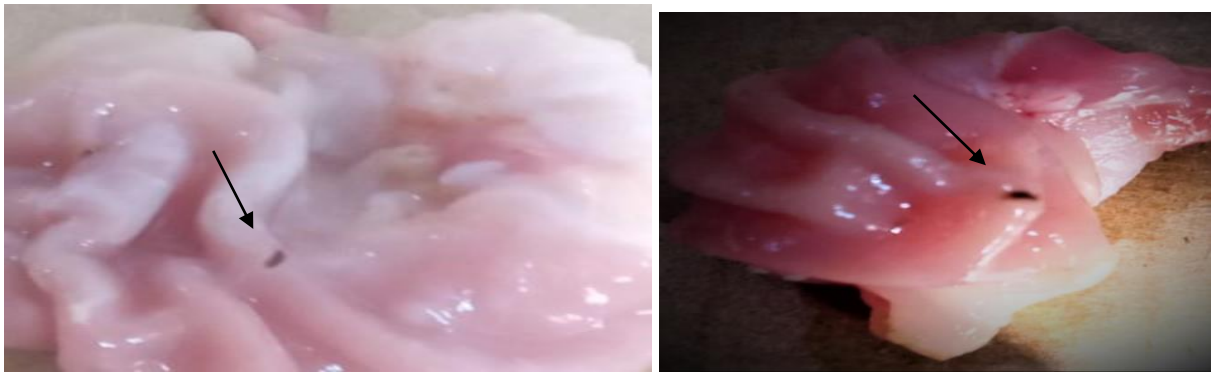

Figure 1: Gross pictures for the gastric ulcer induced by piroxicam.

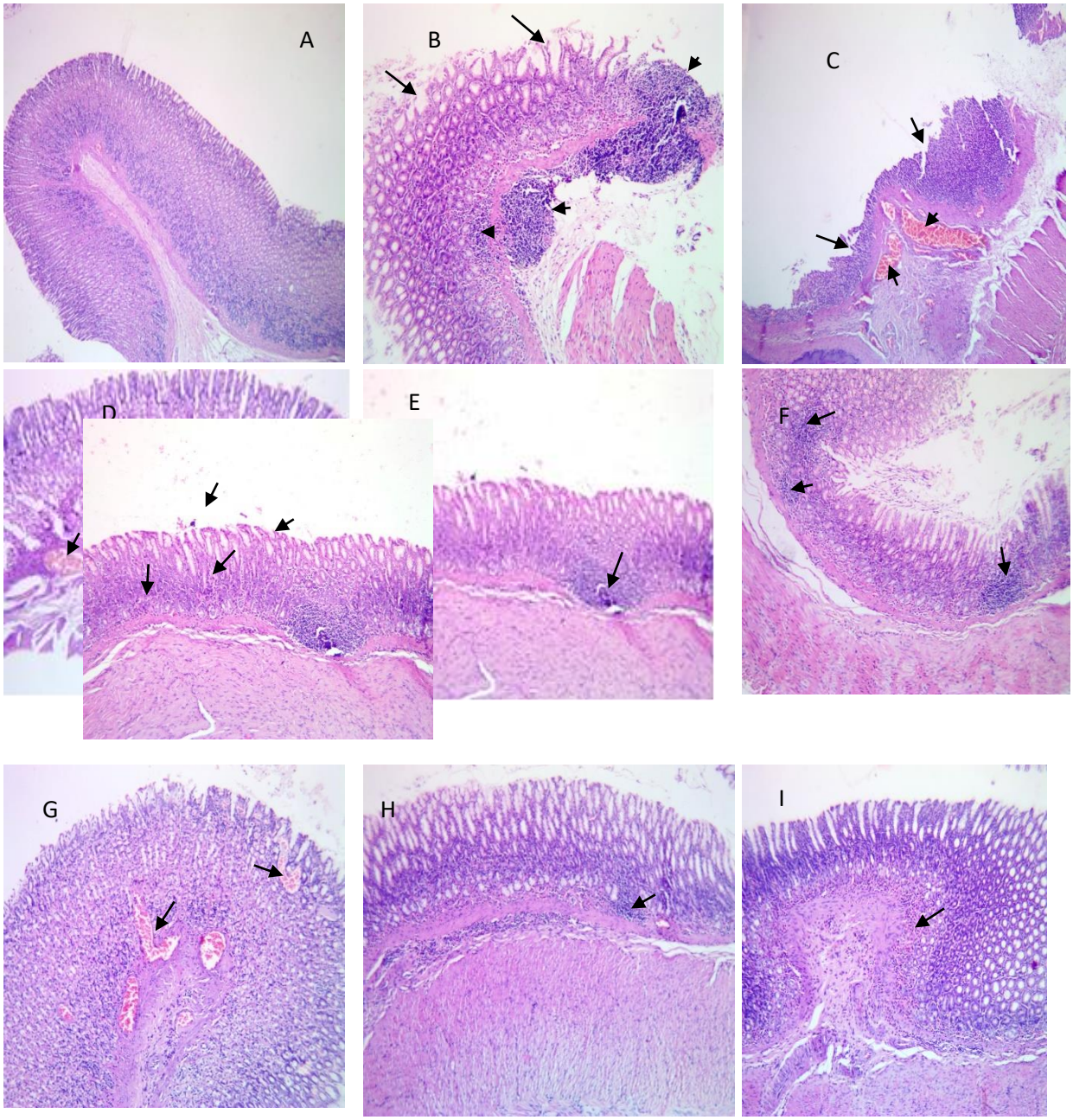

Figure 2: Representative photomicrographs for histopathological examination of stomach in different groups. A: Section of control group stomach shows normal histological architectures, the mucosa, sub mucosa and the muscular coat are totally normal. B: Section of piroxicam group stomach showing erosive changes (long arrows), superficial mucosal necrosis with presence of detached cells in the lumen of stomach, sever inflammatory changes (short arrows) in the mucosa and sub mucosa. C: Ulcerative lesions (long arrows) and sever congestion of submucosal blood vessels (short arrows). D: Stomach of omeprazole 20-treated rat showing congestion of the mucosal and submucosal blood vessels. E: Focal mucosal inflammatory cell aggregate. F: Stomach of dexlansoprazole 30-treated rat showing multifocal aggregations of inflammatory cell aggregates in the lining mucosaG: Mild vascular congestion of the mucosal blood vessels.H: Stomach of dexlansoprazole 60-treated rat showing almost normal gastric mucosa except for minute inflammatory cell aggregate. I: Eosinophilic infiltration of the lining mucosa.

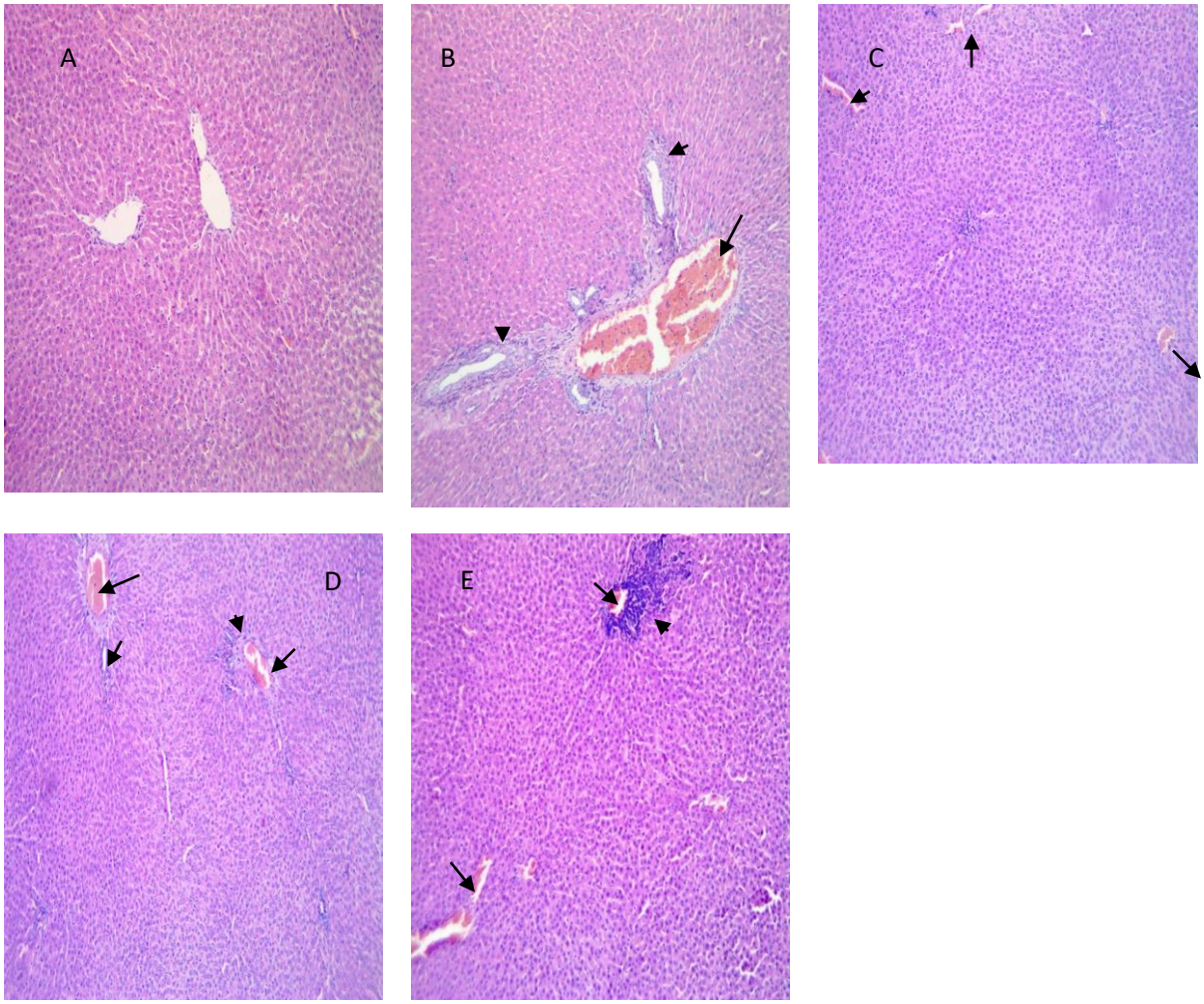

Figure 3: Representative photomicrographs for histopathological examination of liver in different groups A: Liver of control group showing normal histomorphological structure with preserved hepatic lobular patterns, portal triads structures vascular tree and cords arrangement. B: Liver of Piroxicam-treated group showing characteristic portal congestion (long arrow), biliary hyperplasia with periductal fibroblast (short arrow), moderate interstitial round cells accumulations with presence of necrotic hepatocytes.C: Liver of omeprazole 20-treated group showing normal histomorphological structures with preserved hepatic lobular patterns, portal triads structures, vascular tree and cords arrangement except for mild vascular congestion. D: Liver of dexlansoprazole 30-treated group showing apparently normal hepatocytes. However, the portal area showed mild biliary proliferation (short arrows) and portal congestion (long arrows). E: Liver of dexlansoprazole 60-treated group showing normal architecture of liver, portal structures, however portal congestion (long arrows) and mononuclear cell infiltration (short arrow).

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الملخص العربي

الآثار الوقائية المضادة للقرحة من عقار ديكسلانزوبرازول في قرحة المعدة المستحثة تجريبيا في الجرذان

محمد السيد محمد [1]، محمد أحمد كامل [2]، و هيثم سامي عبد الوهاب[2]
[1]قسم الأمراض المشتركة كلية الطب البيطري، جامعة الزقازيق
[2]قسم الفارماكولوجيا كلية الطب البيطري، جامعة الزقازيق

يعتبر الديكسلانزوبرازول من العلاجات المثبطة لمضخة البروتون في حالات التهاب المرئ التاكلي وامراض الارتجاع الغير تاكلي.

اجريت هذه الدراسة لمعرفة تاثير عقار الديكسلانزوبرازول في علاج القرحة التي يسببها البيروكسيكام في ذكور الجرذان البيضاء.

تم تقسيم الجرذان وعددهم خمسين الي خمس مجموعات (عشرة جرذان بكل مجموعة)"المجموعة الاولي لم تعطي اي دواء وتلقت فقط المحلول الملحي (مجموعة ضابطة سالبة)،المجموعة الثانية والثالثة والرابعة والخامسة تلقت بيروكسيكام بجرعة (30 ملجم/كجم) من وزن الحيوان مرة واحدة يوميا ولمدة ثلاثة ايام متتالية عن طريق الفم ،بقيت المجموعة الثانية دون علاج وكانت مجموعة ضابطة ايجابية ، المجموعة الثالثة اعطيت اوميبرازول (0.36 ملجم /كجم) من وزن الجسم ، والمجموعة الرابعة والخامسة اخذوا ديكسلانزوبرازول بجرعة (0.6 ملجم / كجم) و (1.2 ملجم / كجم) علي التوالي ، تم اعطاء المجموعات الثالثة والرابعة والخامسة ادوية عن طريق الفم مرة واحدة يوميا لمدة واحد وعشرين يوما متتالية.

في نهاية التجربة تم قتل الجرذان بطريقة القتل الرحيم وتم جمع عينات الدم لتحديد الاسبرتات امينوترانسفيريز والالانين امينوترانسفيريز والفوسفاتيز القاعدى واليوريا والكرياتينين وحمض البوليك وكذا نسبة البوتاسيوم والماغنسيوم والفسفور والكالسيوم.

تم عزل المعدة وتقييمها من حيث مؤشر القرحة ودرجتها والمؤشر الوقائي وتم تجضير جزء من المعدة لدراسة الاجهاد التاكسدى عن طريق قياس نسبة الكاتاليز و السوبر اكسيد الديسميوتيز والجلوتاثيون بيرواكسيديز ونسبة المالون داي الديهايد ، وتم تحضير جزء من المعدة والكبد لدراسة التغيرات الهيستوباثولوجية والاعراض المرضية الظاهرة علي هذه الانسجة.

اظهرت النتائج ان البيروكسيكام تسبب في حدوث تقرحات علي مستوي المعدة وزيادة في انزيمات الكبد بجانب الاجهاد التاكسدى وكان هناك تحسن ملحوظ في هذه النتائج مع اعطاء الاوميبرازول والديكسلانزوبرازول بجرعتيه المختلفتين. في الختام تشير النتائج الي ان الديكسلانزوبرازول هو علاج واعد لعلاج تلف الغشاء المخاطي المعدى الناتج عن اعطاء البيروكسيكام.