

Comparison between the effect of Leptin, Omega-3 Polyunsaturated Fatty Acids, and Vinegar on the Duodenal Ulcer in Male Albino Rats Through a Histological and Biochemical Study

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Abstract

Background: Duodenal ulcer is a major health problem that many scientists are interested in its management to avoid complications and the side effects of the usual treatments.

Aim of Study: Demonstrating and comparing the possible effects of chronic administration of omega-three polyunsaturated fatty acids, leptin, and vinegar on duodenal ulcer in male albino rats, with the possible underlying mechanisms involved in such effects.

Material and Methods: Four groups of experimental animals were used, with 16 rats in each: the control group (I), ω -3 fatty acids fed (II), Leptin fed (III), and vinegar fed (IV). For each group, we estimated, from the gross duodenal examination, the ulcer score and index, and percentage ulcer protection. Also, histology appearance of the duodenal mucosa was examined together with the measurement of duodenal HCO₃-amount, CCK, and secretin gene expression.

Results: In comparison to control group, the ulcer score and index were diminished significantly while percentage ulcer protection, HCO₃-amount, and expression of secretin and CCK genes were increased significantly in rat groups fed with ω -3, vinegar, and leptin. Vinegar has a more protective effect than ω -3 and leptin.

Conclusion: We conclude that vinegar, ω -3, and leptin have a protective effect against induction of duodenal ulcer, and vinegar had a better effect against ulcer induction followed by ω -3 and finally leptin.

Key Words: Duodenal ulcer – ω -3 fatty acids – Leptin – Vinegar – CCK – Secretin.

Introduction

PEPTIC Ulcer Disease (PUD) is a problem of the GIT, with characteristic damage to the mucosa caused by pepsin and gastric HCl secretion. Such condition usually occurs in the stomach and prox-

imal duodenum, but it can occur in the lower part of the esophagus, the distal part of the duodenum, or the jejunum to less extent, as in unopposed hypersecretory states such as Zollinger-Ellison syndrome, in hiatal hernias (Cameron ulcers), or ectopic gastric mucosa (e.g., in Meckel's diverticulum) [1]. H-pylori infection and the use of Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) are the predominant causes of peptic ulcer [2]. A variety of other infections and comorbidities are accompanied by a higher risk of PUD (e.g., chronic renal failure, Crohn's disease, tuberculosis, cytomegalovirus, myeloproliferative disorder, hepatic cirrhosis, sarcoidosis). Critical illness, surgery, or hypovolemia leading to splanchnic hypoperfusion may result in gastroduodenal ulcers or erosions (stress ulcers); that could manifest with bleeding or perforation or remain silent [3]. Smoking slows ulcer healing and increases the risk of its recurrence [1]. Treatment with proton pump inhibitors and H₂-receptor blockers can decrease mucosal damage [4]. However, various side effects accompany these drugs, such as diarrhea, headache, drowsiness, fatigue, and muscular pain [5]. Hence these days' natural compounds are being explored so that they could replace these drugs.

Leptin, the "satiety hormone," is a hunger inhibitory hormone, that helps regulate energy balance. It is made by adipose cells. Ghrelin, the "hunger hormone," opposes the action of leptin. Both hormones act on receptors in the hypothalamic arcuate nucleus to regulate appetite, achieving energy homeostasis [6]. Decreased sensitivity to leptin usually occurs in obesity, resulting in an inability to detect satiety despite high energy stores [7].

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Over the previous twenty years, there has been a dramatic increase in the scientific and public interest in omega-3 polyunsaturated fatty acids (ω -3 PUFA) and their impact on personal health as they possess anti-inflammatory, anti-arrhythmic, and anti-thrombotic properties [8]. Fish and its oil both are rich sources of ω -3 PUFA, specifically Eicosapentaenoic Acid (EPA) and Docosahexaenoic Acid (DHA) [9,10].

Vinegar, "sour wine," can be made from almost any fermentable carbohydrate source [11]. The chemical and organoleptic properties of vinegar are a function of the starting material and the fermentation method. The tart flavor and biting, pungent odor of vinegar, all are caused by acetic acid. However, the US Food and Drug Administration (FDA) states that diluted acetic acid is not vinegar and so, should not be added to food products [12]. Other vinegar constituents include mineral salts, vitamins, polyphenolic compounds, amino acids, and nonvolatile organic acids [13,14].

This study aimed at demonstrating and comparing the possible effects of chronic administration of omega-3 polyunsaturated fatty acids, leptin and vinegar on duodenal ulcers in male albino rats, with the possible underlying mechanisms involved in such effects. This is in an attempt to prove a hypothetical protective effect of these materials on duodenal mucosa.

Material and Methods

Animals care and housing: A total of 64 adult male albino rats, seven weeks of age, weighing 150-175gm obtained from the Animal House of Kasr Al-Aini Faculty of Medicine, Cairo University, Egypt. The experiment was performed twice with 32 animals each time for six weeks. The first trial started on September 1st and ended on October 12th, 2018 (group a). The second one started on December 1st, 2018 and ended on January 11th, 2019 (group b). Rats were kept under observation for about seven days before the onset of the experiment for adaptation and to exclude any inter-current infection [15]. The animals were then placed in a wire mesh cages (50 X 20 X 20cm, three rats/cage) with well-aerated covers, at normal temperature ($25 \pm 5^\circ\text{C}$) with 12 hours light/dark. Rats were given free water access and supplied daily with laboratory rat diet offered ad-lib. The described experimental protocols in this study were approved by Institutional Animal Care and Use Committee (CU-IACUC), Cairo University.

• **Animals grouping:** Each of the studied groups were further subdivided into four subgroups with eight animals each:

- **Group I (control):** Fed on a standard laboratory rat diet.

- **Group II:** Fed on a standard diet, leptin (10 $\mu\text{g/kg}$, SC) administered twice a day [16].

- **Group III:** Fed on a standard diet enriched with 100g/kg of ω -3 fatty acids [17].

- **Group IV:** Fed on a standard diet enriched with 15% of natural vinegar (5% acetic acid) [18].

• **Determination of ulcer score:** Calculated according to the method of Suzuki et al. [19]. The lesions were counted with the use of a magnifying hand lens (10X), and each was given a severity rating as follows:

A- 1 \rightarrow Less than 1mm (Pinpoint).

B- 2 \rightarrow 1-2mm.

C- 3 \rightarrow Greater than 2mm and above.

• **Determination of ulcer index:** The ulcer score was divided by a factor of 10 to get the ulcer index.

• **Determination of percentage ulcer protection:** According to Takagi et al., [20]:

$$\text{Ulcer protection (\%)} = \frac{U_c - U_t}{U_c} \times 100$$

Where:

U_c = Ulcer index of control group.

U_t = Ulcer index of test group.

• **Techniques:**

A- **Surgical techniques:**

• **Ligation at the duodenojejunal junction:** On the 42nd day, the four groups of rats fasted 24h before any interventions. An aseptic surgical procedure was employed for all subgroups. Intra-peritoneal injection of thiopental sodium (30mg/kg) was used to anesthetize the rats, after that, an approximately 3cm midline incision, at one cm below the xiphoid process was made to open the abdomen. Duodenum was exposed, and a tight knot was applied around the duodenojejunal junction using 4-0 silk ligature. The duodenum was placed carefully, and interrupted sutures were made to close the abdominal wall. After suturing the incision, the wound was immediately cleaned and was covered by local antibiotic ointment (Terramycin). The rats were placed again in their cages and left for 3 hours [21].

• **Induction of ulcer:** Animals were deprived of water during the post-operative period. After that, induction of duodenal ulcer was done by indomethacin, plus histamine. In this model, rats were given indomethacin (5mg/kg) Subcutaneously (SC) followed by histamine dihydrochloride (40mg/kg) SC, 30 minutes later, three times at 2.5 hours intervals. After 3 hours, duodena were excised carefully, cut opened along the antimesenteric side, and the ulcer area(s) was (were) measured. This combined treatment was reported to induce, at an incidence of 100%, one or two round lesions in the proximal duodenum [22].

• **Detection of ulcer formation:** Duodeni of subgroups were opened at the antimesenteric border, fixed on cork for determination of ulcer index. The hand lens was used to see the mucosal lesions in bright light.

B- Biochemical techniques:

• **Measurement of duodenal HCO₃⁻ secretion:** After collection of duodenal fluid, the total volume of duodenal contents were measured. The duodenal contents were centrifuged at 10.000rpm for 10min. HCO₃⁻ secretion was titrated at pH 7.4 [23].

• **Detection of CCK and secretin genes expression by quantitative real time -polymerase chain reaction (real time-PCR) protocol:** Total RNA was extracted from duodenal tissue using SV Total RNA Isolation System (Promega, Madison, WI, USA) [24].

• **Chemicals:**

A- **Omega-3 fatty acids:** Omax3. Prevention pharmaceuticals. 24 Arnett Avenue, Suite 107, Lambertville, NJ 08530.

B- **Vinegar:** Galletti s.n.c., via Faverzani, 13. 26046 San Danele po. Cremona-Italia-Lic. M.A.F.API 1 CR.

C- **Leptin:** Leptin, L5037-1mg (Sigma Aldrich) recombinant, expressed in E. coli, was lyophilized; 10ccs was dissolved with 1x PBS.

• **Statistical methods:**

The statistical package SPSS version 24 was used for coding and entering data that were summarized using mean and Standard Deviation (SD) for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between analysis of variance (ANOVA) with multiple comparisons post hoc test [25]. *p*-values less than 0.05 were considered as statistically significant. The mean ± SD were calculated with the following formula:

$$S = \sqrt{\frac{\sum (X - \bar{X})^2}{N}}$$

Where:

S = The standard deviation of a sample,

Σ = Means "sum of,"

X = Each value in the data set,

\bar{X} = mean of all values in the data set,

N = Number of values in the data set.

Results

• **Growth (macroscopic) appearance results:**

1- **Ulcer score and index:**

Regarding the first trial (a), the results of the present work showed a statistically significant decrease in ulcer scores and indices; among groups IIIa (-38.63% and -23.99%) and IVa (-57.89% and 47.85%) as compared to the control group Ia and group IIa respectively. There was also a statistically significant increase in group IVa (-31.39%) as compared to group IIIa.

Regarding the second trial (b), the results of the present work showed a statistically significant decrease in ulcer scores and indices; among groups IIb (-35.61%), IIIb (-38.96%), and IVb (-61.04%) as compared to the control group Ib, and in group IVb (-39.5% and -36.17%) as compared to groups IIb and IIIb respectively. Table (1) and Fig. (1).

Table (1): Comparison of different study parameters among the studied groups.

Group	1 st trial (a)				2nd trial (b)			
	I	II	III	IV	I	II	III	IV
Ulcer score	9.5±3.21	7.67±1.37	5.83±1.94*#	4.0±1.10*#	9.83±2.79	6.33±1.21*	6.0±2.28*	3.83±1.17*#
Ulcer index	0.95±0.32	0.77±0.14	0.58±0.19*#	0.40±0.11 *#	0.98±0.28	0.63±0.12*	0.60±0.23*	0.38±0.12*#
Percentage ulcer protection (%)		33.60±0.09	38.67±0.10#	57.67±0.33#		35.60±0.03	38.90±0.07#	65.30±0.04#
Secretin hormone gene expression	1.02±0.12	1.42±0.16*	2.57±0.43*#	4.17±0.67*#	1.03±0.14	1.53±0.31*	2.57±0.37*#	4.08±0.35*#
HCO ₃ ⁻ amount (meq/15min)	0.9±0.21	1.9±0.3*	2.3±0.4*#	3.2±0.15*#	1.2±0.3	2±0.2*	2.5±0.15*#	3.6±0.45*#
CCK hormone gene expression	1.05±0.14	1.50±0.33*	4.58±0.63*#	5.82±0.71 *#	1.03±0.16	1.62±0.19*	4.43±0.85*#	5.08±0.62*#

Values were presented as mean ± SD.
Group (I) control, group (II) leptin.
Group (III) treated ω-3 fatty acids fed.

Group (IV) vinegar fed.
Statistically significant (*p*<0.05) compared to the corresponding values in:
(*) Group I, (#) Group II, and (\$) Group III.

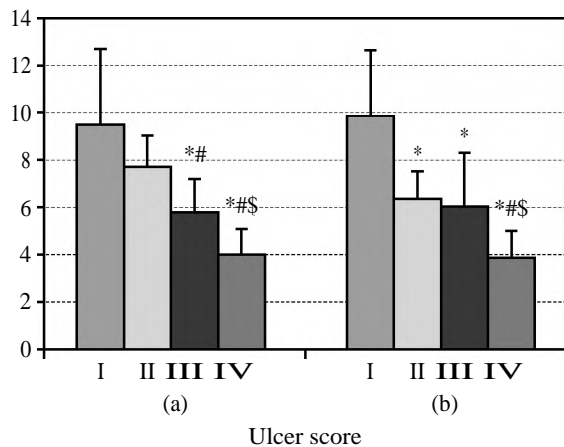


Fig. (1): Ulcer score among the studied groups of the two trials.

2- Percentage ulcer protection:

Regarding the first trial (a), the results of the present work showed a statistically significant increase in percentage ulcer protection among groups IIIa (14.88%) and IVa (71.64%) as compared to group IIa and in group IVa (49.13) as compared to group IIIa.

Regarding the second trial (b), the results of the present work showed a statistically significant increase in percentage ulcer protection among groups IIIb (9.27%) and IVb (83.43%) as compared to group IIb and in group IVb (67.87) as compared to group IIIb. Table (1) and Fig. (2).

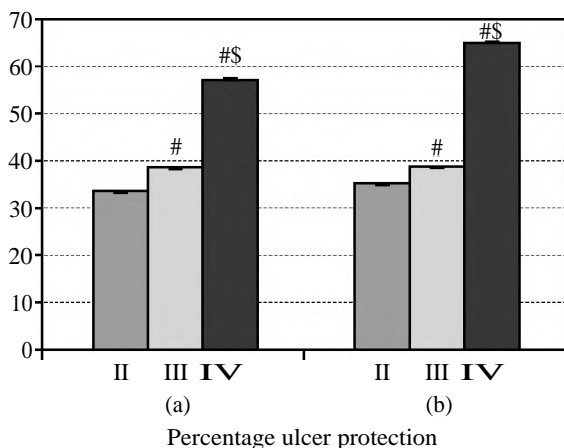


Fig. (2): Percentage ulcer protection among the studied groups of the two trials.

• Results of the biochemical parameters:

1- Secretin hormone gene expression:

Regarding the first trial (a), the results of the present work showed a statistically significant increase in secretin hormone gene expression; among groups IIa (39.22%), IIIa (151.96%) and IVa (299.02%) as compared to the control group Ia, among groups IIIa (80.99%) and IVa (193.66%)

as compared to group IIa, and in group IVa (62.26%) as compared to group IIIa.

Regarding the second trial (b), the results of the present work showed a statistically significant increase in secretin hormone gene expression; among groups IIb (48.54%), IIIb (149.51%) and IVb (296.12%) as compared to the control group Ib, among groups IIIb (67.97%) and IVb (166.67%) as compared to group IIb, and in group IVb (58.75%) as compared to group IIIb. Table (1) and Fig. (3).

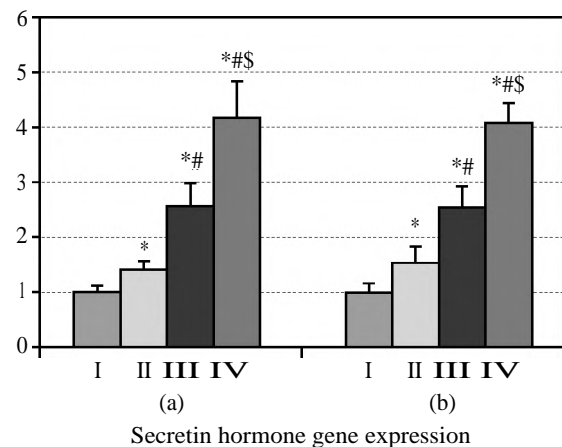


Fig. (3): Secretin hormone gene expression among the studied groups of the two trials.

2- Amount of HCO_3^- secretion:

Regarding the first trial (a), the results of the present work showed a statistically significant increase in HCO_3^- secretion; among groups IIa (111.11%), IIIa (155.56%) and IVa (255.56%) as compared to the control group Ia, among groups IIIa (21.05%) and IVa (68.42%) as compared to group IIa, and in group IVa (39.13%) as compared to group IIIa.

Regarding the second trial (b), the results of the present work showed a statistically significant increase in secretin hormone gene expression; among groups IIb (66.67%), IIIb (108.33%) and IVb (200%) as compared to the control group Ib, among groups IIIb (25%) and IVb (80%) as compared to group IIb, and in group IVb (44%) as compared to group IIIb. Table (1) and Fig. (4).

3- Cholecystokinin (CCK) hormone gene expression:

Regarding the first trial (a), the results of the present work showed a statistically significant increase in CCK hormone gene expression; among groups IIa (42.86%), IIIa (336.19%) and IVa (454.29%) as compared to the control group Ia, among groups IIIa (205.33%) and IVa (288%) as

compared to group IIa, and in group IVa (27.07%) as compared to group IIIa.

Regarding the second trial (b), the results of the present work showed a statistically significant increase in secretin hormone gene expression; among groups IIb (57.28%), IIIb (330.1%) and IVb (393.2%) as compared to the control group Ia, among groups IIIb (173.46%) and IVb

(213.58%) as compared to group IIb. Table (1) and Fig. (5).

• Results of microscopic examination:

1- Hx and E staining:

The results of the present study demonstrated that vinegar has the highest protective effect on duodenal mucosa. Omega 3 was superior to Leptin but less effective than vinegar. Figs. (6-13).

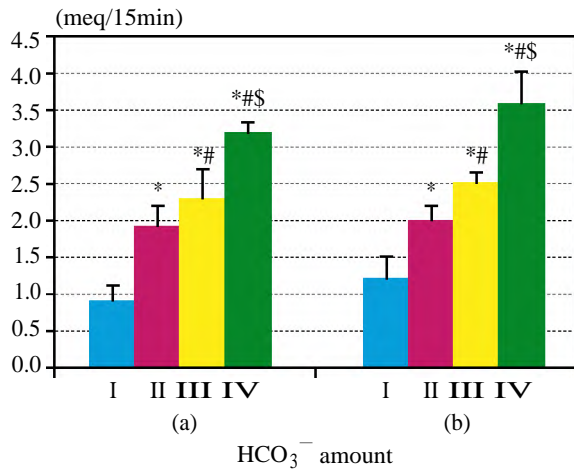


Fig. (4): HCO₃⁻ amount among the studied groups of the two trials.

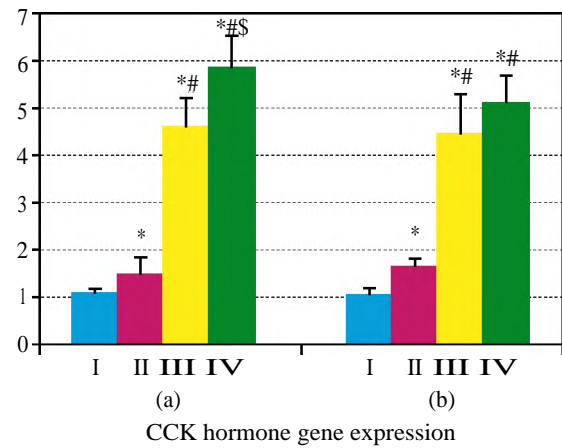


Fig. (5): CCK hormone gene expression among the studied groups of the two trials.

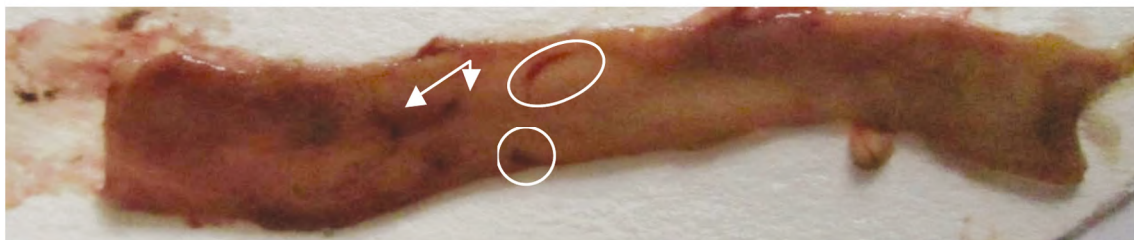


Fig. (6): Macroscopic representation of duodenal mucosa of (control group) showing multiple ulcers (arrows and circles).

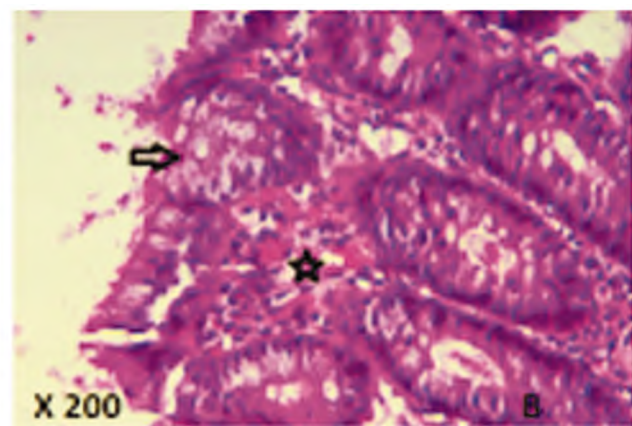
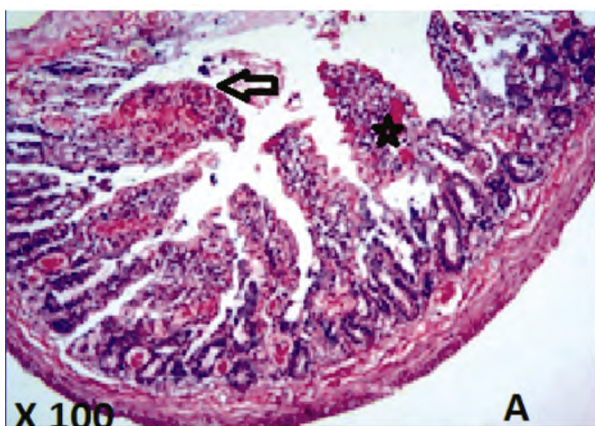


Fig. (7): Serial sections examined from the duodenal wall of (control group) revealed disorganized villous architecture in the form of broadening and shortening associated with focal surface erosion (arrow). The lamina propria showed edema, congested vessels and moderate exudation of lymphocytes and plasma cells with few neutrophils and eosinophils (asterisk).

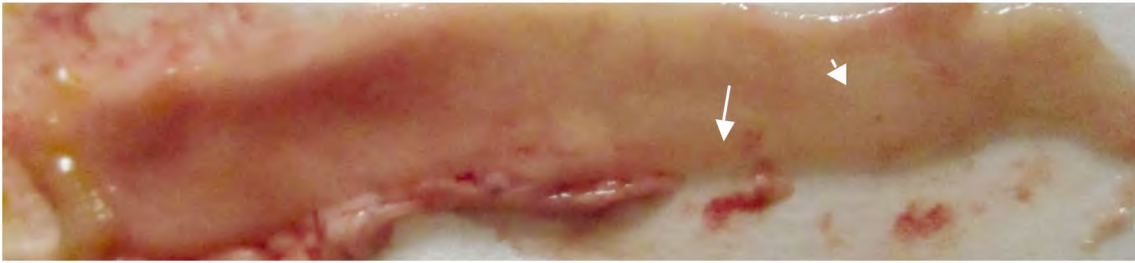


Fig. (8): Macroscopic representation of duodenal mucosa of vinegar fed group.

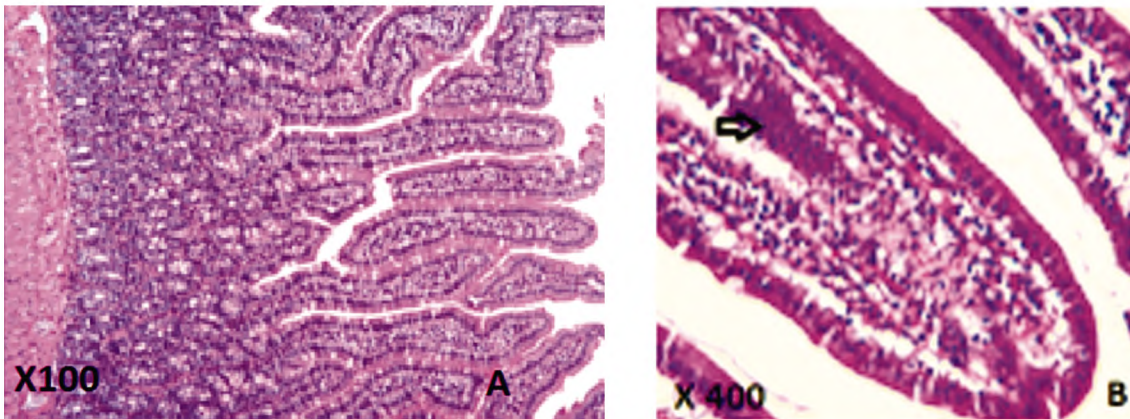


Fig. (9): Serial sections examined from the duodenal wall of (Vinegar-treated group) revealed preserved normal villous architecture and mucogenic activity. The lamina propria showed mild exudation of lymphocytes and plasma cells (arrow).



Fig. (10): Macroscopic representation of duodenal mucosa of w-3 fatty acids fed rats treated group.

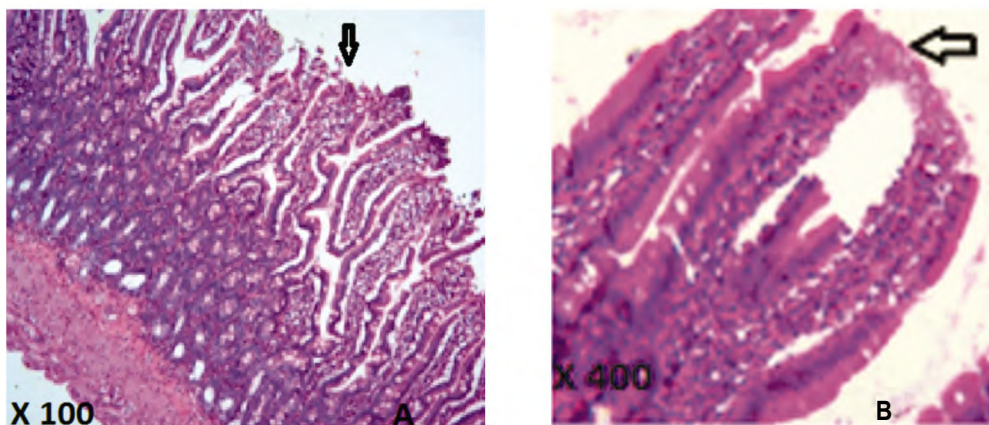


Fig. (11): Serial sections examined from the duodenal wall of (Omega 3-treated group) revealed disorganized villous architecture in the form of broadening and shortening associated with focal surface erosion and granulation tissue formation. The lamina propria showed edema, congested vessels and moderate exudation of lymphocytes and plasma cells with few neutrophils and eosinophils.

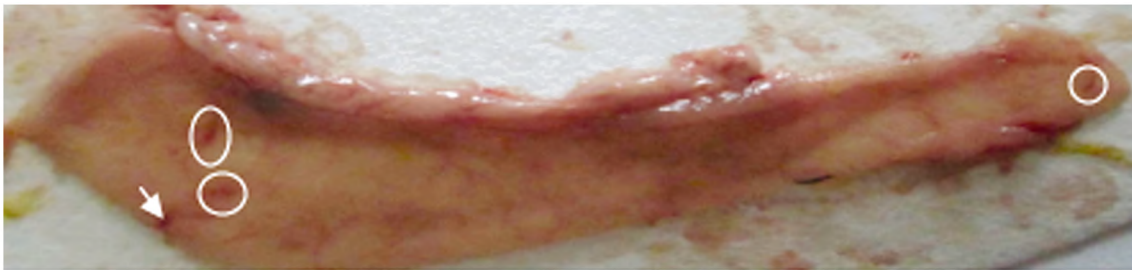


Fig. (12): Macroscopic representation of duodenal mucosa of leptin treated group.

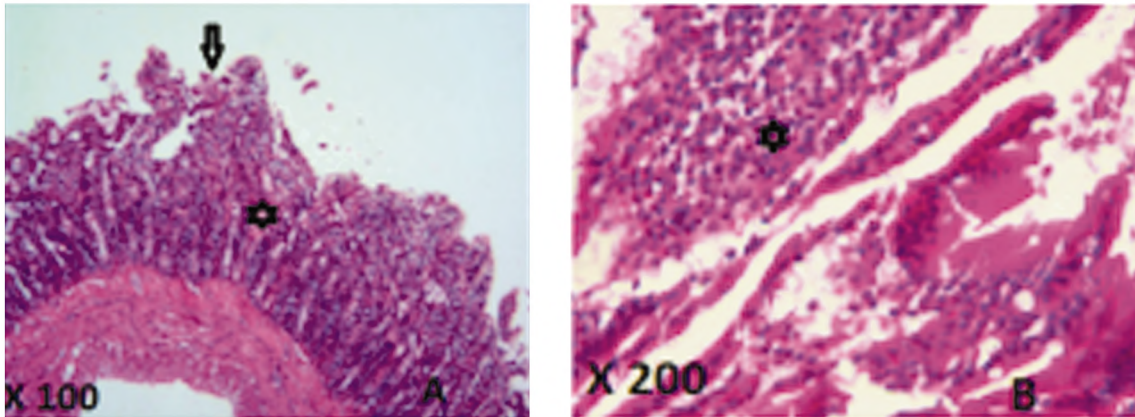


Fig. (13): Serial sections examined from the duodenal wall of (Leptin-treated group) revealed disorganized villous architecture. The lamina propria showed edema and moderate exudation of lymphocytes and plasma cells with few neutrophils and eosinophils.

Discussion

Peptic Ulcer Disease (PUD) is the most prevalent gastrointestinal disorder. The pathophysiology of PUD involves an imbalance between offensive (acid, pepsin, and *H. pylori*) and defensive factors (prostaglandin, mucin, nitric oxide, bicarbonate, and growth factors) [26]. Free radicals, oxidants, physical, chemical factors are also involved in the pathogenesis of PUD [27]. Many drugs are used in the treatment of ulcers, but its clinical evaluation shows the incidence of relapses, side effects with the interaction of other drugs. Currently, there are different classes of drugs like proton pump inhibitors, H₂ receptor blockers [4], antibiotics and antiacids are available for the treatment of peptic ulcer, but all these drugs have side effects and limitations [5].

The results of the present work illustrated that treating rats with vinegar, ω -3 FA, and leptin produced a significant reduction in indomethacin and histamine-induced duodenal ulcer compared to control group. These results are consistent with the work of Shu and colleagues [28]. On the other hand, Faust and colleagues denied the presence of any cytoprotective effect of ω -3 FA on the gastric ulcer as it had no significant effect on mucosal

prostaglandin E₂ or F₂ alpha content or the damaging effect on the stomach [29].

Regarding the mean values of both ulcer score and ulcer index, the present work results showed a statically significant decrease among groups IIIa and IVa compared to the control group Ia, among groups IIb, IIIb, and IVb compared to the control group Ib, among groups IIIa and IVa compared to group IIa, in group IVa compared to group IIIa, and in group IVb compared to both group IIb and IIIb. These results are consistent with that of Jaccob [30] and Hader et al., [31,32]. However, concerning leptin, our results are on contrary to those of Soghra and colleagues [33].

Leptin acts as a trophic factor in the GI tract and can stimulate gut epithelial cell proliferation when given exogenously [34]. In neonatal piglets, leptin has been shown to have a stimulatory effect on the development of intestinal mucosal morphometry, the proliferation of mucosal epithelial cells, enzymatic activity in the brush border of enterocytes, and, as outlined earlier, in nutrient absorption [35]. After massive small bowel resection, the leptin receptor gene and protein expression were upregulated in residual jejunal and ileal mucosa, concomitant with adaptively increased villus and crypt

growth. Treatment with exogenous leptin enhanced all of these effects [36]. Leptin-deficient ob/ob mice demonstrated decreased cellular proliferation and increased apoptosis in intestinal cells after massive small bowel resection [37]. The leptin-induced inhibition of food intake and the stimulation of pancreatic exocrine secretions can be blocked by a cholecystinin-1 (CCK-1) receptor antagonist [38]. STC-1 cells that secrete CCK have leptin receptors and are stimulated by the presence of leptin. Duodenal delivery of leptin *in vivo* increases the concentration of CCK in the serum. Feeding decreases the amount of leptin in the gastric juice and increases the amount of leptin in the duodenum even in leptin receptor-deficient mice; however, a surge of serum CCK after feeding is not observed in such mice [39]. CCK itself increases the release of leptin from gastric glands, suggesting that leptin and CCK comprise a positive feedback loop [40].

O-3 PUFAs attenuate the inflammatory response through minimizing tissue injury while avoiding suppression of necessary inflammatory components of subsequent wound healing, thus facilitating the resolution of inflammation and transition to wound healing [41]. Novel lipid mediators derived from ω -3 PUFAs, such as resolvins and protectins that are synthesized during the later stages of inflammation, promote inflammation resolution. They enhance macrophage engulfment of apoptotic neutrophils and the efflux of macrophages to local lymph nodes [42,43]. Resolvins were shown to enhance the resolution of inflammation and microbial clearance in experimental critical illness. It is possible, therefore, that locally formed resolvins/protectins and n-3-derived PPAR-g agonists may induce a 'wound-healing' phenotype in tissue macrophages [44]. Resolvins such as resolvin D2 have been shown to reduce the trafficking of leukocytes to inflammatory loci and to reduce CD26L and CD 18 [45]. This further inhibits the inflammatory infiltration and initiates the transition to a reparative stage of healing (inflammation resolving type macrophages). Finally, nutritional support with fish oil may prevent hypotension and improve oxygenation in critical illness [46], thus maintaining cutaneous blood flow and oxygen supply and facilitating the healing of ulcers.

O-3 PUFAs have pleiotropic properties during inflammation through the production of weaker eicosanoids, inhibition of nuclear factor κ B, and direct promotion of resolution [47]. O-3 PUFA had proved its cytoprotective action by its antioxidant mechanism [48]. The beneficial effect of fish consumption with high contents of Eicosapentaenoic Acid (EPA) and Docosahexaenoic Acid (DHA)

might be attributed to the displacement of AA from the cell membrane phospholipid and to a preferential formation of less pro-inflammatory PGs (such as PGE3, PGF3(ξ), TXA3), and LTs (such as LTB5, LTC5, and LTD5) [49].

Health benefits of apple have been reported [50], and one of important category of active apple constituents is phenols. Phenols are secondary plant metabolites and act as an antioxidant, antibacterial [51], and antiviral agents [52]. Variety of substances, such as carotenoids, flavonoids, polyphenols, phenolic acid, and uric acid are very famous antioxidants. Among these substances, polyphenols and their by-products are the most important antioxidants in plants. Several studies in humans or animals have demonstrated that polyphenols possess significant chemopreventive properties due to their antioxidant capacity [53]. Polyphenols are present in fruits, wines, and their by-products like vinegar [54]. Due to the wide variety of antioxidants present in vinegar, and perhaps, the additive, interactions among these molecules and other nutrients present in them, do not necessarily reflect their total antioxidant capacity [55]. Antioxidant capacity was found to be positively correlated with both, sugar and phenol content of vinegar. Regular apple vinegar exhibited improved health benefits with the presence of residual phenols in addition to acetic acid [56].

Superoxide dismutase, active constituents in vinegar, would have effects on maintaining normal vascular function [57]. Free and bound phenolics are known to play a crucial role in the defense mechanism, offering protection against Oxidative Stress (OS) caused by both biotic and abiotic factors. Phenolics from grape seed [58], cacao liquor [59] and others have been shown to possess antiulcer activity. The antioxidant activity of phenolics may be an important contributing antiulcer factor since Free Radicals (FR)/Reactive Oxygen Species (ROS) are related to the occurrence of ulcers [60].

The results also showed a statistically significant increase in the mean values of both secretin gene expression and HCO₃ amount among groups IIa, IIIa and IVa compared to the control group Ia, among groups IIb, IIIb, and IVb compared to the control group Ib, among groups IIIa and IVa compared to group IIa, among groups IIIb and IVb compared to group IIb, and in groups IVa and IVb compared to groups IIIa and IIIb respectively.

The secretin hormone is a peptide hormone produced in duodenal S cells. It influences the duodenal environment by regulating secretions in

the stomach, pancreas, and liver [61]. Secretin helps regulate duodenal pH by inhibiting gastric acid secretion from the parietal cells of the stomach directly or indirectly by inhibiting the release of gastrin in the pyloric antrum and stimulating the release of somatostatin [62]. It also stimulates HCO_3^- production from pancreatic centro-acinar cells and intercalated ducts [63]. Secretin primarily functions to neutralize the pH in the duodenum, allowing digestive enzymes from the pancreas to function optimally. Secretin targets the pancreatic centro-acinar cells that show secretin receptors in their plasma membrane [64]. Secretin also increases water and bicarbonate secretion from duodenal Brunner's glands to buffer the incoming protons of the acidic chyme [65].

The total amount of HCO_3^- secreted by the gastric mucosa is relatively small when compared to maximal gastric H^+ secretion. However, due to HCO_3^- secretion into the thin adherent mucus gel layer, it is highly effective in neutralizing the penetrating luminal H^+ . By contrast, the duodenum does not have the inherent acid protective structural properties of the stomach or tight intercellular junctions; however, it is covered by a leaky epithelium and has thicker mucus gel with more abundant HCO_3^- secretion which is the primary defense mechanism against the discharged H^+ . This HCO_3^- secretion originates from the pancreas and biliary tree and secreted in response to duodenal acidification due to release of secretin and due to local action of numerous mediators on duodenocytes (e.g., PG, NO, melatonin, VIP) [66].

Regarding the mean values of CCK gene expression, our results showed a statistically significant increase among groups IIa, IIIa and IVa compared to the control group Ia, among groups IIb, IIIb, and IVb compared to the control group Ib, among groups IIIa and IVa compared to group IIa, among groups IIIb and IVb compared to group IIb, and in group IVa compared to group IIIa.

CCK is a gastrointestinal peptide hormone responsible for stimulating fat and protein digestion. It is synthesized and secreted by entero-endocrine cells, called I cells, in the small intestine mucosal lining, neurons of the enteric nervous system, and neurons in the brain [67]. By inhibiting gastric emptying, CCK mediates digestion in the small intestine. It stimulates pancreatic acinar cells to release a juice rich in pancreatic digestive enzymes that catalyze fat, protein, and carbohydrates digestion [68]. CCK also is responsible for the increased hepatic bile production, the stimulation of the gall bladder to contract and the sphincter of Oddi (Glis-

son's sphincter) to relax, that results in the delivery of bile into the duodenum [67]. Konturek and colleagues showed that, in humans, endogenous CCK exerts an inhibitory influence on gastric acid secretion and gastrin release [69]. This could be explained by a negative feedback mechanism controlling gastrin secretion. CCK can potentially stimulate somatostatin release from isolated canine fundic mucosal cells [70]. It is also well documented that gastrin secretion is under somatostatin control in rats [71].

Conclusion and Recommendation:

The present study revealed the presence of a protective effect of omega-3 PUFA, vinegar and leptin on indomethacin and histamine dihydrochloride induced duodenal ulcer, with vinegar having more protective effect followed by omega-3 PUFA and finally comes leptin.

Conflict of interest: There is no conflict of interest.

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مقارنة بين تأثير الأحماض الدهنية الغير مشبعة أوميغا ٣ واللبتين والخل على قرحة الإثني عشر في الفئران البيضاء الذكور من خلال دراسة نسيجية كيميائية حيوية

يعتبر مرض القرحة الهضمية من مشكلات الجهاز الهضمي التي عادة ما تنتج من تلف الغشاء المخاطي نتيجة إفراز البيسين وحامض المعدة. يحدث هذا عادة في المعدة وبدايات الإثني عشر، ولكن يمكن أيضاً أن يحدث في نهايات المرئ أو نهايات الإثني عشر أو الصائم بدرجة أقل كما هو الحال في متلازمة "زولينجر إليسون" أو فتق الحجاب الحاجز أو تواجد غشاء مخاطي معدى خارج المعدة. تعد العدوى بالبكتريا الحلزونية واستخدام العقاقير المضادة للإلتهابات غير الإستيرويديه من الأسباب السائدة للقرحة الهضمية. هناك مجموعة متنوعة من الإصابات والأمراض مصحوبة بارتفاع خطر الإصابة بمرض القرحة الهضمية مثل: الفشل الكلوي المزمن ومرض "كرون" والسل والفيروس المضخم للخلايا، وإضطراب تكاثر النخاع، والتليف الكبدى والساركويد. كذلك قد يؤدي المرض المفاجئ أو الخضوع لعملية جراحية أو نقص حجم الدم المصحوب بنقص تدفق الدم السطحي إلى تقرحات أو تآكل في المعدة والأمعاء وهو ما يعرف بإسم قرحة الإجهاد، والتي يمكن أن تظهر مع نزيف أو ثقب أو حتى دون أعراض. من المعروف أيضاً أن التدخين يبطل إنتام القرحة ويزيد من خطر تكرارها. العلاج بمثبطات مضخة البروتون وحاصرات مستقبلات الهيستامين يمكن أن يقلل تلف الغشاء المخاطي. ولكن هناك العديد من الآثار الجانبية تصاحب هذه الأدوية كالإسهال والصداع والنعاس والتعب وآلام العضلات. وبالتالي يتم حالياً إستكشاف المركبات الطبيعية كبديل لهذه الأدوية.

يعد اللبتين - هرمون الشبع الذي يُصنع في الخلايا الدهنية - مثبطاً للجوع مما يساعد على تنظيم توازن الطاقة ويزيده في العمل الجريلى (هرمون الجوع). كلا الهرمونين يعمل على مستقبلات موجودة في النواة المقوسة بالمنطقة تحت المهادية بالمخ لتنظيم الشهية وتحقيق توازن الطاقة. تحدث الإستجابة المنخفضة للبتين عادة في السمنة مما يؤدي إلى عدم القدرة على الإحساس بالشبع بالرغم من مخزون الطاقة العالى.

كانت هناك زيادة كبيرة على مدار السنوات الماضية في الإهتمام العلمى والعام بالأحماض الدهنية الغير مشبعة أوميغا ٣ وتأثيرها على الصحة الشخصية، حيث أنها تعتبر مضادة للإلتهابات ومضادة لإضطراب أنظمة الجسم ومضادة للغط القلب كما أنها أيضاً مضادة للتخثر. الأسماك وزيتونها كلاهما مصدران غنيان للأحماض الدهنية الغير مشبعة أوميغا ٣، وتحديدأ حمض الإيكوزابنتانويك وحمض الدوكوزاهيكسانويك.

الخل - النبيذ الحامض - يمكن أن يصنع تقريباً من أى مصدر كربوهيدراتي متخمر. تنجم الخواص الكيميائية والحسية للخل عن المادة المتخمرة وطريقة التخمر. يعتبر حمض الخليك هو المسؤول عن النكهة الحامضية والرائحة اللاذعة للخل. تنص إدارة الغذاء والدواء الأمريكية على أن حمض الخليك المخفف ليس بالخل وبالتالي لا ينبغي إضافته إلى المنتجات الغذائية. المكونات الأخرى للخل تشمل الفيتامينات والأملاح المعدنية والأحماض الأمينية والمركبات البوليفينولية والأحماض العضوية غير المتطايرة.

تهدف هذه الدراسة إلى توضيح ومقارنة الآثار المحتملة للتعاظم المزمّن للأحماض الدهنية الغير المشبعة أوميغا ٣ واللبتين والخل على قرحة الإثني عشر في الفئران البيضاء الذكور، مع الآليات الكامنة لمثل هذه الآثار، في محاولة لإثبات وجود تأثير وقائى إفتراضى لهذه المواد على الغشاء المخاطي المبطّن للإثني عشر.