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Effect of Garlic in Comparison with Misoprostol and Omeprazole on Aspirin Induced Peptic Ulcer in Male Albino Rats

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ABSTRACT

Aiming to evaluate the protective effect of garlic on aspirin induced peptic ulcer in comparison with misoprostol and omeprazole drugs and its possible mechanisms. Forty white male albino rats were used. Total acid content, ulcer area/mm^2, histological study, mucosal & serum Total Antioxidant Capacity (TAC) by calorimetry and mucosal & serum PGE_2 and serum TNF-α by ELISA were assayed. Titrable acidity and total acid output decreased in garlic, misoprostol and omeprazole treated groups. Garlic, misoprostol and omeprazole improved gastric mucosa and decreased ulcer formation and ulcer area/mm^2. Aspirin decreased PGE_2 in gastric mucosa and serum. Co-administration of garlic to aspirin significantly increased PGE_2 near to normal in gastric mucosa. Aspirin significantly increased serum TNF-α than control and other groups. Garlic is suggested to protect the stomach against ulcer formation induced by aspirin by reducing gastric acidity, ulcer area, improve gastric mucosa, increasing PGE_2 and decreasing TNF-α.

Keywords: Aspirin, Garlic, Misoprostol, Omeprazole, Peptic ulcer

INTRODUCTION

Peptic ulcer is a worldwide problem, that present in around 4% of the population [1]. About 10% of people develop a peptic ulcer in their life [2]. Peptic ulcer is due to many causes include *Helicobacter pylori* and non-steroidal anti-inflammatory drugs [1]. Less common causes include smoking, stress due to serious illness, Behcet disease, Zollinger-Ellison syndrome, Crohn disease and liver cirrhosis [3]. Peptic ulcer is treated usually by proton pump inhibitors like omeprazole, H_2 blocker, prostaglandin-like substance (misoprostol) and ulcers due to *H. pylori* are treated with a combination of amoxicillin and clarithromycin antibiotics [1].

Aspirin is one of NSAIDs; act as an analgesic, an antipyretic and as an anti-inflammatory medication to relive pain, fever and inflammation [4,5]. It is used for the treatment of rheumatoid arthritis and related diseases as well as the prevention of cardiovascular thrombotic diseases. Salicylic acid, the main metabolite of aspirin, is an integral part of human and animal metabolism. Gastric ulcer is associated with aspirin usage [6].

Garlic (*Alliums sativum*) has been used as a food and remedy of many diseases for centuries. It is used as oils, ointments, poultices and powders. Garlic has been extensively used in the Indo-Pak subcontinent; it is used as a medicine for treatment of hypertension, atherosclerosis, rheumatism, bronchial asthma, and as a spasmolytic, vermifuge and antiseptic [7]. Garlic has anti-inflammatory effect and anti-Helicobacter activity [8]. The effect of garlic on healing of gastric ulcer in experimental rats has been investigated by many gastric ulcer studies [9-12]. However, the mechanism of the protective effects of garlic against gastric damage is unclear. In our research, we investigated the effect of garlic in comparison to misoprostol and omeprazole and its possible mechanisms on aspirin induced peptic ulcer in male albino rats.

MATERIALS AND METHODS

Forty white male albino rats of local strain weighing 150 ± 20 g were fed with standard laboratory diet and water “ad libitum” and housed in animal house at Faculty of Medicine, Menoufia University under normal light/dark cycle and room temperature. The study protocol was approved by the Ethics Committee of Faculty of Medicine, Menoufia University. The animals were acclimatized to these conditions for 10 days before the experiment. The animals were classified into five groups of eight animals each.

Group 1 control group: received only vehicle 1 ml of 1% carboxy methyl cellulose (CMC) solution orally by oral gastric tube once daily for 5 days. Group 2 aspirin induced peptic ulcer group: Aspirin was suspended in 1 ml of 1% CMC and was given orally in the dose of 200 mg/kg in rats once per day for 5 days [13]. Group 3 garlic and aspirin group: garlic powder was suspended in 0.5 ml of 1% CMC and was given orally in the dose of 200 mg/kg, 30 min before each aspirin administration (200 mg/kg suspended in 0.5 ml of 1% CMC solution), once daily for 5 days [13]. Group 4 misoprostol and aspirin group: Misoprostol was suspended in 0.5 ml of 1% CMC and was given orally in the dose of 50 µg/kg, 30 min before each aspirin administration (200 mg/kg suspended in 0.5 ml of 1% CMC solution), once daily for 5 days [14]. Group 5 omeprazole and aspirin group: omeprazole 2.3 mg/kg intraperitoneally injected once daily for 5 days, 30 min before each aspirin administration (200 mg/kg suspended in 1 ml of 1% CMC solution) [14].

On the 6^{th} day, pylorus ligation was performed [13]. The rats were fasted for 24 h, before surgery and allowed free access to drinking water. The animals were then anesthetized using thiopental sodium (50 mg/kg) intraperitoneally, the abdomen was opened. The pyloric end of stomach was ligated without damaging to its blood supply. Then, the stomach was replaced, and the abdominal wall was closed. After recovery from the anesthesia, the previous groups took their medication, as mentioned before (Group 1 orally received 1 ml of 1% CMC. Group 2 received aspirin (200 mg/kg orally) suspended in 1 ml of 1% CMC. Group 3 received aspirin together with garlic powder orally suspended in 1 ml of 1% CMC. Group 4 received aspirin together with misoprostol orally suspended in 1 ml of 1% CMC Group 5 received aspirin in 1 ml of 1% CMC and omeprzole intraperitoneally injected. After four hour of drug administration, the animals were anesthetized and then retro orbital blood samples were collected. About 3 ml of blood was collected in a sterile tube and kept at 37° for 30 min. After centrifugation at 3000 rpm for 15 min, the serum was collected using a sterile pipette [13]. The collected serum was then used for the estimation of prostaglandin E_2 (PGE_2), total antioxidant capacity (TAC) and Tumor necrosis Factor -α (TNF-α).

The oesophageal end was tied and the stomach was removed [15-17]. The stomach was cut along the greater curvature, and the gastric juice was collected [15]. The contents were collected in tubes and centrifuged at 3000 for 10 min. The supernatant was used for the estimation of gastric juice volume, titrable acidity and the total acid output. Then the stomach was washed with warm saline, and the inner surface was photographed. The gastric mucosal tissues were removed and used for estimation of PGE_2 and TAC.

Measurement of total acid content (Titrable acidity)

The total acid content of the gastric juice was calculated by titrating it with 0.01 N NaOH and was expressed as mEq/L [17,18]. The total acid content estimated by multiplying gastric juice volume ml/4 h and titrable acidity and was expressed as mEq/4 h [13].

Measurement of the gastric hemorrhagic ulcer area using image-J software

The photographs of the stomach were digitized and analyzed using image-J software product of the National Institute of Health (NIH), the area of gastric hemorrhagic ulcers (mm^2) was calculated [19].

Histopathological studies

Paraffin sections from gastric tissue samples from each group were performed and stained with haematoxylin and eosin and evaluated by light microscope.

Measurement of mucosal and serum PGE_2

For mucosal PGE_2, gastric mucosa was scraped with glass slide and put in a tube containing 5 mL homogenization buffer (0.1 M phosphate, pH 7.4), 1 mM Ethylenediaminetetraacetic acid (EDTA) and 10 µM indomethacin) and homogenized. Then, the lysate was centrifuged at 16,000 × g at 2-8°C for 15 min. The supernatant was collected and its total protein content was analyzed. To determine serum PGE_2, Blood samples were centrifuged at 1000 × g for 10 min at 4°C. The supernatant serum was collected and freeze at -20°C until usage. PGE_2 concentrations were investigated using the PGE_2 enzyme linked immunosorbent assay (ELISA) Kit (DRG International, Inc., USA) [15].

Determination of mucosal and serum TAC

To determine mucosal total antioxidant capacity, gastric mucosa was washed using saline then put in homogenized phosphate buffer (K_2HPO_4 and KH_2PO_4). The homogenized tissues were then centrifuged using a cold centrifuge at 1000 × g for 10 min at 4°C. The supernatant was collected and freeze at -20°C [20]. Mucosal and serum samples were used to determine TAC using colorimetric method (Biodiagnostic Company, Egypt).

Determination of serum TNF-α

The levels of TNF-α was determined by ELISA (Assaypro LLC, Charles, MO, USA).

Reagents

Aspirin (Aspocid) 75 mg was purchased from Chemical Industry Development (CID), Egypt. Garlic powder was purchased from Lu Hypermarket, Egypt. Misoprostol (Misotac tablet 200 µg), omeprazole (Losec injection 40 mg) and CMC were purchased from Sigma Company, Egypt.

Statistical analysis

The SPSS version 16.0 statistical tool was used for data analysis. The results of experiments were expressed as means ± standard error of the mean (S.E.M). The significance of differences between groups was determined by one-way analysis of variance (ANOVA) and the proper post-hoc test. The significance of differences was determined at $p<0.05$.

RESULTS

Gastric secretion parameters

Table 1, gastric volume was significantly decreased in both aspirin and (garlic & aspirin) groups ($p<0.001$) when compared to control group. Titrable acidity was significantly increased in aspirin group ($p<0.001$), while significantly decreased in other groups when compared to control group. Titrable acidity was significantly decreased in both (garlic & aspirin) ($p<0.05$) and (omeprazole and aspirin) ($p<0.01$) groups when compared to (misoprostol & aspirin) group.

Total acid output was significantly decreased after administration of garlic ($p<0.001$), misoprostol ($p<0.001$) and omeprazole ($p<0.001$) to aspirin induced peptic ulcer, but total acid output was significantly decreased in both (garlic & aspirin) ($p<0.001$) and (omeprazole and aspirin) ($p<0.01$) groups when compared to (misoprostol & aspirin) group.

Table 1: Gastric volume (ml/4 h), titrable acidity (mEq/L) and total acid output (mEq/4 h) in control, aspirin, (garlic & aspirin), (misoprostol & aspirin) and (omeprazole & aspirin) groups

Groups/Parameters	Control	Aspirin	Garlic and aspirin	Misoprostol and aspirin	Omeprazole and aspirin
Volume (ml/4 h)	1.03 ± 0.05	0.52 ± 0.037[a]	0.406 ± 0.042[a]	1.01 ± 0.036	1.07 ± 0.04
Titrable acidity (mEq/L)	3.76 ± 0.26	6.6 ± 0.15[a]	1.95 ± 0.18[a-c]	2.42 ± 0.15[ab]	1.6 ± 0.08[a-c]
Total acid output (mEq/4 h)	3.8 ± 0.22	3.4 ± 0.21	0.76 ± 0.08[a-d]	2.4 ± 0.15[b]	1.78 ± 0.11[a]

Values are shown as mean ± S.E.M. [a]Significant when compared to control group, [b]Significant when compared to aspirin group, [c]Significant when compared to (misoprostol & aspirin) group, [d]Significant when compared to (omeprazole & aspirin) group

Histopathological result

The macroscopic findings of the opened stomach are shown in Figure 1. Aspirin induced multiple ulcers with some hemorrhage. Pinpoint ulcers were sometimes seen in control group. Co-administration of garlic to aspirin decreased ulcer formation. Misoprostol and omeprazole with aspirin decreased aspirin induced ulcer formation.

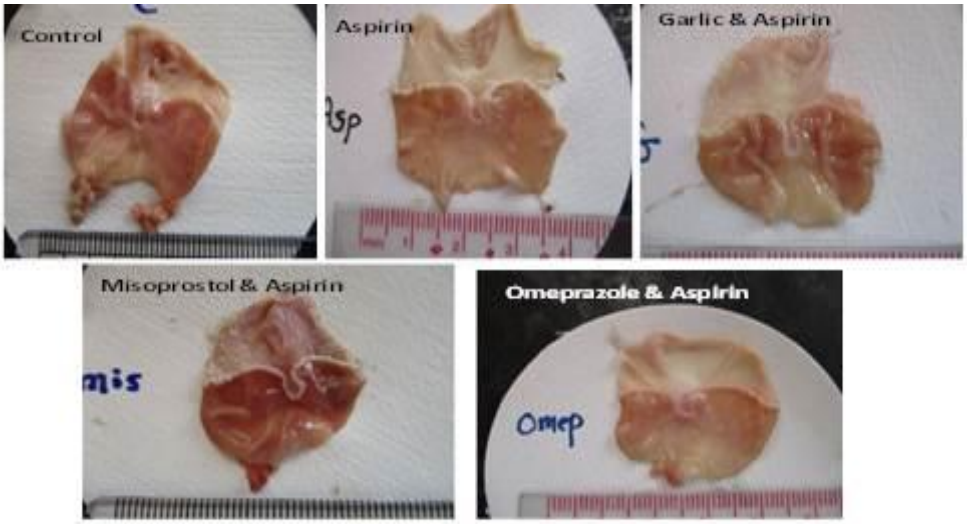
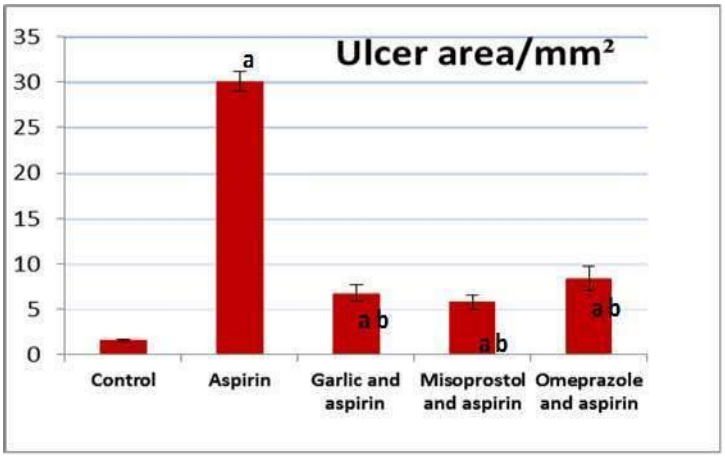


Figure 1: Photographs of opened stomach in control, aspirin, (garlic & aspirin), (misoprostol & aspirin) and (omeprazole & aspirin) groups

Figure 2, showed the mean area of gastric hemorrhagic ulcers (mm^2) in each group. Aspirin significantly increased ulcer area (30.1 ± 1.05 mm^2) ($p<0.001$) than control, (Garlic & aspirin), (misoprostol & aspirin) and (omeprazole &aspirin) (1.59 ± 0.17, 6.78 ± 0.88, 5.81 ± 0.77 and 8.42 ± 1.32 mm^2 respectively). Co-administration of garlic, misoprostol and omeprazole to aspirin significantly decreased ulcer formation ($p<0.001$) when compared to aspirin group, there was no significant difference between them.



Values are shown as mean ± S.E.M. [a]Significant when compared to control group, [b]Significant when compared to aspirin group

Figure 2: Ulcer area/mm^2 in control, aspirin, (garlic & aspirin), (misoprostol & aspirin) and (omeprazole & aspirin) groups

Figure 3a, high power image (H & E × 400) of the gastric mucosa showed the numerous gastric pits, gastric glands and intact gastric epithelium in control group. Figure 3b, distorted gastric glands; a damaged mucosal epithelium and cell debris with ulcer formation are shown in aspirin group. Co-administration of garlic and misoprostol to aspirin protected against previous changes, resulted in the maintenance of gastric glands and gastric mucosa. Omeprazole co-administration to aspirin decreased gastric mucosal damage with little ulcer formation (Figure 3).

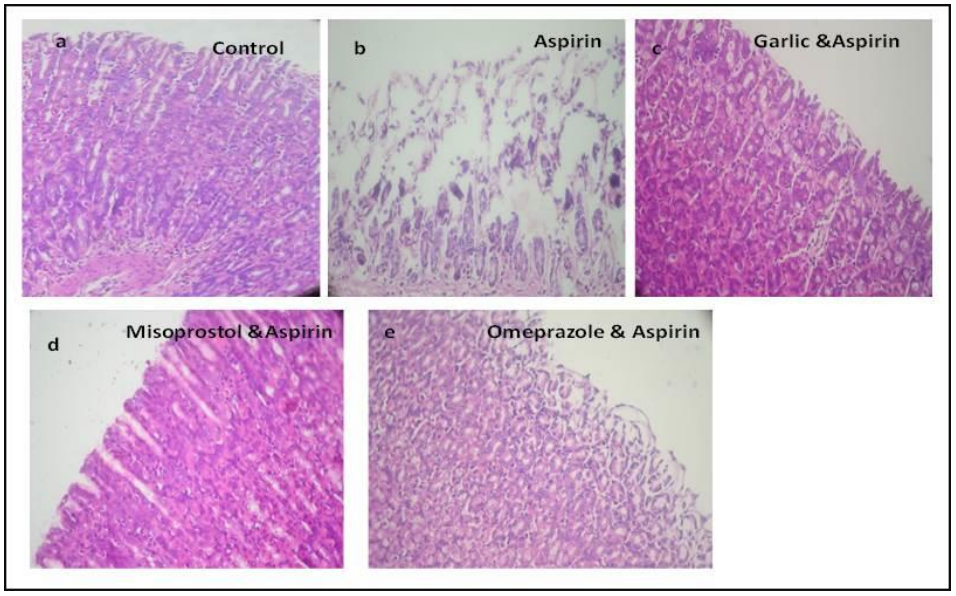


Figure 3: Histological sections of stomach in control, aspirin, (garlic & aspirin), (misoprostol & aspirin) and (omeprazole & aspirin) groups (H&E × 400)

Figure 4a and 4b showed PGE_2 pg/ml in gastric mucosa and serum in all groups. Aspirin significantly decreased mucosal and serum PGE_2 (962.52 ± 355 and 1888.2 ± 255.11 pg/ml, respectively) ($p < 0.01$ and $p < 0.001$ respectively) than control group (2316.5 ± 179.59 and 20100 ± 1472.12 pg/ml, respectively). Co-administration of garlic to aspirin attenuated the reduction of mucosal PGE_2 caused by aspirin more than serum PGE_2 (2111.5 ± 484.28 pg/ml mucosa and 9494.4 ± 2363.9 pg/ml serum). Co-administration of misoprostol and omeprazole to aspirin failed to inhibit the reducing effect of aspirin on mucosal and serum PGE_2.

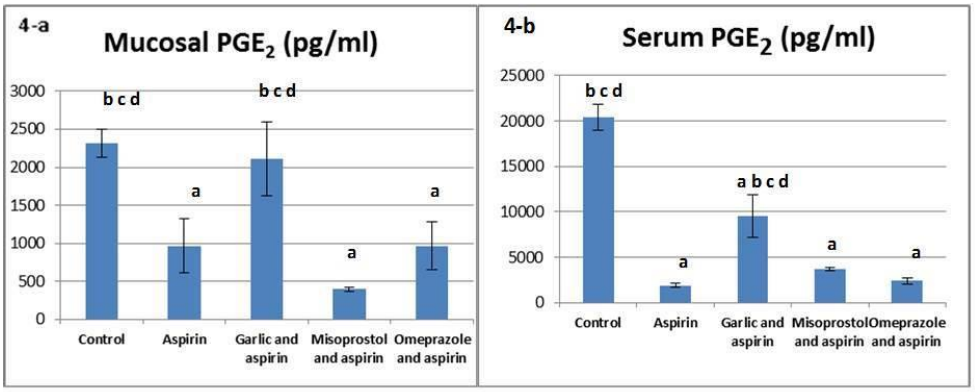
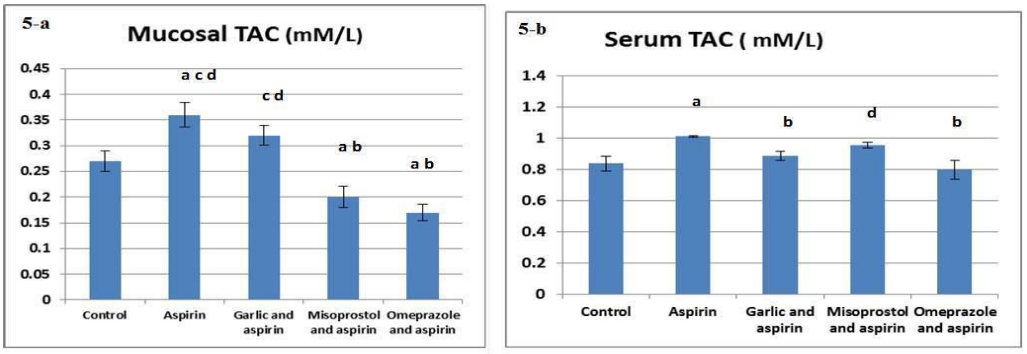


Figure 4: Mucosal and serum PGE_2 (pg/ml) in control, aspirin, (garlic & aspirin), (misoprostol & aspirin) and (omeprazole & aspirin) groups

Figure 5a and 5b showed mucosal and serum TAC mM/L in all groups. Aspirin group showed significant increase in mucosa and serum (0.36 ± 0.024 and 1.01 ± 0.007 mM/L, respectively) ($p<0.01$) than control. (Garlic & aspirin) group showed insignificant increase in mucosa and serum (0.32 ± 0.019 and 0.887 ± 0.03 mM/L, respectively) than control (0.27 ± 0.02 and 0.838 ± 0.048 mM/L, respectively), it also showed significant increase ($p<0.001$) than (misoprostol & aspirin) and (omeprazole & aspirin) groups (0.2 ± 0.021 and 0.17 ± 0.016 mM/L, respectively) in mucosa only. Misoprostol & aspirin group showed significant increase (0.955 ± 0.02 mM/L) when compared to (omeprazole & aspirin) group (0.797 ± 0.058 mM/L) in serum. (Misoprostol & aspirin) and (omeprazole & aspirin) groups showed significant decrease ($p<0.05$ and $p<0.001$ respectively) than control group in mucosa only.

Figure 6 shows serum TNF-α (pg/ml) in all groups. Aspirin significantly increased serum TNF-α (57.8 ± 7.3 pg/ml) ($p<0.001$) than control group (31.13 ± 6.4 pg/ml). Co-administration of garlic, misoprostol and omeprazole to aspirin significantly decreased the level of serum TNF-α near to normal (28.38 ± 6.9, 31.88 ± 0.97 and 24.38 pg/ml, respectively) (($p<0.001$, $p<0.01$ and $p<0.001$ respectively) when compared to aspirin group. There is no significant difference between control, (garlic &aspirin), (misoprostol &aspirin) and (omeprazole & aspirin).



Values are shown as mean ± S.E.M. [a]Significant when compared to control group, [b]Significant when compared to aspirin group, [c]Significant when compared to (misoprostol & aspirin) group, [d]Significant when compared to (omeprazole & aspirin) group

Figure 5: Mucosal and serum TAC (mM/L) in control, aspirin, (garlic & aspirin), (misoprostol & aspirin) and (omeprazole & aspirin) groups

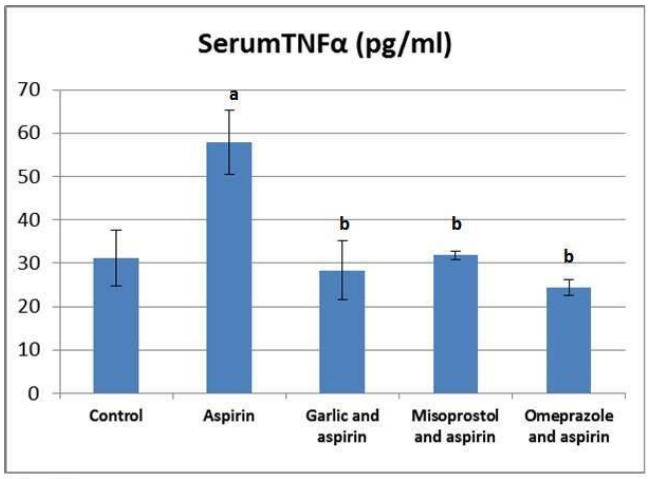


Figure 6: Serum TNF-α (pg/ml) in control, aspirin, (garlic & aspirin), (misoprostol & aspirin) and (omeprazole & aspirin) groups

DISCUSSION

Garlic has been used as a food and remedy of different diseases for centuries. The antiulcer effect of garlic has been investigated by many experimental gastric ulcer models [9,10,20]. However, the mechanism of the protective effects of garlic against gastric damage is unclear. In the present study the antiulcer effect of garlic in comparison with misoprostol and omeprazole was investigated in aspirin induced peptic ulcer in male albino rats. As regard to gastric secretion parameters, aspirin significantly decreased gastric volume, increased titrable acidity and increased ulcer area when compared to control group. These results were in agreement with previous studies [15,18], they reported that aspirin decreased gastric mucosal blood flow (GMBF), synthesis of gastric mucus, increased gastric acid secretion, decreased PGE_2 and affected the quality of ulcer healing.

Co-administration of garlic with aspirin significantly decreased gastric volume, titrable acidity, total acid output and ulcer area when compared to control group. This may be due to garlic increasing effect on PGE_2. Prostaglandins have protective effects against different gastric ulcer models [21,22]. Prostaglandins stimulate mucus and bicarbonate secretion in the stomach and many sites in the gastrointestinal tract. Thus, they decrease ulcer area and promote its healing [23,24]. At least in rodents, these effects appear to be mediated via prostaglandin receptors [25]. The cause of decreased gastric volume with garlic administration is not fully understood, as previous studies reported increase in the gastric volume [19,26].

Garlic also contains sulphur compounds. These compounds form H_2S when combined with gastric acid. H_2S donors increase the resistance of the gastric mucosa to injury that caused by NSAIDs and other noxious substances [27] so, they accelerate healing of ulcers in rodents [24,28]. Misoprostol, a synthetic prostaglandin analogue, specially a prostaglandin E_1 analogue. It is used in the prevention of NSAID-induced gastric ulcers. It acts upon gastric parietal cells by inhibiting the secretion of gastric acid by G-protein coupled receptor-mediated inhibition of adenylate cyclase, which leads to decreased intracellular cyclic-AMP levels and decrease proton pump activity at the apical surface of the parietal cell [29]. These results were in agreement with our results that reported that co-administration of misoprostol to aspirin significantly decreased titrable acidity, total acid output and ulcer area when compared to control group. Also co-administration of omeprazole to aspirin significantly decreased titrable acidity, total acid output and ulcer area when compared to control group. These results may be due to blocking effect of omeprazole on H^+K^+ ATPase pump which is responsible for final secretion of gastric acid secretion. These results were in agreement with Walan et al. [30], who reported that omeprazole is highly effective inhibitor of acid secretion and has been shown to promote rapid healing of duodenal ulcer and reflux oesophagitis.

The significant decrease in total acid output in both (garlic & aspirin) and (omeprazole and aspirin) groups when compared to (misoprostol & aspirin) group may be due to effect of misoprostol on gastric secretion occurs at high doses only. This result was in agreement with Bauer [31], who reported that misoprostol has been shown to protect against gastric ulceration in various rat models at doses 10 fold lower (10-150 ug/kg) than the dose required to decrease acid secretion (1000 ug/kg).

Gastric cellular epithelia and tight junction among gastric cellular epithelia form a mucosal barrier. This mucosal barrier constitutes a line of defense that protects the gastric mucosa from harmful factors. The deformed gastric mucosa weakens barrier function [18]. Ulcers associated with distorted gastric glands, a damaged mucosal epithelium, cellular debris, and inflammatory exudates were found in the stomachs of the aspirin-treated rats [9]. This result was in agreement with our result about aspirin induced peptic ulcer. Garlic has protective effect against aspirin induced peptic ulcer. Garlic increases mucus secretion, improves gastric mucosal structures, this result was in agreement with Badr and Al-Mualhim [10]. Misoprostol, a prostaglandin analogue, improved gastric mucosa and increased mucus secretion Prostaglandins increased the resistance of epithelial cells to damage caused by Non-steroidal Anti-inflammatory Drugs (NSAID) or ethanol [32]. Omeprazole protected against aspirin induced gastric ulcer with improvement of gastric mucosal structures [33].

Aspirin has been shown to reduce the mucosal and serum PGE_2 [18,34]. The key enzyme for synthesis of prostaglandins is Cyclooxygenase (COX) enzyme. Aspirin administration was accompanied by the suppression of COX-1 and COX-2 activity [35]. Inhibition of prostaglandin synthesis weakened the function of the gastric mucosal defense [36] and inhibits pain transmission to the brain [37].

Garlic attenuated the decreasing effect of aspirin on PGE_2 and elevated its level near to normal especially in gastric mucosa. This result was in agreement with Hussain and Khan [38], they reported that garlic extract has got prostaglandin activity. The chemistry of garlic reveals presence of sulphur containing fatty acids and various actions of garlic extract were assigned to these fatty acids, (active principles) and prostaglandins are also fatty acids. The effect of garlic on PGE_2 in mucosa is more than serum. This result may be due to little effect of garlic on prostaglandins synthesis in blood. Ali [39] reported that cyclooxygenase activity of rabbit platelets was more sensitive to inhibition by raw garlic. Also, Al-Qattan et al. [40] reported that garlic inhibits cyclooxygenase activity that would allow for the production of thromboxane B2. This change in balance towards PGE_2 favors vasodilation.

Co-administration of misoprostol to aspirin failed to inhibit the reducing effect of aspirin on mucosal and serum PGE_2. This result may be due to that misoprostol is a selective prostaglandin E_1 analogue and it doesn't affect PGE_2 level and also, it acts locally and replaces prostaglandin whose synthesis in the gastro-duodenal mucosa is inhibited by NSAIDs. These results coincide with (Simon et al.; Moskowitz et al. [41,42].

Omeprazole failed to inhibit the aspirin -induced reduction of mucosal and serum PGE_2. The main action of omeprazole in peptic ulcer treatment is to inhibit of gastric acid production. Anti-secretory therapy like omeprazole may also affect the production of factors involved in primary gastric mucosal defense like PGE_2 and decreases their levels [43].

Aspirin has been shown to decease TAC, as reported by many researches [44-46], but our research reported that aspirin significantly increase both mucosal and serum TAC. We attributed this rise to the short period of aspirin administration and increased generation of reactive oxygen species (ROS), which will induce a specific compensatory increase in antioxidant enzyme activities and over expression of the antioxidant complex enzymes. TAC is major mechanisms by which cells counteract the deleterious effects of ROS and protect themselves from oxidative damage. Koseoglu et al. [47] reported that low-dose aspirin supplementation in a short time period significantly increases total antioxidant activity and improves the general antioxidative potency of blood.

Garlic is an important source of antioxidant phytochemicals such as diallyl sulfide, S-allylmercaptocysteine, and ajoene, which is the optimal assurance for neutralizing free radical-mediated inflammation [10,48,49], but our result reported that co-administration of garlic with aspirin shows insignificant increase in TAC in mucosa and serum when compared to control group. These results may be due to the short period of the garlic administration and protective effect of garlic on mucosa and decrease its damage, so it decreases release of ROS, since gastric mucosa and mucus act as a potent scavenger of ROS [44].

Misoprostol, a prostaglandin analogue has protective effect on gastric mucosa and increase mucus secretion, it showed significant decrease in TAC in gastric mucosa when compared to control. In fact, this result was not clearly understood, as other researchers reported increase antioxidant enzymes with misoprostol administration [50,51], the insignificant increase in TAC in serum after administration of misoprostol coincide with Smirnova et al. [52].

Omeprazole has been shown antioxidant effect in gastric mucosa and blood, as reported by other research [53-55], but our research reported a decrease in TAC after co-administration of omeprazole to aspirin. This result may be due to the low dose of omeprazole or due to the short period of omeprazole administration.

Inflammation and neutrophil infiltration are important in the pathogenesis of the gastric damage caused by NSAIDs [15,56,57]. The inflammation induced by aspirin in the gastric mucosa is accompanied by increased inflammatory cytokines like TNF-α [16,58]. These result coincided with our result. Co-administration of garlic to aspirin decreased the level of serum TNF-α near to normal, this result coincide with (Makrisa et al.; Badr and Al-Mualhim [10,59]. Garlic allicin inhibited the TNF-α secretion assessing the anti-inflammatory effect of allicinon intestinal epithelial cells [60].

Prostaglandin E compounds (Misoprostol) have been shown to reduce inflammation and tissue injury. Misoprostol decrease acute inflammation induced by TNF-α [61]. Misoprostol has anti-inflammatory effect and decrease TNF-α in NSAIDs induced intestinal injury in mice [62]. These results agreed with our result that detected that misoprostol decreased TNF-α level. Omeprazole also significantly decreased TNF-α. This result agreed with Gao et al. [33].

CONCLUSION

Garlic powder is suggested to protect the stomach against the ulcer formation caused by aspirin by reducing gastric acidity, ulcer area, improve gastric mucosa, increasing PGE_2 and decreasing TNF-α. These provide strong interest in developing natural drug that produce the desired antiulcer effect without the undesired effect of other drugs.

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REFERENCES

[1] W.I. Najm, *Primary Care*., **2011**, 38, 383-394.
[2] F.M. Snowden, *Immunol. Rev.*, **2008**, 225, 9-26.
[3] K.P. Steinberg, *Crit. Care Med.*, **2002**, 30, S362-S364.
[4] W. Sneader, *BMJ*., **2002**, 321, 1591-1594.
[5] C. Lampl, M. Voelker, H.C. Diener, *J. Neurol.* **2007**, 254, 705-712.
[6] J.R. Paterson, G. Baxter, J.S. Dreyer, J.M. Halket, R.L. Flynn, R. James, *J. Agric. Food. Chem.*, **2008**, 5, 11648-11652.
[7] A. Rashid, H.H Khan, *J. Pak. Med. Assoc.*, **1985**, 35, 357-62.
[8] T.B. Hadda, N.A. ELSawy, E.A.M. Header, Y.N. Mabkhot, M.S. Mubarak, *Med. Chem. Res.*, **2014**, 23, 5110-5119.
[9] S.A. Tope, O.F. Sunday, A.T. Gabriel, *Int. J. Inter Med*., **2013**, 8, 119-123.
[10] G.M. Badr J.A. AL-Mulhim, *Evid. Based. Complement. Alternat. Med.*, **2014**, 2014, 1-9.
[11] J.J. Park, *Gut. Liver.*,**2016**, 10, 321-322.
[12] N.E. El-Ashmawy, E.G. Khedr, H.A. El-Bahrawy, H.M. Selim, *Nutr.*, **2016**, 32, 849-854.
[13] M. Khushtar, V. Kumar, K. Javed, U. Bhandari, *Ind. J. Pharm. Sci.*, **2009**, 71, 554-558.
[14] M. Sancar, T. Hantash, B. Okuyan, S. Apikoglu-Rabus, Z. Cirakli, M.G. Gulluoglu F.V. Izzettin, *Afr. J. Pharm. Pharmacol*., **2009**, 3, 615-620.
[15] Z. Wang, J. Hasegawa, X. Wang, A. Matsuda, T. Tokuda, N. Miura, T. Watanabe. *Yonago. Acta. Medica.*, **2011**, 54, 11-19.
[16] M. Jainu, C.S.S. Devi. *Chem. Biol. Interact.*, **2006**, 161, 262-270.
[17] M. Jainu, K.V. Mohan, C.S.S. Devi, *Indian. J. Med. Res*., **2006**, 123, 799-806.
[18] G.Z. Wang, G.P. Huang, G.L. Yin, G. Zhou, C.J. Guo, C.G. Xie, B.B. Jia, J.F. Wang, *Cell. Physiol. Biochem.*, **2007**, 20, 205-212.
[19] H.A. Khan, *J. Pharmacol. Toxicol. Methods*., **2004**, 9, 89-90.
[20] M.A. Mabrouk, F.A. Nnawodu, Y. Tanko, F. Dawud, *Curr. Res. J. Biol. Sci*. **2009**, 1: 15-19.
[21] J.L. Wallace, *Gastroenterol, Clin, North, Am*., **1992**, 21, 631-641.
[22] T. Brzozowski, P.C. Konturek, S.J. Konturek, I. Brzozowska, T. Pawlik. *J. Physiol. Pharmacol.*, **2005**, 56, 33-55.
[23] S. Chu, S. Tanaka, J.D. Kaunitz, M.H. Montrose, *J. Clin. Invest*., **1999**, 103, 605-612.
[24] J.L. Wallace. *Physiol. Rev*., **2008**, 88, 1547-1565.
[25] K. Takeuchi, A. Tanaka, S. Kato, E. Aihara, K. Amagase, *J. Pharmacol. Exp. Ther.*, **2007**, 322, 903-912.
[26] F.N. Rafsanjani, M. Shahrani, J. Vahedian, *Pak. Med. Sci*., **2006**, 22, 1-7.
[27] S. Fiorucci, E. Antonelli, E. Distrutti, A. Mencarelli, S. Orlandi, R. Zanardo, B. Renga, G. Rizzo, A. Morelli, G. Cirino, J.L. Wallace, *Gastroenterology*, **2005**, 129, 1210-1224.
[28] S.N. Elliott, W. McKnight, G. Cirino, J.L. Wallace, *Gastroenterology*, **1995**, 109, 524-530.
[29] C.J. Hawkey, J.A. Karrasch, L. Szczepañski, D.G. Walker , A. Barkun, A.J. Swannell, N.D. Yeomans, *N. Engl. J. Med.*, **1998**, 338, 727-34.
[30] A. Walan, J.P. Bader, M. Classen, C.B.H.W. Lamer, D.W. Piper, K. Rutgesson, S. Eriksson, *N. Engl. J. Med.*, **1989**, 320, 69-75.
[31] R. Bauer, *Dig. Dis. Sci.*, **1985**, 30, 118S-125S.
[32] A. Tarnawski, T. Brzozowski, I.J. Sarfeh, W.J. Krause, T.R. Ulich, H. Gergely, D. Hollander, *J. Clin. Invest.*, **1988**, 81, 1081-1089.
[33] W. Gao, H.Y. Li, L.X. Wang, L.J. Hao, J.L. Gao, R.J. Zheng, C.J. Cai, Y.L. Si. *Asian. Pac. J. Trop. Med.*, **2014**, 7, 402-406.
[34] L.M. Lichtenberger, J.J. Romero, E.J. Dial, *Br. J. Pharmacol*., **2007**, 150, 913-919.
[35] T. Brzozowski, *J. Physiol. Pharmacol.*, **2003**, 54, 99-126.
[36] F.K. Chan, W.K. Leung, *Lancet.*, **2002**, 360, 933-941.
[37] H. Tohgi, S. Konno, K. Tamura, B. Kimura, K. Kawano, *Stroke.*, **1992**, 23, 1400-1403.
[38] A.M. Hussain, H.H. Khan, *JPMA.*, **1986**, 36, 138-141.
[39] M. Ali, *Prostaglandins. Leukot. Essent. Fatty. Acids.*, **1995**, 53, 397-400.
[40] K.K. Al-Qattan, I. Khan, M.A. Alnaqeeb, M. Ali, *Prostaglandins. Leukot. Essent. Fatty. Acids.*, **2001**, 64, 5-10.
[41] L.S. Simon, H.T. Hatoum, R.M. Bittman, M.T. Archambault, R.P. Polisson, *Fam. Med.*, **1996**, 28, 202-208.
[42] R.W. Moskowitz, R.D. Altman, M.C. Hochberg, J.A. Buckwalter, V.M. Goldberg. Lippincott Williams & Wilkins, a Wolter Kluwer Business, Philadelphia. USA. **2007**, 15, 267-280.
[43] K.I. Yoshimura, S.G. Delbarre, E. Kraus, C.R. Boland, *Aliment Pharmacol. Ther*., **1996**, 10, 111-7.
[44] Y. Mitobe, H. Hiraishi, T. Sasai, T. Shimada, A. Terano, *Aliment. Pharmacol. Ther.*, **2000**, 14, 10-17.
[45] S. Sarkar, D. Buha, *Indian J. Exp. Biol*., **2008**, 46, 639-645.
[46] K. Shyamal, R. Chandan, *Saudi. J. Gastroenterol*., **2012**, 18, 188-194.
[47] M.H. Koseoglu, S. Cuhadar, A. Atay, Y. Yigit, Y. Akcay, *Siriraj. Med. J.*, **2014**, 66, 42-44.
[48] C. Borek, *J. Nutr.*, **2001**, 131, 1010-1015.
[49] H. Amagase, *J. Nutr.*, **2006**, 136, 716-725.
[50] S. Bhattacharya, D. Banerjee, A.K. Bauri, S. Chattopadhyay, S.K. Bandyopadhyay, *World. J. Gastroenterol.*, **2007**, 21, 3705-3713.
[51] M.S. Ali Khan, A.M. Mais Jais, A. Afreen, *Bio. Med. Res. Int*., **2013**.
[52] G.A. Smirnova, V.I. Pogorel'tsev, F.M. Faĭzrakhmanova, *Klin. Lab. Diagn.*, **2009**, 8, 14-15.
[53] T.R. Koch, L.X. Yuan, A. Petro, E.C. Opara, *Dig. Dis. Sci.* **2002**, 47, 2486-2492.
[54] K. Biswas, U. Bandyopadhyay, I. Chattopadhyay, A. Varadaraj, E. Ali, R.K. Banerjee. *Ame. Soc. Biochem. Mol. Biol. Inc.*, **2003**, 1-48.
[55] K.K. Abdul-Aziz, *Food, Nutr. Sci*., **2011**, 2, 628-640.
[56] J.L. Wallace, C.M. Keenan, D.N. Granger, *Am. J. Physiol.*, **1990**, 259, G462-G467.
[57] M.H.L.P. Souza, H.P. Lemos, R.B. Oliveira, F.Q. Cunha, *Gut*., **2004**, 53, 791-796.
[58] Y. Naito, T. Yoshikawa, N. Yagi, K. Matsuyama, N. Yoshida , K. Seto, T. Yoneta, *Dig. Dis. Sci*., **2001**, 46, 845-851.
[59] A. Makrisa, C.E. Thorntona, B. Xua, A. Hennessya, *Placenta.*, **2005**, 26, 828-834.
[60] A. Lang, M. Lahav, E. Sakhnini, I. Barshack , H.H. Fidder , B. Avidan , E. Bardan , R. Hershkoviz , S. Bar-Meir, Y. Chowers, *Clinical. Nutr.*, **2004**, 23, 1199-1208.
[61] R.G. Rossetti, C.M. Seiler, K. Brathwaite, R.B. Zurier, *Am J. Ther.*, **1995**, 2, 600-606.
[62] J. Jin, F. Wu , Z. Xiao , Z. Liu , X. Xie, H. Zhou, *Xi Bao Yu Fen Zi Mian Yi Xue Za Zhi*, **2015**, 31, 928-932.