

ANTI-ULCEROGENIC EFFECT OF WATER EXTRACT OF SOME HERBS ON ASPIRIN INDUCED GASTRIC ULCER IN RATS

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ABSTRACT: *Stomach ulcer still a medical problem that face several patients in a wide range of age of both sexes worldwide. Long term uses of nonsteroidal anti-inflammatory drugs (NSAIDs) such as Aspirin are the second most common cause of ulcers after H. pylori. Enormous drugs are available for the treatment of gastric ulcers, but these drugs proclaim serious side effects. Therefore the aim of this study was to evaluate the antiulcerative effects of the water extracts of four plant herbs individually and in a mixture toward Aspirin namely, chamomile (Matricaria chamomilla), turmeric (Curcuma longa), ginger (Zingiber officinale Rosc.) and licorice (Glycyrrhiza glabra). Sixty five male albino wistar rats were divided into 13 groups, two different concentration 200 and 400 mg/kg bodyweight of herb extracts or their mixture against 400 mg/kg Aspirin were used. Additionally, Omeprazole 20 mg/kg was used as standard antiulcer drug. Gastric juice volume, acidity, pH value, ulcer index and histological changes were measured to determine the antiulcerative effects of these herbs. Results showed that a single dose of Aspirin (400mg/kg) for two consequence days was able to induce severe ulcer on stomach of 5.50 ± 0.25 mm length. All herb extracts as well as Omeprazole significantly alleviated and cured Aspirin induced ulcer ($P \leq 0.01$). The percentage of recovery ranged from 69.64 to 87.82. Chamomile 200 mg, Omeprazole 20 mg, Turmeric 400mg and Licorice 200 mg expressed the highest curative effects respectively. In general, herb extracts were ordered descendingly according to their curative effects as follow: Chamomile 200 mg> Turmeric 400 mg> Licorice 200 mg> Chamomile 400 mg> Licorice 400 mg> Ginger 200 mg> Ginger 400 mg> Mixture 200 mg> Mixture 400 mg> Turmeric 200 mg. significant difference between groups was also observed for gastric volume, acidity and pH values. Data suggested a potential role of these herbs on Aspirin induced gastric ulcer.*

Key words: *Ulcer Herb Aspirin Omeprazole Rats*

INTRODUCTION

Gastric ulcer is a lesion penetrating through the entire thickness of the mucosa and muscularis mucosa of the stomach. It still a medical problem that face many patients in a wide range of age of both sexes worldwide . Many pathogens induce gastric ulcer such as *H. pylori*, gastric acid secretions, NSAIDs (Non-steroidal anti-inflammatory drugs), reserpine, ethanol, cytokines, NO (Nitric oxide), prostaglandins, LTs (leukotrienes), endothelin and apoptosis (Ge *et al.*, 2007, Kaur *et al.*, 2012, Chan *et al.*, 2013).

The long-term use of NSAIDs is the second most common cause of ulcers after *H. pylori*. About 25% of chronic users of these drugs develop gastric ulcer disease. The most common NSAIDs are Aspirin,

naproxen and ibuprofen (Shrestha *et al.*, 2009).

Different mechanisms are involved in NSAIDs/Aspirin induced gastric ulcer. These includes, inhibiting the prostaglandin synthesis which causes the activation of neutrophils and local release of reactive oxygen species (ROS) thus initiates the gastric injury, overcoming the expression of enzyme cyclo-oxygenase (COX) which inhibits the conversion of arachidonic acid (AA) to prostaglandins (PG's) that impairs the mucosal barrier (Chan *et al.*, 2013), Further NSAIDs/Aspirin also causes marked reduction in mucosal blood flow, mucus-bicarbonate secretions, impaired platelet aggregation, reduced epithelial cell renewal and increased leukocyte adherence that are responsible for pathogenesis of ulceration (Shiotani *et al.*, 2009).

A wide range of drugs are available for the treatment of peptic/gastric ulcers including H₂ antagonists, anticholinergics and proton pump inhibitors. Unfortunately these drugs proclaim serious side effects like impotence, headache, skin rash, arrhythmias, hypergastrinemia, atrophic gastritis, constipation, ulcer perforation, urinary retention, diarrhoea, dizziness, edema, hypophosphatemia, blurred vision, xerostomia and precipitation of glaucoma (Akhtar *et al.*, 1992, Franko and Richter, 1998, Reilly, 1999).

Due to the mentioned reasons, there was an importance to find out other natural strategies with few side effects. Herbs and herbal drugs have preserved their importance due to effective, easy availability, relatively less adverse effects and economical (Padhye *et al.*, 2010). Furthermore herbs possess wide range of health properties other than antiulcer including, anti-inflammatory, immunomodulatory, antihyperglycemic, anti-cancer, antipruritic, wound healing, antimicrobial, anti-allergic, prevent osteoporosis and antiulcer potential (McKay and Blumberg, 2006, Ali *et al.*, 2008, Asl and Hosseinzadeh, 2008).

In the present work, the therapeutic effect of the water extracts of four plant herbs individually and in a mixture including, Chamomile (*Matricaria chamomilla*), Turmeric (*Curcuma longa*), Ginger (*Zingiber officinale* Rosc.) and Licorice (*Glycyrrhiza glabra*) toward gastric ulcer induced by Aspirin using rats are studied.

MATERIAL AND METHODS

Plants

Chamomile, Turmeric, Ginger and Licorice were obtained as crude dried materials from local markets of Egypt. Plants were free of diseases and authenticated at Faculty of Pharmacy, Tanta University, Egypt.

Chemicals and Drugs

Aspirin (acetylsalicylic acid) Aspegic © and Omeprazole 20 mg (Epirazole capsules, 20mg) were obtained from Egyptian International Pharmaceutical Industries Co.

(EIPICO) Cairo, Egypt. All other chemicals were obtained from Al- Gomhoriya Co. for pharmaceutical industries Cairo, Egypt.

Experimental animals

This study was carried out in the animal house of faculty of Home Economics, Minufiya University using albino wistar rats weighing 150–200 g. All rats were obtained from the animal house colony of the National Research Centre, Dokki, Giza, Egypt. Rats were housed in clean wire mesh cages under standard conditions of humidity (50 ± 5 %), temperature (25±3°C), light (12 h light/12 h dark cycle) and accumulated for one week before starting the experiment using free access standard basal diet and water ad libium. Basal diet was formulated to contain 14% casein, 10% sucrose, 5% corn oil, 5% fiber (cellulose), 3.5% mineral mixture, 1% vitamin mixture, 0.25% choline chloride, 0.3 % D-L methionine, and 60.95% corn starch (Reeves *et al.*, 1993). All animals were handled with humane care. The experiment was carried-out in accordance with the national regulations on animal welfare and Institutional Animal Ethical Committee, Minufiya University, Egypt.

Preparation of aqueous extract

The dried plant herbs were ground for 5 min to pass through a 60 mesh sieve using Wiley mill. The ground powder was soaked in distilled water (1:10) over night at 4 °C. Samples were then boiled for 15 min in a water bath. The supernatant was centrifuged and recovered through vacuum filtration using filter paper No.1 then through Millipore filters (0.45 µm). The filtrate was then dried in vacuum oven at 45 °C and stored in airtight containers at -20 °C until use.

Experimental design

Induction of gastric ulceration and treatment protocol:

Sixty five male Albino Wistar rats were randomly divided into thirteen groups with five rats each as follows:

Group 1: served as normal control without any treatment (control).

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All other groups were administered orally with single dose of Aspirin (400mg/kg b.wt.) for two consequence days and then treated for further seven days as following:

Group 2: Without treatment as ulcerogenic control (control⁺).

Group 3: treated with Omeprazole (20mg/kg b.wt.).

Group 4 and 5: treated with aqueous extract of Chamomile at two concentration levels, (200 and 400 mg /kg b.w.), respectively.

Group 6 and 7: treated with aqueous extract of Turmeric at two concentration levels, (200 and 400 mg /kg b.w.), respectively.

Group 8 and 9: treated with aqueous extract of Ginger at two concentration levels, (200 and 400 mg /kg b.w.), respectively.

Group 10 and 11: were treated with aqueous extract of Licorice at two concentration levels, (200 and 400 mg /kg b.w.), respectively.

Group 12 and 13: treated with a mixture consisted of equal volumes of aqueous extract of Chamomile, Turmeric, Ginger and Licorice at two concentration levels, (200 and 400 mg /kg b.w.) respectively

Aspirin was freshly prepared by dissolving one vial (1g) in 5 ml distilled water. It was orally given to the rats on an empty stomach at a single dose of 2 ml (equal to 400 mg/kg Aspirin). The standard drug (Omeprazole 20 mg/kg) and the other aqueous extracts were administered orally to the respective groups one hour before giving the diet. At the end of experiment rats were fasted and only allowed to drink water for 16 hours then they were humanely sacrificed using diethyl ether.

Determination of gastric juice volume

The stomach was removed after legend the cardiac and pyloric opening and injected with 3ml distilled water. The gastric contents were collected into graduated centrifuge tubes and centrifuged at 3000 rpm for 10 min. Volume was then recorded and expressed as ml. The gastric juice decrease percentage was calculated for each group

according to (Parmar and Desai, 1993) as following: The gastric juice decrease percentage = [volume of gastric juice of control positive - volume of gastric juice of treated group / volume of gastric juice of control positive) × 100].

Determination of gastric juice acidity and pH value

One ml of gastric juice was adjusted to 10 ml using distilled water. The pH value was then measured by pH meter. Total acidity was determined by titrating gastric juice with 0.01N sodium hydroxide using phenolphthalein as indicator according to (A.O.A.C., 1995). The decrease in total acidity of gastric juice percentage was calculated for each treated group according to (Paiva *et al.*, 1998) as following: Decrease in total acidity percentage = [total acidity of gastric juice of control positive group - (total acidity of gastric juice of treated group / total acidity of gastric juice of control positive group) × 100].

Determination of Ulcer Index (UI)

Stomachs were opened longitudinally, washed with saline and examined under dissecting microscope for gastric ulcer. The length of gastric ulcer was measured for each group to determine of ulcer index (UI) and the curative ratio according to (Parmar and Desai, 1993). The ulcerative index was calculated by severity of gastric mucosal lesions 1mm or less, 1-2 mm and more than 2 mm and graded as 1, 2 and 3 score, respectively. Then the UI was calculated by using the formula: UI = 1 × (number of lesions of grade 1) + 2 × (number of lesions of grade 2) + 3 × (number of lesions of grade 3). Then the overall score was divided by a factor 10, which was designated as ulcer index. The curative ratio was calculated for each group as following: Curative ratio=(length of gastric ulcer in control positive group - length of gastric ulcer in treated group / length of gastric ulcer in control positive group) ×100.

Histological examination

Sections of tissue from stomach was examined histopathologically to study the

antiulcerogenic activity of plant extracts . Tissue samples were fixed in 10% buffered formalin (pH 7.4) for 24h and afterward processed using tissue processor. The processed tissue was embedded in paraffin blocks and about 5 µm thick sections were prepared a rotary microtome. These sections were stained with Hematoxylin and Eosin. The slides were then examined microscopically for pathomorphological changes such as congestion, hemorrhage, edema and erosions (Price, 1991).

Statistical analysis

Data were expressed as mean ± SD. The statistical significance of differences between groups was assessed using one-way analysis of variance (ANOVA). The Mann-Whitney U test was used to compare the difference between two groups. A value of $p < 0.05$ was considered for significance. Statistical analysis was performed using SPSS 17 for Windows software (SPSS Inc, Chicago, IL, USA).

RESULTS AND DISCUSSION

Effect of Aspirin, Omeprazole and herb extracts on gastric juice volume

As illustrated in table (1) revealed no significant difference for gastric juice volume between positive and negative control group ($P \leq 0.05$). Contrary Omeprazole and all other herb extracts showed significant elevation ($P \leq 0.05$) in gastric juice volume compared to control positive group suggesting increasing in gastric secretion. Chamomile 400 mg, Turmeric 200 mg and Ginger 200 mg showed the greatest gastric juice volume respectively. These data are in correspondence with that of (Shea-Donohue *et al.*, 1990, Wang *et al.*, 2011).

Effect of Aspirin, Omeprazole and herb extracts on gastric juice acidity

Although results illustrated in table (1) showed reduction in total acidity in control positive group compared to negative control. Moreover, Omeprazole and all herb extracts recorded slight elevation than those of control positive. Statistically these

differences were not significant. These findings agreed with several studies (Khayyal *et al.*, 2006, Kim *et al.*, 2006, Wang *et al.*, 2011).

Since gastric juice acidity has not been significantly changed by any treatments; it was therefore suggested that the changes in the volume of gastric juice and acid production induced by Aspirin are not the major factor in ulcer formation or the protective activity of herb extracts seen in these experimental ulcer model rats.

Effect of Aspirin, Omeprazole and herb extracts on gastric juice pH

As represented in table (1), the pH values of gastric juice varied significantly between groups ($P \leq 0.05$). The pH value of control positive was significantly lower than that of control negative ($P \leq 0.05$). These findings are in agreement with (Wang *et al.*, 2007, Wang *et al.*, 2011) demonstrated that the pH, mucus, and PGE2 were significantly decreased in Aspirin treated rats compared with those of untreated suggesting that Aspirin reduce mucous secretion and inhibit prostaglandins.

On the other hand Omeprazole treated group showed significant increase in the pH value compared to positive group ($P \leq 0.05$). Similar data were reported by (Hsu *et al.*, 2004) who demonstrated that the administration of Omeprazole was more effective than anti H₂-blocker at maintaining a persistent elevation of gastric pH. Omeprazole may inhibit of gastric acid secretion through very selective inhibition of the proton-pumping enzyme H⁺,K⁺-ATPase (Larsson *et al.*, 1988).

Herb extracts also showed significant elevation on the pH values compared with those of control positive group ($P \leq 0.05$). Whereby, between herbs treatment, nonsignificance difference has been noticed. Chamomile, ginger and licorice respectively gave the greatest effect where, turmeric and mixture showed the lowest effects. These data are in correspondence with many studies (Khayyal *et al.*, 2006, Mukherjee *et al.*, 2010).

Table (1): Effect of Aspirin, Omeprazole and herb extracts on ulcer parameters

Groups	Ulcer Index	Curative Ratio	juice volume	Acidity (mEq/mL)	pH
1 Control -	0.00±0.00	100±0.00*	0.46±0.07	52±1.19	4.65±0.16
2 Control +	5.50±0.25*	0.00±0.68*	0.42±0.12	48±1.12	3.51±0.19*
3 Omeprazole	0.71±0.23*	87.09±1.61*	0.93±0.05*	47±1.34	5.83±0.14*
4 Chamomile 200 mg	0.67±0.13*	87.82±1.05*	0.67±0.06*	50±1.54	4.95±0.08*
5 Chamomile 400 mg	1.13±0.20*	79.45±2.01*	1.03±0.09*	52±1.38	4.76±0.13*
6 Turmeric 200 mg	1.67±0.33*	69.64±1.45*	0.97±0.09*	53±2.05	4.16±0.11*
7 Turmeric 400 mg	0.82±0.04*	85.09±1.36*	0.80±0.08*	51±2.18	4.40±0.16*
8 Ginger 200 mg	1.40±0.90*	74.55±1.96*	0.87±0.06*	50±1.45	4.79±0.18*
9 Ginger 400 mg	1.55±0.08*	71.82±1.25*	0.63±0.15*	50±2.17	4.86±0.12*
10 Licorice 200 mg	0.84±0.10*	84.73±0.89*	0.63±0.11*	52±2.35	4.60±0.15*
11 Licorice 400 mg	1.16±0.68*	78.91±1.75*	0.770.12*	53±2.20	4.73±0.17*
12 Mixure 200 mg	1.60±0.25*	70.91±1.09*	0.53±0.11*	50±1.17	4.27±0.14*
13 Mixure 400 mg	1.65±0.20*	70.00±2.09*	0.70±0.10*	49±1.85	4.12±0.12*

Data represented as Mean ± SD. * (P ≤ 0.05) between control positive and other treatments.

Modulatory effect of herb extract on the pH may attribute to increase gastric sulfhydryl groups bioavailability or act effectively as an H₂ blocker (Dehpour *et al.*, 1994, Fukai *et al.*, 2002, Asl and Hosseinzadeh, 2008).

Effect of Aspirin, Omeprazole and herb extracts on ulcer parameters

Different ulcer parameters were recorded in table (1) and figure (1). As shown, a single dose of Aspirin (400mg/kg) for two consequence days was able to induce sever ulcer on stomach of 5.50±0.25 mm length. Several mechanisms were documented to explain how Aspirin helps in the progression of ulceration. Of these mechanisms; overcoming the expression of enzyme COX which inhibits the conversion of AA to PGs. The later impairs the mucosal barrier and results in corrosive action with pepsin results in the progression of peptic ulcers. Further, PGs cause the activation of neutrophils and the local release of ROS and thus induce the gastric injury. Aspirin also causes increased production of NO due to the overexpression of iNOS; it may also induce marked reduction in mucosal blood flow; mucus-bicarbonate secretions; increasing

acid secretion and back diffusion of H ions; reduced epithelial cell renewal and increased leukocyte adherence that are responsible for pathogenesis of ulceration (Voutilainen *et al.*, 2001, Shiotani *et al.*, 2009, Hunt and Yuan, 2011, Chan *et al.*, 2013).

Data also demonstrated that all herb extracts as well as Omeprazole significantly alleviated and cured Aspirin induced ulcer (P ≤ 0.01). The percentage of recovery ranged from 69.64 to 87.82. Chamomile 200 mg, Omeprazole 20 mg, turmeric 400mg and licorice 200 mg expressed the highest curative effects respectively. In general, herb extracts were ordered descendingly according their curative effects as follow Chamomile 200 mg> Turmeric 400 mg> Licorice 200 mg> Chamomile 400 mg> Licorice 400 mg> Ginger 200 mg> Ginger 400 mg> Mixure 200 mg> Mixture 400 mg> Turmeric 200 mg.

Statistically, results of present study showed significant positive correlation between ulcer index and the pH values of gastric juice (P ≤ 0.01). Therefore it was suggested that the attenuation of gastric juice pH is one of the suspected mechanisms in gastric ulcer healing.

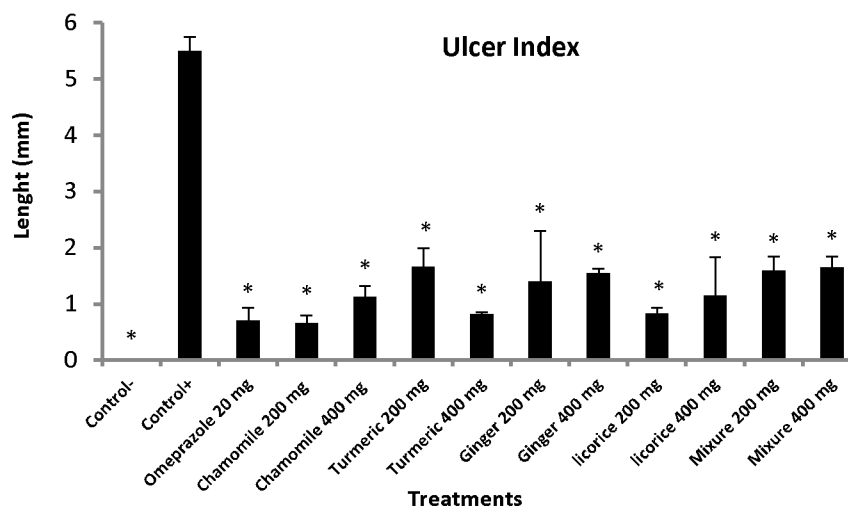


Figure (1): The effect of Aspirin, Omeprazole and plant herb extracts on (a): Ulcer index. Data represented as Mean \pm SD. * ($P \leq 0.05$) between control positive and other treatments.

It was suggested that plant herb extracts exert their antiulcer effects through various mechanisms including a) reducing lipid peroxidation, b) increase GSH levels, c) augmentation antioxidant activity d) increase of gastric sulfhydryl groups bioavailability, e) raising the local concentration of prostaglandins that promote mucous secretion and cell proliferation in the stomach, leading to healing of ulcers, f) suppression of iNOS and attenuation of the recruitment of neutrophils (Fukai *et al.*, 2002, Aly *et al.*, 2005, Asl and Hosseinzadeh, 2008, Khushtar *et al.*, 2009, Cemek *et al.*, 2010, Rocha *et al.*, 2010, Wang *et al.*, 2011, Gupta *et al.*, 2013).

These data are in agreement with many previous studies. For example, hydroalcoholic extract of chamomilla showed clearly protective effect against ethanolinduced gastric mucosal lesions. It exhibited the antiulcerative effect, through reducing lipid peroxidation, increase GSH levels, augmentation antioxidant activity and increase of gastric sulfhydryl groups bioavailability (Shikov *et al.*, 2008, Al-Hashem, 2010, Cemek *et al.*, 2010, Rocha *et al.*, 2010)

Furthermore, ginger provided gastric protection against Aspirin and pylorus ligation induced ulcer in rats. It reduced iNOS activity and inhibited the production of gastric ulcers, even in the presence of Aspirin (Mahady *et al.*, 2003, Sharma *et al.*, 2008, Khushtar *et al.*, 2009, Wang *et al.*, 2011, Singh and Kaur, 2012).

It was observed that licorice components and their derivatives protect against gastric-ulcer induced by Aspirin in rats by raising the local concentration of PGs. In addition its aqueous extract could heal ulcers as effectively as an h2 blocker (Dehpour *et al.*, 1994, Fukai *et al.*, 2002, Aly *et al.*, 2005, Asl and Hosseinzadeh, 2008).

Moreover curcumin significantly attenuate gastric ulcer induced by different pathogens including Aspirin. The antiulcerative effects of curcumin are associated with a reduction in (i) upregulation of proinflammatory Th1 cytokine response leading to the suppression of iNOS and attenuation of the recruitment of neutrophils, (ii) lipid peroxidation and (iii) ultimately tissue injury (Prucksunand *et al.*, 2001, De *et al.*, 2009, Gupta *et al.*, 2013).

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Histological evaluation

Histopathological examination for the stomach sections of all groups showed; an intact cellular architecture and normal gastric layers without any histopathological changes in negative control group (Figure 2). In contrast ulcers combined with distorted gastric glands, a damaged mucosal epithelium, inflammatory exudates and cellular debris, local mucosal necrosis, submucosal edema and mucosal leucocytic inflammatory cell infiltration were found in the stomachs of the Aspirin-treated rats. Previous histopathological investigations confirmed results of present study concerning the impact of Aspirin on ulcer parameters including ulcer index, acidity and gastric juice volume (Shiotani *et al.*, 2009, Choi *et al.*, 2010, Hunt and Yuan, 2011, Chan *et al.*, 2013).

Significant protection against these histopathological changes has been recovered by the co-administration of Omeprazole, resulted in the maintenance of glandular organization and the structure of the muscularis mucosa (Figure 2). Omeprazole may inhibit gastric ulcer through a dual mechanism of action including inhibition of H(+)K(+) ATPase and gastric mucosa carbonic anhydrase (Larsson *et al.*, 1988, Puscas *et al.*, 1999).

With exception of chamomile (400 mg) which showed submucosal edema, and turmeric (200 mg) that showed submucosal edema and few mucosal leucocytic cell infiltrations (Figure 3), all other herb extracts showed great recovery of gastric ulcer to normal gastric structure without any pathological changes.

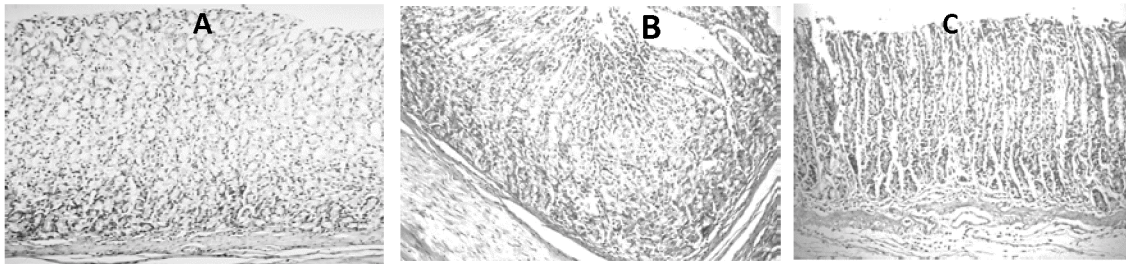


Figure (2): Photomicrograph of (A); stomach section of normal rats (-ve control) showing normal histological gastric layers. (B); stomach section of Aspirin ulcerative rats (+ve control) showing histological changes including ulcer, local mucosal necrosis, submucosal edema and mucosal leucocytic inflammatory cell infiltration. (C); stomach section of Omeprazole treated rats (group3) showing normal histological gastric layers (H and E x200).

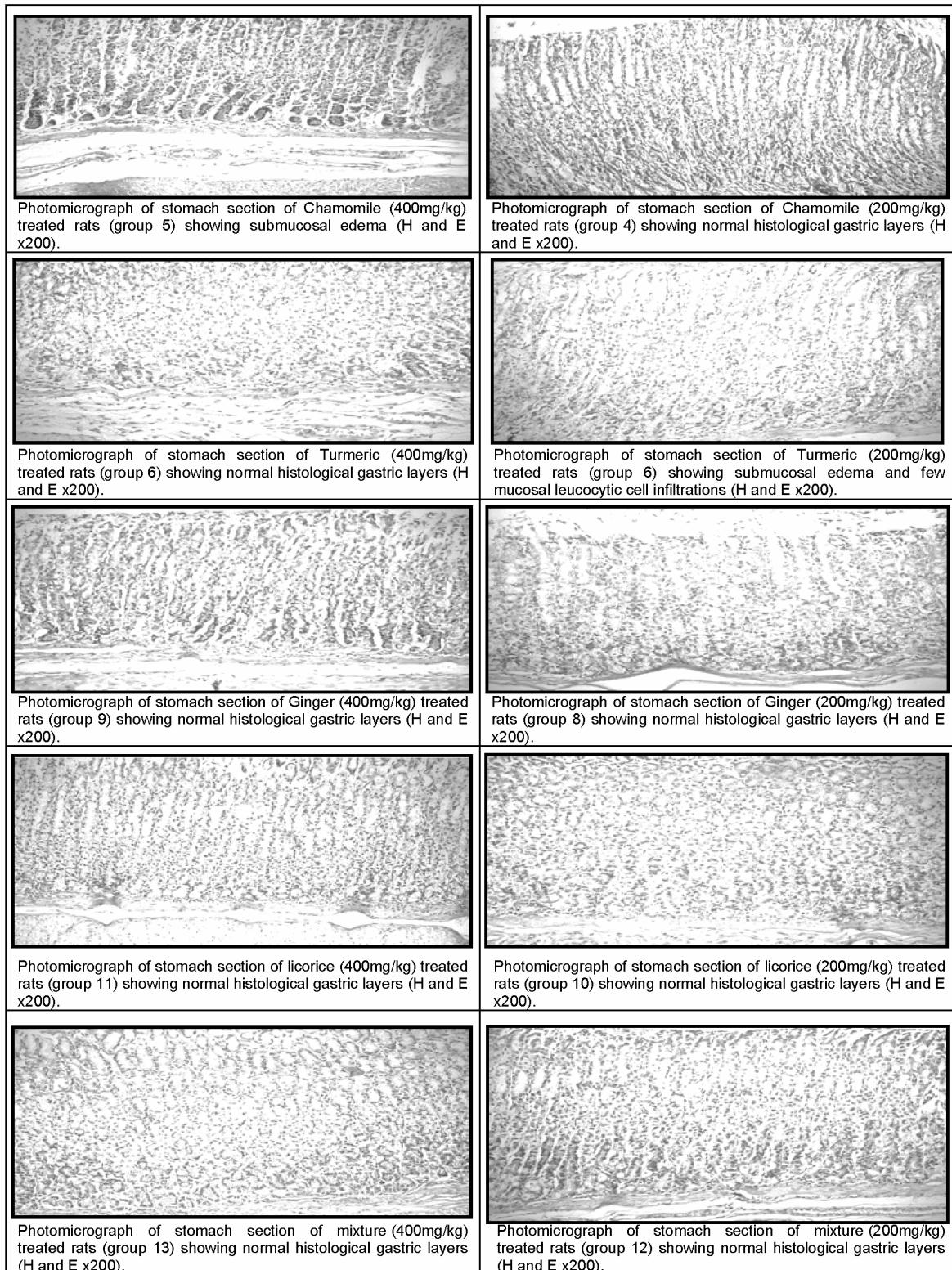


Figure (3): Histopathological effects of different extracts on rats stomach .

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التأثير العلاجي للمستخلصات المائية لبعض الاعشاب ضد قرحة المعدة المحدثه بواسطة الاسبرين في فئران التجارب

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المخلص العربي

لا تزال قرحة المعدة مشكلة طبية معقدة تواجه العديد من المرضى في مراحل عمرهم المختلفة وفي مناطق واسعة من العالم. ويعد الاستخدام طويل المدى من الأدوية المسكنة المضادة للالتهابات مثل الأسبرين اكثر الاسباب خطورة بعد بكتريا هليكوباكتر بيلورى فى احداث قرحة المعدة. وبالرغم من توافر عدد هائل من العقاقير الطبية فى علاج القرحة، الا ان استخدامها لا يخلو من العديد من الآثار الجانبية. ولذا كان الهدف من هذه الدراسة هو تقييم التأثير العلاجي للمستخلصات المائية لبعض الاعشاب ضد قرحة المعدة المحدثه بواسطة الاسبرين فى فئران التجارب. حيث استخدم المستخلص المائى لاربعه اعشاب هى البابونج ، الكركم، الزنجبيل و العرقسوس منفردة وفى صورة خليط عند تركيزات ٢٠٠، ٤٠٠ ملجم / كجم من وزن الفئران وذلك ضد الاسبرين (٤٠٠ ملجم/ كجم) المستخدم لاحداث القرحة. وقد استخدم عقار الوميرازول بتركيز ٢٠ ملجم/ كجم كعلاج قياسى للمقارنة. وقدر حجم العصير المعدى وحموضته ودلائل القرحة الاخرى وكذا التغيرات النسيجية لجدار المعدة لتحديد مدى التأثير العلاجي لهذه الاعشاب. وقد اظهرت النتائج ان اعطاء جرعة واحدة من الاسبرين (٤٠٠ ملجم / كجم) كانت قادرة على احداث قرحة حادة بجدار المعدة وصل طولها الى 0.5 ± 0.25 مم. كما اظهرت جميع الاعشاب قدرة عالية على تخفيف وعلاج هذه القرحة بنسب تراوحت بين ٦٩.٦٤ حتى ٨٧.٨٢. وكان البابونج ٢٠٠ ملجم، أوميرازول ٢٠ ملجم، الكركم ٤٠٠ ملجم والعرقسوس ٢٠٠ ملجم أعلى الآثار العلاجية على التوالي. وعموما رتبت جميع الاعشاب تنازليا فى تأثيرها العلاجي كما يلى: البابونج ٢٠٠ ملجم < الكركم ٤٠٠ ملجم < العرقسوس ٢٠٠ ملجم < البابونج ٤٠٠ ملجم < العرقسوس ٤٠٠ ملجم < الزنجبيل ٢٠٠ ملجم < الزنجبيل ٤٠٠ ملجم < الخليط ٢٠٠ ملجم < الخليط ٤٠٠ ملجم < الكركم ٢٠٠ ملجم. وقد اكدت دلائل القرحة جميعها بالاضافة الى التغيرات النسيجية مدى فاعلية هذه الاعشاب فى علاج قرحة المعدة المحدثه بتأثير الاسبرين.

