World Journal of Dairy & Food Sciences 14 (2): 161-168, 2019

ISSN 1817-308X

© IDOSI Publications, 2019

DOI: 10.5829/idosi.wjdfs.2019.161.168

Gastroprotective Effect of Aqueous Extract of Chamomile and Arabic Gum on Indomethacin- Induced Gastric Ulcer in Male Rats

Suzan S. Ibraheim

Nutrition and Food Science Department, Faculty of Home Economics, Al-Azhar University, Tanta, Egypt

Abstract: This study was carried out to investigate the gastroprotective effect of aqueous extract of chamomile (CHAE) and Arabic gum (AGAE) on indomethacin (IND) induced gastric ulcer in experimental rats. Thirty albino rats weighing 185 ± 195 g were used in this study and divided into 6 equal groups, one was kept as a control –ve group, while the other 5 groups were treated with one oral dose daily of 25mg / kg b.w indomethacin throughout experimental period. One group was kept as (+ve) control group, while others were given administration of CHAE and AGAE (500 and 1000 mg/kg)] orally for six weeks. Biological evaluation including feed intake (FI), body weight gain % (BWG %) and feed efficiency ratio (FER) was carried out. Gastric glutathione (GSH), Malondialdehyde (MDA) and Nitric oxide (No) were estimated. PH of gastric content, Ulcer Index (UI) and the preventive index (PI) were measured. Also, histopathological changes for stomach tissues were examined. The obtained results concluded that using CHAE and AGAE improved all pervious parameters. Also, histopathological examination confirmed biochemical results. The best results were found by using high doses (1000mg / kg) of CHAE and AGAE. According to the results, CHAE and AGAE could be used as protective agent against non-steroidal anti-inflammatory drugs (NSAIDs) - induced gastric ulcer.

Key words: Gastric ulcer · chamomile · Arabic gum · Biological evaluation · Histopathological examination

INTRODUCTION

Gastric ulcer is one of the most common diseases in the digestive tract where the lesions occur in any part of it. This disease is caused by imbalance between aggressive factor such as acid and pepsin on one hand and digestive factor especially prostaglandins and blood flow on the other hand [1]. Incidence of gastric ulcer is increased by *Helicobacter pylori* infection and administration of non-steroidal anti-inflammatory drugs (NSAIDs) in particular as well as some factors such as stress, smoking and alcohol consumption [2]. Indomethacin is one of the most drugs used to treat pain and inflammation by elder patients but it has dangerous side effects on gastrointestinal tract induced ulceration and may up to perforation [3].

Natural products are an important source for the prevention and treatment of gastric ulcer [1] Chamomile (*Matricaria recutita L.*) is one of the most widely used medicinal plants in the world. Chamomile contains several

flavonoids (the most abundant phenolic compounds in herbs) and the core structure consists of either flavone (apigenin and luteolin) or flavonol-derivatives (quercetin and patuletin). Previous studies demonstrated that aqueous chamomile extract is used as herbal medicine as to possess antiinflammatory and antioxidant properties that have useful effect for ulcers and gastrointestinal disorders [4].

Arabic Gum (*Acacia Senegal*) is used throughout the world for various purposes including food additive and pharmaceutical excipient [5]. Arabic Gum is reported to possess antioxidant, renal protective, antidiabetic effects and anti-ulcerogenic protective activity. Arabic gum is a branched chain, complex polysaccharide, either neutral or slightly acidic. It contains phenolic compounds and flavonoids [6].

Therefore, this study aimed to investigate the gastroprotective effect of aqueous extract of chamomile and Arabic gum on indomethacin- induced gastric ulcer in rats.

MEATERIALS AND METHODS

Materials: Chamomile and Arabic Gum were purchased from the local company for medicinal plants and herbs, Cairo Governorate, Egypt. Indomethacin (Liometacen) was purchased from (The NILE Co. for Pharm. and Chemical Ind., Cairo, Egypt). Casein (85%), Vitamins mixture and salt mixture and all chemicals used for blood biological measurements were purchased from Modern Lab Company, Dokki, Giza, Egypt.

Preparation of Aqueous Extracts:

- The aqueous extract of chamomile was prepared using 10g dried material/100 ml distilled water and boiling for 5 min at 100°C. Then it was filtrated, concentrated at 50°C under reduced pressure using a Rota vapor. The extract was kept at -15°C until it was used in the experiment according to Kassi *et al.* [7].
- Fine powder of Arabic gum was dissolved in distilled water to prepare 10 % extract solution. Afterwards, the extract was leaved for 3 days, filtered by Whatman No. 1 filter paper according to Ayaz *et al.* [8].

Animals: Thirty male albino rats of Sprague Dawley strain (185±10 g) were obtained from the animal colony, Helwan farm, Vaccine and Immunity Organization, Ministry of Health, Cairo Governorate, Egypt.

Experimental Design: A total of 30 mature male rats weighing between 185-195 g were housed in clean metabolic cages. The rats were adapted for one week before the beginning of the experiment. The rats were fed on basal diet according to Jerome *et al.*[9] and divided into 6 groups each group contained 5 rats as follows:

Group 1: Fed on basal diet (B.D) as a control (- ve) group

Group 2: Fed on B.D. and treated with one oral dose daily of 25mg / kg b.w Indomethacin and used as control (+ ve) group.

Group 3: Fed on B.D. and treated with one oral dose daily of 500 mg/kg b.w chamomile aqueous extract + 25 mg /kg Indomethacin.

Group 4: Fed on B.D. and treated with one oral dose daily of 1000 mg/kg b.w chamomile aqueous extract + 25 mg /kg Indomethacin.

Group 5: Fed on B.D. and treated with one oral dose daily of 500 mg/kg b.w Arabic gum aqueous extract + 25 mg /kg Indomethacin.

Group 6: Fed on B.D. and treated with one oral dose daily of 1000 mg/kg b.w Arabic gum aqueous extract + 25 mg/kg Indomethacin.

Induction of Gastric Mucosal Damage: A single dosage of 25 mg/kg indomethacin dissolved in sterilized distilled water was orally administered in accordance with the Kwon and Kim [10] method to induce gastric mucosal damage.

Biological Evaluation: Body weight, food consumption were measured twice a week and total food intake of the experimental period (6 weeks) was calculated according to Chapman *et al.* [11]. The feed efficiency ratio was calculated according to Hosoya [12].

Determination of Gastric Glutathione (GSH), Malondialdehyde (MDA) and Nitric Oxide (NO): MDA, NO and glutathione (GSH) levels were measured in stomach tissues according to the method of Ohkawa *et al.* [13], Montgomery and Dymock [14] and Beutler *et al.*[15] respectively.

Measurement of pH of Gastric Content, UI and PI %: One ml of the gastric juice was collected and the pH was directly measured by using Digital pH meter. The gastric mucosal lesions were expressed in terms of ulcer index (UI) according to Peskar et al. [16] which depends on the calculation of the severity of each lesion by using 0-3 scoring system. The severity factor was defined according to the length of the lesions, where severity factor 0 = no lesions; severity factor 1 = lesionsless than 1 mm length, severity factor 2 = lesions 2-4 mmin length and severity factor 3= lesions greater than 4 mm in length. The lesion score for each rat was calculated as the number of lesions in the rat multiplied by their respective severity factor. The UI for each group was taken as the mean lesion score of all the rats in that group. The preventive index (PI) of a given Chamomile and Arabic Gum was calculated by the equation of Hano et al.

 $PI = [(UI \text{ of IND group} - UI \text{ of treated group}) \div UI \text{ of IND group}] \times 100$

Histopathology Examination: For histopathology assessment, stomach tissues were fixed in 10% buffered

formalin solution and were embedded in paraffin. Sections were deparaffinized and stained with hematoxylin and eosin (H&E).

Statistical Analysis: Statistical analysis was carried out using one way analysis of variance (ANOVA) test followed by Duncan test through the programme of statistical packages for the social science (SPSS) version 16. Results were expressed as mean \pm SD. The differences among means at p < 0.05 are considered significant [18].

RESULTS

Effect on Feed Intake, Body Weight Gain and Feed Efficiency Ratio: Administration of indomethacin showed a significant decrease (p<0.05) in feed intake (FI), body weight gain (BWG) and feed efficiency ratio (FER) when compared with normal (- control) group. However, these parameters were improved in all treated groups with IND + CHAE and IND +AGAE. The highest improvement was observed in the treated group with IND + CHAE at dose (1000mg/kg) and closed to normal group (Table 1).

Effect on GSH, MDA and NO in Gastric Tissue in Different Experimental Groups: There was a significant (p<0.05) decrease in gastric tissue GSH and NO in IND (+ control) group. While, MDA levels were increased in IND (+ control) when compared with normal (- control) group. However, the reverse was recorded for all treated rats with IND + CHAE and IND + AGAE, in particular for IND + AGAE (1000 mg/kg) group, followed by that of IND + CHAE (1000 mg/kg) group which recorded the best results (Table 2).

Effect on Gastric pH, Ulcer Index and Preventive Index in Different Experimental Groups: Administration of indomethacin showed a significant decrease in gastric pH (2.65±0.20) when compared with normal control group (5.08±0.13). Treatment with IND + CHAE and IND + AGAE significantly raised the gastric pH. The best result observed was in group treated with IND + AGAE at dose 1000mg/kg. Indomethacin administration in (+ control) group resulted in a significant (p<0.05) increase in ulcer index (20.4±3.29) compared with Normal (- control) group (0.00±0.00), while all treated groups with IND + CHAE and

Table 1: Effects of aqueous extracts of Chamomile and Arabic gum on feed intake, body weight gain and feed efficiency ratio in different experimental groups (mean±SD, n=5)

Groups	FI (g)	BWG (%)	FER
Normal (- control)	24.92±1.15 a	24.25± 2.07°	0.045 ±0.005 ^a
IND (+ control)	11.17±0.97 ^f	4.33 ± 0.38^{d}	0.023 ± 0.004^{d}
IND +CHAE (500mg/kg)	19.90±1.09°	17.84±3.63 ^b	0.040±0.001 bc
IND + CHAE (1000mg/kg)	$22.47 \pm 0.64^{\text{ b}}$	23.29 ±2.66 a	$0.042\pm\ 0.002^{ab}$
IND + AG (500mg/kg)	15.36±1.67 ^e	14.10±1.00°	$0.036 \pm 0.003^{\circ}$
IND + AG (1000mg/kg)	18.35±1.12 ^d	16.91±3.42b°	0.038 ±0.001 bc

Means in the same column with completely different letters are significantly different at p<0.05.

Table 2: Effects of aqueous extracts of Chamomile and Arabic gum on GSH, MDA and NO in gastric tissue in different experimental groups (mean±SD, n=5)

MDA (nmol/g)
141D11 (IIIIO1/5)
2.08±0.14e
5.90±0.25a
3.16 ± 0.33^{b}
2.51 ± 0.04^{d}
2.89±0.05°
2.42 ± 0.14^{d}

Means in the same column with completely different letters are significantly different at p<0.05.

Table 3: Effects of aqueous extracts of Chamomile and Arabic gum on Gastric pH , Ulcer index and Preventive Index in different experimental groups (mean±SD, n=5)

Groups	Gastric pH	Ulcer index	Preventive Index
Normal (- control)	5.08±0.13 ^a	0.00 ± 0.00	
IND (+ control)	2.65 ± 0.20^{e}	20.4 ± 3.29^{a}	
IND + Chamomile (500mg/kg)	4.49 ± 0.03^{d}	9.20±2.68 ^b	54.90%
IND + Chamomile (1000mg/kg)	$4.66\pm0.05^{\circ}$	3.40±0.55 ^{cd}	83.33%
IND + Arabic gum (500mg/kg)	4.65±0.07°	4.80±1.10°	76.47%
IND + Arabic gum (1000mg/kg)	4.93±0.02 ^b	1.80 ± 0.45^{d}	91.17%

Means in the same column with completely different letters are significantly different at p<0.05

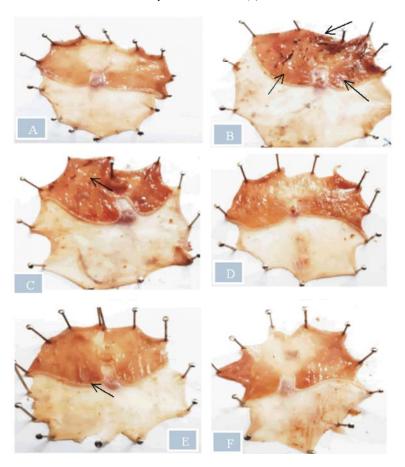


Fig. 1: Showing the appearance of the gastric mucosa in experimental groups. (a) The gastric mucosa in control group (Normal - control)) revealed no lesions in gastric mucosa. (b) The gastric mucosa in Indomethacin group (positive + control) revealed multiple hemorrhagic lesions in gastric mucosa (arrows). (c) The gastric mucosa in Indomethacin +Chamomile (500mg/kg) group revealed minimal lesions in gastric mucosa (arrows). (d) The gastric mucosa in Indomethacin +Chamomile (1000mg/kg) revealed no lesions in gastric mucosa. (E) The gastric mucosa in Indomethacin +Arabic gum (500mg/kg) revealed minimal lesions in gastric mucosa. (F) The gastric mucosa in Indomethacin +Arabic gum (1000mg/kg) revealed no lesions in gastric mucosa

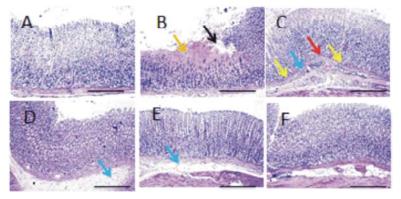


Fig. 2: Microscopic images of hematoxylin and eosin (H & E) stained glandular gastric sections showing (A) Normal (- control) group. (B) indomethacin (+ control) group. (C) Indomethacin +Chamomile (500mg/kg) group. (D) Indomethacin +Chamomile (1000mg/kg) group (E) Indomethacin +Arabic gum (500mg/kg) group. (F) Indomethacin +Arabic gum (1000mg/kg) group. X: 100 bar 100

IND +AGAE showed significant decreases compared to IND (+ control) group. The best result recorded for treated groups was with IND + Arabic gum (1000mg/kg) significantly decreased (p<0.05) ulcer index when compared with IND (+ control) group from 20.4±3.29 to 1.80± 0.45, with preventive index 91.17 % followed by treated group with IND + Chamomile (1000mg/kg) group with preventive index 83.33 % (Table 3 and Fig. 1).

Histological Results: The results obtained from histological gastric sections stained with H&E are illustrated in Fig. 100 bar 100. Gastric sections, show no lesions in Normal (-control) group (A). However, Gastric sections from indomethacin (+control) group showed severe mucosal necrosis and ulceration (B), while moderate multifocal congestion and inflammation observed in Indomethacin +Chamomile (500 mg/kg) group (C) when compared to mild submucosal edema in Indomethacin + Chamomile (1000 mg/kg) group (D). While, Mild submucosal edema was observed in Indomethacin +Arabic gum (500 mg/kg) group (E) when compared to normal mucosa (no lesion) in Arabic gum (1000mg/kg) group (F).

DISCUSSION

Indomethacin has been widely used as anti-inflammatory agent which is a well-known non-steroidal anti-inflammatory drug (NSAID) [19]. Inhibitory action of indomethacin on prostaglandin synthesis coupled with free radicals formation has been opined as critical biochemical events in the pathogenesis of gastric ulceration [20]. In the present study, we reported that indomethacin decreased BWG%, FI and FER because it interfered with metabolic pattern of experimental rats and caused poor gastro intestinal functions with less absorption of nutrients according to Bagoji *et al.* [21]. These results agree with Fjære *et al.* [22] who reported that indomethacin reduces Feed efficiency and obesity in mice treated with high fat/high sucrose and indomethacin due to reduced energy intake, feed intake was monitored.

On the other hand, chamomile aqueous extract at 1000 mg/kg improved BWG%, FI and FER and achieved the best result that closed to normal. The positive improvement in theses parameters might be related to the active compounds which influence the gastrointestinal ecosystem, increasing production of digestive enzymes, improving utilization of digestive products according to Al-Mashhadani *et al.* [23]. In this respect, Al baroudi [24] reported that Chamomile aqueous extract increased the

body weight in 2, 4-Dichlorophenoxyacetic acid intoxicated rats treated with Chamomile when compared to positive control rats. That due to the high content of flavonoids (63.3%) and total phenolic compounds (23.2%) in Chamomile, so enhancing food consumption by rats given Chamomile. Also, in the present study the increased in body weight gain by Arabic gum aqueous less than chamomile aqueous extract might be due to the high dietary fiber content of GA which has an effect on fat metabolism or lowering caloric density of food according to Ahmed *et al.* [25]. However, Fedail *et al.* [26] that reported no significant differences were observed in final body weight in diabetic rat or diabetic rat treated with GA groups when compared to the control group.

In the current study indomethacin produced free radical caused stomach damage which was confirmed by determination of oxidative stress markers in gastric tissue according to Saad et al. [3]. This was evident by the significant decrease in GSH & NO and increase in MDA level in IND (+ control) group. Our findings are in line with El-Komy and Mouaf [27] who showed that indomethacin-treated rats, reduced glutathione (GSH) content were significantly diminished in gastric mucosa while the lipid peroxidation products malondialdehyde (MDA) were significantly increased. Also, Katary and Salahuddin [28] indicated that nitric oxide production was decreased in positive (+ control) group treated with indomethacin that due to decreased cytoprotective endothelial (eNOS) gene expression as well as gastric level of NO leading to decreasing mucus synthesis plus the depleted gastric mucus levels. Meanwhile, Arabic gum aqueous extract increased GSH in gastric tissue. It plays a role in reducing oxidative stress and lipid peroxidation and restore No production. The potential mechanism of GA has been explained by Helal et al. [29] who clarify that GA refers to a group of closely related polysaccharides including arabinose and galactose and arabinogalactan. Plant polysaccharides have been reported to possess antiulcer activities. Polysaccharides have ability to bind to the mucosal surface and to function as a protective coating, by diminishing the secretory activities of acid and pepsin and protecting the mucosa by increasing mucus synthesis or scavenging radicals.

Similarity, chamomile aqueous extract, in the present study, lowered MDA level and raised GSH and No in gastric tissue that might due to the presence of high concentrations of total polyphenols, total flavonoids and condensed tannins. These results agree with Jabri *et al.* [30] who studied protective effect of chamomile (*Matricaria recutita* L.) decoction extract

against alcohol-induced injury in rat gastric mucosa. The phytomolecules such as gallic acid, protocatechuic acid, chlorogenic acid, caffeic acid, caffeoylquinic acid, salicylic acid, quercetin, quinic acid derivative, hydroxybenzoic acid-O-hexoside, 5, 7, 4-Trihydroxy 6, 3-dimethoxyflavone have been shown to be responsible for the antioxidant and bio-functional properties of many plant extracts. Also, Al-Hashem [31] demonstrated that daily treatment of rats with the administered aqueous extract of *Chamomile* led to an increase in GSH levels. It has gastroprotective effects against ethanol-induced gastric ulcers in male rats.

In our findings we found that Indomethacin administration in (+ control) group resulted in a significant (p<0.05) decrease in gastric pH with increase in ulcer index compared with Normal (- control) group. These findings supported by Ibrahim et al. [19] who showed that administration of IND led to hemorrhagic lesions and increase in ulcer index due to IND comprises polar lipids that have a high affinity for the lipophilic areas of cell membranes, where their polar groups trigger membrane disruption, with loss of structural phospholipids and membrane proteins. In addition, this leads to reduced hydrophobicity of the mucosal coat adherent to the mucosal cell surface. Such loss of hydrophobicity facilitates the entry of water soluble agents of injury (e.g. acid, pepsin, bile salts, etc.) and also alter membrane fluidity that play a key role in the development of the gastric mucosal lesions induced by IND. Also, Sabiu et al. [20] concluded that oral administration of indomethacin caused a significant (p < 0.05) increase in the degree of ulceration (ulcer index) in the rats. Our results are in agreement with El-Ashmawy et al. [32] who reported that indomethacin given orally to rats produced an increase of gastric acidity and ulcer index, compared with normal group. The results showed that indomethacin has higher ulcerogenic ability than other NSAIDs, so it is used to induce gastric ulcer in experimental rats. Meanwhile, Arabic gum and chamomile increase gastric pH and decrease in ulcer index. Previous studies have proved that Chamomile is one of the richest natural sources of apigenin which is a naturally occurring compound, present in many plants and possesses chemopreventive, antioxidant, anti-inflammatory and ulcer healing activity in experimental rats. Additionally, á-bisabolol, luteolin and quercetin are also known to possess antiulcer activity. The influence of flavonoids on gastric secretion has been studied using pylorus ligated rats. Intraduodenal administration of flavonoid increased the gastric pH according to Cemek et al. [33]. In harmony with these

findings, Gohar and Zaki [34] observed that the aqueous extract of chamomile decreases the gastric secretions and acidity so, increases the curative ratio of gastric ulcer. Jabri et al. [30] showed that chamomile extract exhibited significant reduction of gastric lesions (ulcer index) with protection percentage up to 90.95%, when compared to positive control group. Also, AL-Yahya and Asad [5] reported that Arabic gum increased the healing of gastric ulcers. It also produced a significant protection in the development of the gastric ulcers. It was concluded that Arabic gum have beneficial effect in preventing and healing of gastric ulcers due to both gastric antisecretory and cytoprotective effects. Khedr [6] observed an increase in pH and preventive index in the groups treated with Arabic gum and produced a higher increase in preventive index due to Arabic gum is a known antioxidant and this would have contributed to its antiulcer action. Arabic gum contain an arabinogalactan, has been reported to possess antiulcer effect in rats.

Moreover. these results are confirmed histopathological examination as gastric sections in indomethacin (+control) group showed severe mucosal necrosis and ulceration. The inflammatory insult produced by indomethacin could be mediated by induction of oxidative stress [32]. These results agree with Ibrahim et al.[19] who showed that IND-administered rats led to necrosis and loss of epithelial cells, submucosal edema, marked infiltration with inflammatory cells and congested blood vessels. Also, Lim et al. [35] reported that severe desquamation of focal epithelium, focal extensive superficial epithelial damage, congestion/ hemorrhages and necrosis of ulcerative lesions and gastric glands were observed following treatment with IND in rats.

Administration of IND + CHAE at dose (1000 mg/kg b.wt.) and IND + Arabic gum at dose (500 mg/kg b.wt.) improved to some extent the histopathological picture but mild submucosal edema. While administration of IND + AG at dose (1000 mg/kg) showed normal mucosa (no lesion). These results are supported by Abid et al. [36] who detected that the lesion of gastric mucosa show less severe effects with protection of the glandular stomach when treated with CHAE. This may be explained by various constituent of chamomile that have protection of lining epithelium against gastric ulcer. Also, AL-Yahya and Asad [5] reported that treated with Arabic gum improved histological examination wherein regeneration of lining epithelium was more prominent. In harmony with our results Helal et al. [29] demonstrated that treated rats with GA showed near normal gastric mucosa with atrophied surface epithelium, some collagen fibers in the lamina propria and between the near normal gastric glands and mild PCNA reaction in the gland cells. The antiulcer effects of polysaccharides lie in their ability to bind to the mucosal surface and to function as a protective coating, by diminishing the secretory activities of acid and pepsin and protecting the mucosa by increasing mucus synthesis or scavenging radicals.

CONCLUSIONS

Overall, the attenuation of gastric affronts of indomethacin by administration of aqueous extracts of chamomile and Arabic gum at two doses (500, 1000 mg/kg) is indicative of their excellent gastroprotective and antioxidative potentials in rats which confirmed by biochemical results and histological findings. Therefore, it could be used as protective agents against gastric injury

REFERENCES

- Karampour, N.S., A. Arzi, A. Rezaie, M. Pashmforoosh and F. Kordi, 2019. Gastroprotective Effect of Zingerone on Ethanol-Induced Gastric Ulcers in Rats. Medicina (Kaunas), 55(3): 64.
- Kim, Y.S., H.J. Park, H. Kim, J. Song and D. Lee, 2019. Gastroprotective Effects of Paeonia Extract Mixture HT074 against Experimental Gastric Ulcers in Rats. Hindawi. Evidence-Based Complementary and Alternative Medicine, 2019, Article ID 3546258, 13 pages. https://doi.org/10.1155/2019/3546258
- 3. Saad, A.A.E., M.G. Tadros, D.A. Elsherbiny and T.E. Menze, 2017. Therapeutic effects of pinocembrin on indomethacin-induced gastric ulcer model in rats. Az. J. Pharm. Sci., 56: 1-9.
- Mannaa, F.A., N.A. Ibrahim, S.S. Ibrahim, K.H.G. Abdel-Wahhab, N.S. Hassan and S.G. Mohammed, 2015. Preventive role of chamomile flowers and fennel seeds extracts against liver injury and oxidative stress induced by an immunosuppressant drug in rats. Hepatoma Res., 1: 125-35.
- AL-Yahya, A.A. and M. Asad, 2016. Antiulcer activity of gum Arabic and its interaction with antiulcer effect of ranitidine in rats. Biomedical Research, 27(4): 1102-1106.

- Khedr, A.A., 2017. Antiulcer protective activity of gum Arabic (Acacia Senegal) in adult rats. Bulletin of the National Nutrition Institute of the Arab Republic of Egypt, 49(1): 1-28.
- Kassi, E., Z. Papoutsi and N. Fokialakis, 2004. Greek plant extracts exhibit selective estrogen receptor modulator (SERM)-like properties. J. Agric. Food Chem., 52: 6956-6961.
- Ayaz, N.O., K.H.S. Ramadan, H.E. Farid and H.S. Alnahdi, 2017. Protective role and antioxidant activity of Arabic gum against trichloroacetateinduced toxicity in liver of male rats. Indian J. Anim. Res., 51(2): 303-309.
- Jerome, B., G. Elyett, R. Edmond, M. Andrzej and R.Yves, 2002. Substituting honey for refined CHO protects rats from hypertriglyceridemic and prooxidative effects of fructose. J. Nutr., 132(11): 3379-82.
- Kwon, H.W. and D.J. Kim, 2015. Protective Effects of BK-1202 on the Indomethacin-induced Gastric Ulcer in Rats. J. Korean Med., 36(4): 42-55.
- Chapman, D.G., R. Castilla and A.J. Cambell, 1959.
 Evaluation of protein in food. In Method for the Documentation of protein Efficiency Ratio. Can. J. Biochem. Physiol., 37: 679-686.
- Hosoya, N., 1980. Determination of feed efficiency ratio. Cited in Hosoya, N.; Inami, S. and Goto, S., eds. Nutrition Experiments Using Small Animals. Daiichi Shuppan, Tokyo, Japanese, pp. 71.
- 13. Ohkawa, H., W. Ohishi and K. Yagi, 1979. Assay for lipid peroxides in animal tissues by Thiobarbituric acid reaction. Anal. Biochem., 95: 351-358.
- 14. Montgomery, H.A.C. and J.F. Dymock, 1961. colorimetric determination of nitrite. Analyst, 86: 414.
- 15. Beutler, E., O. Duron and M.B. Kelly, 1963. Improved method for the determination of blood glutathione. J. Lab. Clin. Med., 61: 882.
- Peskar, B.M., K. Ehrlich and B.A. Peskar, 2002. Role of ATP-sensitive potassium channels in prostaglandin-mediated gastroprotection in the rat. J. Pharmacol. Exp. Ther., 301: 969-974.
- 17. Hano, J., J. Bugajski and L. Danek, 1976. Effect of adrenergic blockade on gastric secretion altered by catecholamines in rats. Arch Immunol. Ther. Exp. (Warsz), 24: 507-524.
- Sneddecor, George, W. and G. Cochran, William, 1989. Statistical Methods. Eighth Edition, Iowa State University Press.

- Ibrahim, R.M., M.M. Allam, O.A. El-Gohary, A.E.A. El-Talees and M.S. El-Hamady, 2018. Protective effect of obestatin on indomethacininduced acute gastric ulcer in rats: role of VEGF and TNF-α. Benha Medical Journal, 35(3): 369-377.
- Sabiu, S., T. Garuba, T. Sunmonu, E. Ajani, A. Sulyman, I. Nurain and A.Balogun, 2015. Indomethacin-induced gastric ulceration in rats: Protective roles of Spondias mombin and Ficus exasperate. Toxicol Rep., 2: 261-267.
- Bagoji, I.B., M.A. Doshi, S. Yendigeri, B.G. Patil, B.B. Patil and K.K. Das, 2014. Black tea extract ameliorates indomethacin induced changes in testicular histopathology of albino rats. Journal of Young Pharmacists, 6(3): 53-57.
- 22. Fjære, E., U.L. Aune, K. Røen, A.H. Keenan, T. Ma, K. Borkowski, D.M. Kristensen, G.W. Novotny, T. Mandrup-Poulsen, B.D. Hudson, G. Milligan, Y. Xi, J.W. Newman, F.G. Haj, B. Liaset, K. Kristiansena and L. Madsen, 2014. Indomethacin Treatment Prevents High Fat Diet-induced Obesity and Insulin Resistance but Not Glucose Intolerance in C57BL/6J Mice. The Journal of Biological Chemistry, 289(23): 16032-16045.
- Mashhadani, E.H., H. Al-Mashhadani and J.S. Al-Shamire, 2013. Effect of Supplementing Different Levels of Chamomile Oil on Broiler Performance and Some Physiological Traits. International Journal of Poultry Sci., 12(7): 426-429.
- 24. Al baroudi, D.A., 2013. Hepatoprotective Effect of Chamomile Capitula Extract against 2, 4-Dichlorophenoxyacetic Acid- Induced Hepatotoxicity in Rats. M.Sc. Thesis, Faculty of home Economics, king Abdul Aziz University.
- Ahmed, A.A., J.S. Fedail, H.H. Musa, A.A. Kamboh, A.Z. Sifaldin and T.H. Musa, 2015. Gum Arabic extracts protect against hepatic oxidative stress in alloxan induced diabetes in rats. Pathophysiology, 22: 189-194.
- Fedail, J.S., A.A. Ahmed, H.H. Musa, E. Ismail, A.Z. Sifaldin and T.H. Musa, 2016. Gum Arabic improves semen quality and oxidative stress capacity in alloxan induced diabetes rats. Asian Pacific Journal of Reproduction, 5(5): 434-441.
- El-Komy, M.M. and F.E. Mouaf, 2016. Mitigating effect of Avicenna marina on indomethacin induced gastric ulcer in male albino rats. Egyptian Journal of Basic and Applied Sciences, 3: 155-163.

- Katary, M.A. and A. Salahuddin, 2017.
 Gastroprotective Effect of Vanillin on Indomethacin-Induced Gastric Ulcer in Rats: Protective Pathways and Anti-Secretory Mechanism. Clin Exp. Pharmacol., 7: 232. doi:10.4172/2161-1459.1000232
- 29. Helal, O.K., M.M. Yousef and M. Elnaa, 2011. Possible protective effect of gum Arabic on experimentally induced gastric ulcer in adult male albino rats: a histological and immunohisto chemical study. The Egyptian Journal of Histology, 34: 546-553.
- Jabri, M.A., N. Aissani, H. Tounsi, M. Saklya, L. Marzouki and H. Sebai, 2016.Protective effect of chamomile (*Matricaria recutita* L.) decoction extract against alcohol-induced injury in rat gastric mucosa. Pathophysiology, 24(1): 1-8.
- 31. Al-Hashem, F.H., 2010. Gastroprotective effects of aqueous extract of Chamomilla recutita against ethanol-induced gastric ulcers. Saudi Med. J., 31(11): 1211-6.
- El-Ashmawy, N.E., E.G. Khedr, H.A. El-Bahrawy and H.M. Selim, 2016. Gastroprotective effect of garlic in indomethacin induced gastric ulcer in rats. Nutrition, 32: 849-854.
- 33. Cemek, M., Yilmaz, E. and M.E. Büyükokuroğlu, 2010. Protective effect of Matricaria chamomilla on ethanol-induced acute gastric mucosal injury in rats. Pharmaceutical Biology, 48(7): 757-763.
- 34. Gohar, A.A. and A.A. Zaki, 2014. Assessment of some Herbal Drugs for Prophylaxis of Peptic Ulcer. Iranian Journal of Pharmaceutical Research, 13(3): 1081-1086.
- Lim, J., C. Song, S. Park, D. Park, G. Jung, H. Cho, K.M.I. Bashir, S.K. Ku and J. Choi, 2019. Protective effects of triple fermented barley extract (FBe) on indomethacin-induced gastric mucosal damage in rats. BMC Complementary and Alternative Medicine, 19(49): 1-11.
- 36. Abid, S.A., N.J. Mohammed and H.A. Al-Kaffaji, 2012. Effect of Liqurice and Chamomile Extracts in the Management of Gastric Ulcer in Rats. Medical Journal of Babylon, 9(3): 583-597.