

Gastroprotective Effect of Borago Extracts against Indomethacin-Induced Gastric Ulcer in Rats

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ABSTRACT

Gastric ulcer stays one of the perilous sicknesses in the world. In spite of the fact that there are numerous medications utilized for the treatment of gastric ulcer, the vast majority of these deliver a few adverse impacts. The aim of this investigation was to assess the antiulcer effects of Borago (*Borago officinalis L*) leaves extract (BL), flowers extract (BF) and the mixture of leaves and flowers extracts (Mix) against gastric ulcer induced by indomethacin in rats and compared with ranitidine as a reference drug. Gastric ulceration was stimulated by indomethacin at one dose (30 mg/kg b.w. Intraperitoneal (i.p)). BL and BF were administered orally at two doses of 100 and 200 mg/kg b.w, Mix was given orally at a dose of 200 mg/kg b.w. and ranitidine at a dose of 20 mg/kg b.w. for three weeks before the injection of indomethacin. The results appeared that indomethacin significantly decreased pH value, mucin content, catalase activity (CAT) and nitric oxide (NO), while, increased ulcer index, total acidity, free acidity and malondialdehyde (MDA) comparing with control group. While, pretreatment with Borago extracts provided a significant decrease in ulcer index, total acidity, free acidity, MDA, and associated with a significant rise in pH value, mucin content, CAT and NO compared to indomethacin group. The protection provided by the extracts of Borago is similar to ranitidine. Histological studies of stomach mucosa affirmed these outcomes. Borago has protective against indomethacin which caused gastric ulcer because of it contains antioxidant properties. The results of the present suggest that Borago can be utilized against gastric ulcer impacts as well as to decrease antagonist drugs adverse effects.

Keywords: Gastric ulcer, Borago, Indomethacin, Ranitidine, CAT, MDA.

INTRODUCTION

Gastric ulcer is a disease that affects a large number of people in the world. It is corroded in the duodenum or the lining of the stomach happening on a site where the mucosal epithelium is presented to pepsin and acid and it is instigated by numerous factors, including smoking, stress, alcohol consumption, nutritional deficiencies and regular ingestion of non-steroidal anti-inflammatory drugs (NSAIDs) (Belaiche *et al.*, 2002). Gastric ulcers related to the usage of NSAIDs stay one of the major clinical issues everywhere throughout the world (Dhiyaaldeen *et al.*, 2014). Tulassay and Herszényi (2010) detailed that the pathophysiology of gastric ulcers depends on the imbalance between defensive factors and the aggressiveness of the gastric mucosa. Indomethacin is one of NSAIDs family, is known to induce serious side impacts in gastric mucosa, for example, ulcerative lesions and erosions (Prasad *et al.*, 2012). The mechanism of indomethacin in gastric ulcers involves the inhibition of prostaglandin synthesis and the generation of reactive oxygen species (ROS) (Takeuchi *et al.*, 2011). An extensive variety of medication is as of now accessible for the to treat gastric ulcer that include H₂- blockers, proton pump inhibitors, anticholinergics, and antacids. Although the use of H₂ antagonists and proton pump inhibitors in treatment caused a high healing rate of 80-100% after 1-2 month of therapy, but after one year, stopping treatment, the rate of recurrence of ulcers is between 40 and 80% (Miller and Faragher, 1989). Also, these medications caused a few adverse impacts (Ariyphisi *et al.*, 1986), for example, hypersensitivity, hypergastrinemia, gynecomastia, blood dyscrasias, impotence, and arrhythmia. These impacts sire the rationale for the improvement of new antiulcer drugs. Consequently, the research is still ongoing to find a natural drug that has antiulcerogenic properties.

Borago (*Borago officinalis L*) family Boraginaceae is used as an ornamental plant (Kaskoos *et al.*, 2012) and folk medicinal purposes (Gilani *et al.*, 2007). Borago plant has numerous health impacts, for example, antispasmodic, antipyretic, antihypertensive, diuretic properties, kidney ailments, and useful to treat palpitations and bronchitis

(Gilani *et al.*, 2007). In the food application, a meal of Borago extracts has been utilized as successful antioxidants in the model system of meat (Wettasinghe and Fereidoon, 1999). Bandoniene and Murkovic (2002) demonstrated that the extract of borage leaf was as an efficient antioxidant in rapeseed oil. Borage contains polyphenols such as rosmarinic acid, which is in charge of some of the antioxidant activities of rosemary extracts, which is likewise generally utilized by the food industry. Borage leaves are an inexpensive crude material for the production of polyphenols, and disposal of these leaves needs a high cost, which can be limited by its utilization (Krishnaiah *et al.*, 2011). Many unsaturated fatty acids, for example, palmitic, stearic, linoleic and α -linolenic acids are found in flowers of borage (Morteza *et al.*, 2014 and Ramandi *et al.*, 2011).

The objective of the present study was designed to investigate the role of Borage leaves and flowers extracts of healing gastric ulcer was induced by indomethacin in rats.

MATERIALS AND METHODS

Materials

Chemicals

Indomethacin was obtained from Bio-diagnostic Company. Ranitidine was purchased from a pharmacy, El-Minia, Egypt. All kits were purchased from Bio-diagnostic Company, Cairo, Egypt.

Plant material

The Flowers and leaves of Borago were collected from the Faculty of Agriculture, Minia University, Egypt.

Experimental Animals:

Eighty female albino rats of Sprague-Dawley albino strain weighing (200 \pm 10g), were obtained from the Animal House of Faculty of Agriculture, Minia University.

Methods

preparation of Borago extracts

The plant material was dried at room temperature and ground to powder. Leaves and flowers powder were soaked in ethanol (70% v/v) at 1:10 (w/v) at room temperature with stirring for three hours and filtered. The soaking and filtration were repeated twice. The extracts were dried in a rotary evaporator at 40 °C.

Experimental design:

Rats were used after acclimatization for a period of 1 week in animal house conditions and had free access to water and food. Rats were placed in a mesh-bottomed cages to reduce coprophagia and were fasted for 24 hours before the experiment. Rats had free access to water, excluding the last hour before the experiment. All experiments were conducted at the same time of the day to avoid differences due to the daily rhythms of the supposed organizations of the functions of the stomach (Bregonzio *et al.*, 2003).

The animals were randomly classified into 8 groups (10 rats per each):

- Group (1):**Control group; Rats were received only distilled water.
- Group (2):** IND group; Rats were received a single dose of indomethacin (30 mg/ kg b.w. i.p.Khattab *et al.*, 2001) to induce ulcer
- Group (3):**RAN group; Rats were treated with ranitidine (20 mg/kg b. w. Bharat *et al.*, 2013) daily for, three weeks before indomethacin injection.
- Groups (4) and (5):** BL1+IND and BL2+IND groups; Rats were treated with Borago leaves extract (BL) (100 and 200 mg/kg b. w., respectively) daily for three weeks before indomethacin injection
- Group (6) and (7):** BF1+IND and BF2+IND groups; Rats were treated with Borago flowers extract (BO) (100 and 200 mg/kg b. w., respectively) daily for three weeks before indomethacin injection.
- Group (8):** MIX+IND group;Rats were treated with BL and BF (200 mg/kg b. w.)daily for three weeks before indomethacin injection.

At the end of experiment, the blood samples were taken from the retro orbital plexus in a glass tube and left for 20 minutes to coagulant at room temperature and then centrifuged at 3000 rpm for 15 minutes, to obtain serum samples which kept at -20°C until used for subsequent biochemical analysis. The animals were sacrificed.

Biochemical analysis

Serum alanine and aspartate aminotransferase enzymes activity (ALT and AST, respectively), total protein, and albumin were measured according to Reitman and Frankel (1957), and Dumas *et al.*,(1971) respectively. Serum uric acid and urea levels were assayed in the samples by a colorimetric methods (Fossati *et al.*,1980 and Fawcett and Scott 1960, respectively) .Serum cholesterol, triglycerides (TG) and glucose were estimated according to (Abell *et al.*, 1952; Bucolo and David, 1973 and Trinder 1969, respectively).

Evaluation of mucosal lesions in gastric:

After three hours of indomethacin injection, the animals were killed with an overdose of the ether.Each stomachs were obtained and opened along a larger curvature, and the gastric juice was obtained.The stomachs were washed with a cold saline solution and were examined for microscopic mucosal lesions. Mucosal lesions in gastric were expressed in terms of ulcer index (U.I) according to the method of Peskar *et al.*, (2002).Prevention (P.I) was calculated from a given drug by the equation Hano *et al.*, (1976).

Analysis of gastric juice

The juice of gastric was centrifuged at 2000 x g for 15 min .The volume of the supernatant , pH and the concentration of mucin were estimated by using methods (Moore,1968 and Winzler, 1955 , respectively). Total and free acid outputs were calculated according to (Hara *et al.*, 1991 and Feldman, 1998, respectively).

Determination of gastric oxidative stress

Oxidative stress was measured in gastric tissue homogenates included catalase enzyme activity (CAT), malondialdehyde concentration (MDA) and nitric oxide (NO) (Mihara and Uchiyama ,1978; Aebi, 1984 and Green *et al.*, 1982,respectively).

Histopathological studies

Histological examination of stomach tissues was based on the method described by Bancroft and Stevens,(1977) using stained with haematoxylin& eosin.

Statistical analysis

The results obtained in the present study were evaluated by One Way ANOVA test followed by Tukey Dunken SPSS. The results were expressed as mean ± standard error and values of P<0.05 were considered statistically significant (Snedecor and Cochran, 1986).

RESULTS AND DISCUSSION

Phytochemical screening

Table (1) shows the presence of phytoconstituents such as flavonoids, glycosides, terpenoids, tannins, phenolic acids and, alkaloids and the absence of saponins in both BL and BF extracts. Steroids were no appearance of in BF extract.

These compounds have antioxidant properties (Nayak *et al.*, 2011) and it's found in Borago (Farhadi *et al.*,2012) . Also, these components known to influence the safety of membranes of mucous (Oliver, 1960).Tannins could be impacted worthwhile in averting ulcer advancement (Aguwa and Nwako, 1988) and it is an astringent, which forms a protective layer of Pellicle (precipitation of microproteins)over the lining in the site of ulcer thereby to prevent the absorption of substances toxic and to resist the attack of enzymes of proteolytic (John and Onabanjo, 1990 and Nwafor *et al.*, 1996).

Table 1. Preliminary phytochemicals screening of Borago leaf and flower extracts

Phytochemical Tests	BL	BF
Flavonoids	+	+
Glycosides	+	+
Steroids	+	-
Saponins	-	-
Terpenoids	+	+
Phenolic Acids	+	+
Tannins	+	+
Alkaloids	+	+

+: presence - : Absence

Ulcer index and prevention

Indomethacin group appeared a remarkable high ulcer index (35). our results agree with other reports (Heeba *et al.*,2009; Kim *et al.*,2011 and Moram *et al.*, 2016).While, pretreatment with extracts of Borago (BL1, BL2, BF1,BF2 and MIX) had significantly decreased ulcer index to 15, 4, 3,2 and 2 respectively. BF groups (100 and 200 mg / kg.b.w) showed protection (91.42 and 94.29 %, respectively) against ulceration. Whereas BL groups (100 and 200 mg / kg.b.w)

exhibited protection (57.14 and 88.57 %, respectively) against ulceration. Also, group pre-treated with Borago leaves and flowers extracts (200 mg / kg.b.w) appeared protection (94.29 %) against ulceration. Increasing in ulcer index in the ulcerated rats might be ascribed to either inhibition of prostaglandin synthesis or formation of free radicals. Our outcomes agree with Fathima *et al.*, (2017) who suggested that significant reduction in ulcer index and increase in percentage protection in the ethanolic extract of Borago flowers when compared with indomethacin group. This examination suggests that ethanolic extracts of Borago show antiulcer activity.

Table 2. The effect of Borago leaves, flowers and mixture extracts on the ulcer index and prevention in gastric ulcer caused by indomethacin in rats

Parameters Groups	Ulcer index	Prevention
Control	-	-
IND	35	-
RAN+ IND	1	97.14
BL1+ IND	15	57.14
BL2+ IND	4	88.57
BF1+ IND	3	91.42
BF2+ IND	2	94.29
MIX+ IND	2	94.29

Gastric juice analysis

The pH gives an idea of acidity gastric secretions. Low pH value is a sign of low concentration of hydrogen ions in gastric juice. This was associated with ulcer

Table 3. The effect of Borago leaves, flowers and mixture extracts on gastric juice analysis in gastric ulcer caused by indomethacin in rats

Parameters Groups	pH	Free acidity (µEq/L)	Total acidity (µEq/L)	Mucin content (mg% hexose)
Control	5.11±0.03	40.1±1.39	55.2±1.94	85.16±4.64
IND	2.68 ^a ±0.25	80.2 ^a ±2.39	105.5 ^a ±5.83	41.66 ^a ±3.00
RAN+ IND	4.27 ^{ab} ±0.09	63 ^{ab} ±3.04	75.4 ^{ab} ±2.4	69.18 ^{ab} ±1.57
BL1+ IND	4.02 ^{ab} ±0.02	65 ^{ab} ±4.17	81.1 ^{ab} ±4.85	45.89 ^a ±3.47
BL2+ IND	4.49 ^{ab} ±0.06	50 ^b ±4.76	75.2 ^{ab} ±4.39	53.48 ^{ab} ±3.66
BF1+ IND	4.17 ^{ab} ±0.06	55 ^{ab} ±2.50	70.1 ^{ab} ±2.69	67.28 ^{ab} ±5.24
BF2+ IND	4.81 ^b ±0.08	45 ^b ±4.08	60.3 ^b ±2.23	79.71 ^b ±3.02
MIX+ IND	4.79 ^b ±0.06	46 ^b ±3.89	65.7 ^b ±3.92	74.86 ^b ±1.29

Data represent the mean ± S.E. of observation from 10 rats. ^a significantly different from control group at P ≤ 0.05. ^b significantly different from Indomethacin group at P ≤ 0.05.

Serum biochemical parameters

Indomethacin group produced significant reduction in serum albumin (3.30±0.13 mg/dl) and Uric Acid (2.27±0.53mg/dl) compared to control group (4.12 ± 0.14 and 3.44 ± 0.41 mg/dl , respectively). On the other hand, indomethacin caused a significant increment in ALT, AST, protein, Urea, glucose, total cholesterol, and triglyceride compared to control group. These results agree with El-Metwalley *et al.*, (2016). The increments in the levels of ALT and AST (particularly ALT) are related with liver injury (Bush, 1991). The toxicity of some NSAIDs may be directly related to biliary secretion. A few medications like indomethacin, aspirin and ibuprofen known to have effective anti-inflammatory are related to some side effects such as abdominal ulcers and gastric erosions after a long period of use (Ogbru, 2006). All groups were significantly decreased ALT and AST compared with the indomethacin group (Table 4). Total cholesterol and triglyceride levels were significantly decreased in BL2 and BF2 groups compared with the indomethacin group (Table 4). While, the

disease and gastric harm in animals models (Lüllmann *et al.*, 2000). Administration of indomethacin produced a significant reduction in pH value (2.68±0.25) associated with a significant rise in free acidity (80.2±2.39 µEq/L) and total acidity (105.5±5.83 µEq/L) of gastric juice. This outcome agrees with Beck *et al.*, (2000); Biplab *et al.*, (2011) and Muhammed *et al.*, (2012) who showed indomethacin caused alterations in gastric secretions of rats. The pretreated group with Borago caused significant changes in pH value, free and total acidity comparing with indomethacin group. Treatment rats with RAN drug appeared significant increase in pH value (4.27±0.09 µEq/L) and a significant decrease in free acidity (63±3.04 µEq/L) and total acidity (75.4±2.4µEq/L) comparing with indomethacin group.

Pretreatment of BF and BL exhibited more potent efficacy in decrease of total and free acidity. At the same time, Treated rat with indomethacin significantly decreases in mucin content (41.66±3.0 mg % hexose) compared to control group (85.16±4.64 mg% hexose). All groups of Borago caused a significant change in mucin content comparing with indomethacin group. RAN produced significant increase in mucin content as compared to indomethacin group. Our outcomes are in line with Fathima *et al.*, (2017) who observed that significant raise in pH and diminish in free acidity, total acidity of gastric juice in the ethanolic extract of Borago flowers when comparing with indomethacin group. Borago extracts appear antiulcer activity by repressing harm in the gastric mucosa layer.

levels of albumin, uric Acid was significantly increased and levels of urea and glucose were significantly reduced when compared with the indomethacin group (Table 4). Our results agree with (Hamed and Wahid, 2015) Retrieving high levels of serum enzymes to normal values is an indicator of plasma membrane stability and tissues repair. Our results agree with previous reports confirming the high antioxidant activity of Borago because of their high content of phenolic compounds, which have high free radical scavenging activity (Samy *et al.*, 2016).

Oxidative stress

Injection of indomethacin significantly raised the concentration of MDA in the mucosa of the stomach about three times, reaching (16.76 ±2.21 nmol/g tissue) comparing with the control group (5.29±1.44 nmol/g tissue). These results agree with many authors (Kim *et al.*, 2011 ; Allam and EL-Gohary, 2017 and Nwaonukuru *et al.*, 2018). BL pretreatment (100 and 200 mg/kg b.w respectively) significantly decreased MDA to 10.36 ± 1.97nmol/g and 9.10±0.81nmol/g when compared to

indomethacin group. BF pretreatment (100 and 200 mg/kg b.w respectively) diminished MDA to 7.96±0.77 nmol/g and 6.15±0.55 wet tissue, respectively. While RAN pretreatment diminished MDA to 6.83±0.76 nmol/g tissue, Mixture extracts BL and BF altogether expanded the reduction of MDA to 6.62 ±1.47nmol/g tissue. Ranitidine has often been accounted to possess immunosuppressive actions and antioxidant , which might be in charge of its

antiulcerogenic activity (Ardestani *et al.*, 2004). Borago introduced a noticeable repression of oxidative damage because of its phenomenal radical scavenging capacity, It conveyed MDA level nearer to ordinary levels. This is because of the activated components in Borago extract that contain the antioxidant components, for example, non - enzymatic like Vit. C and enzymatic like catalase which are keeping up the living cell membranes (Jaeschke,2000).

Table 4. The effect of Borago leaves, flowers and mixture extracts on some biochemical parameters in gastric ulcer caused by indomethacin in rats

Parameters Groups	ALT (U/L)	AST (U/L)	Protein (mg/dl)	Albumin (mg/dl)	Urea (mg/dl)	Uric Acid (mg/dl)	Glucose (mg/dl)	Cholesterol (mg/dl)	Triglyceride (mg/dl)
Control	23.20±0.81	30.31±5.31	6.28±0.17	4.12±0.14	18.12±4.48	3.44±0.41	70.68±3.78	89.54±6.55	76.07±4.31
IND	37.29 ^a ±0.98	52.83 ^a ±3.81	7.39 ^a ±0.24	3.30 ^a ±0.13	34.70 ^a ±5.46	2.27 ^a ±0.53	95.36 ^a ±6.62	118.32 ^a ±10.60	100.98 ^a ±2.17
RAN+ IND	26.21 ^b ±3.11	34.61 ^b ±3.23	6.64 ^b ±0.51	4.1 ^b ±0.18	22.01 ^b ±3.92	2.94±0.08	80.65±5.43	99.63±3.37	91.49±2.43
BL1+ IND	28.11 ^b ±1.71	40.61 ^b ±3.58	6.92 ^a ±0.22	3.34 ^a ±0.06	26.47±2.14	2.58 ^a ±0.06	86.73±8.64	105.05±9.94	95.62 ^a ±4.85
BL2+ IND	23.65 ^b ±2.71	36.69 ^b ±2.77	6.76 ^b ±0.42	3.59 ^a ±0.27	24.47±3.74	2.88±0.24	82.59±9.49	98.71 ^b ±3.38	88.51 ^b ±2.14
BF1+ IND	26.89 ^b ±1.21	35.81 ^b ±3.23	6.89 ^a ±0.18	3.56 ^a ±0.08	23.45±4.11	2.53 ^a ±0.13	84.75±5.63	100.43±5.62	92.79±4.11
BF2+ IND	21.61 ^b ±2.02	28.61 ^b ±3.52	6.24 ^b ±0.31	4.38 ^b ±0.23	19.47 ^b ±3.76	3.57 ^b ±0.13	78.64 ^b ±5.59	88.21 ^b ±3.98	87.40 ^b ±7.23
MIX+ IND	22.91 ^b ±2.31	31.34 ^b ±4.56	6.32 ^b ±0.26	3.67±0.07	20.38 ^b ±3.19	3.52 ^b ±0.07	81.65±7.72	92.45 ^b ±5.14	90.65±1.56

Data represent the mean ± S.E. of observation from 10 rats. ^a significantly different from control group at P ≤ 0.05. ^b significantly different from Indomethacin group at P ≤ 0.05.

Data presented in Table (5) showed that treated rats with indomethacin significantly decreased catalase activity (0.26 ±0.05 U/g tissue) compared to control group (0.97±0.02 U/g tissue) .BL pretreatment (200 mg/kg b.w) significantly increased catalase activity when comparing with indomethacin group. BF pretreatment (100 and 200 mg/kg b.w respectively) elevated catalase activity to 0.42±0.02 U/g tissue and 0.88±0.05 U/g tissue, respectively. Mean while RAN pretreatment raised catalase activity to 0.48±0.03 U/g tissue, Mixture extracts BL and BF elevated the catalase activity.

Indomethacin stimulates the metabolites of reactive oxygen in animal experiments, which may participate to mucosal damage (Chattopadhyay *et al.*, 2006). Also, these free radicals devastate cellular antioxidant enzymes such CAT that act as the first cellular defense line against oxidative damage. This may damage the aggravated tissue during gastric ulceration (El-Missiry *et al.*, 2001).

Table 5. The effect of Borago leaves, flowers and extracts mixture on nitric oxide, catalase and MDA levels in gastric ulcer caused by indomethacin in rats

Parameters Groups	Nitric oxide (µmol/g tissue)	Catalase (U/g tissue)	MDA (nmol/g tissue)
Control	8.07±0.45	0.97±0.02	5.29±1.44
IND	3.27 ^a ±0.19	0.26 ^a ± 0.05	16.76 ^a ±2.21
RAN+ IND	6.87 ^b ±0.31	0.48 ^{ab} ± 0.03	6.83 ^b ±0.76
BL1+ IND	5.81 ^{ab} ±0.47	0.33 ^a ± 0.04	10.36 ^{ab} ±1.97
BL2+ IND	6.29 ^b ±1.14	0.44 ^{ab} ± 0.03	9.10 ^b ± 0.81
BF1+ IND	6.37 ^b ±0.79	0.42 ^{ab} ±0.02	7.96 ^b ±0.77
BF2+ IND	7.75 ^b ±1.23	0.88 ^b ± 0.05	6.15 ^b ±0.55
MIX+ IND	7.64 ^b ±0.19	0.79 ^{ab} ± 0.03	6.62 ^b ±1.47

Data represent the mean ± S.E. of observation from 10 rats. ^a significantly different from control group at P ≤ 0.05. ^b significantly different from Indomethacin group at P ≤ 0.05.

In indomethacin group, NO levels were significantly decreased (3.27±0.19 µmol/g tissue) compared to control group (8.07±0.45µmol/g tissue). This

result was agreed with Lanas *et al.*, (2000) and Cadirci *et al.*, (2007).The decreasing in NO biosynthesis, due to diminished activity of NO synthase (NOS) which was with an expansion in the degree of damage (Tripp and Tepperman,1995).The indomethacin stimulates the reduction of the activity of endothelial nitric oxide synthase (eNOS) and thus reduces the level of NO (Slomiany *et al.*, 1999).

Interestingly, all groups which used to create a significant increasing in NO levels compared to indomethacin group.The potential mechanism for increasing the NO level in Borago groups might be because of its flavonoids content. Matsuda *et al.*,(2003) announced that flavonoids have many descriptions of antioxidant, gastroprotective properties and antiulcer.

Histological and Macroscopic examination of gastric ulcer

Microscopically, stomach of rats control group appeared the normal histological structure of gastric layers (mucosa, submucosa and serosa) (Fig 1). In contrary , stomach of rats from indomethacin group revealed focal coagulative necrosis of gastric mucosa and submucosa oedema with inflammatory cell infiltration and congestion of mucosal blood vessels (Fig. 1).Moreover, stomach of rats from ranitidine group showed no histological changes (Fig. 1). However, stomach from BL1 group revealed congestion of mucosal and submucosal blood vessel as well as oedema (Fig. 1). Section from BL2 group revealed no histological change (Fig. 1), whereas, other section showed submucosal inflammatory cells infiltration (Fig. 1).However, stomach of rats from BF1 group revealed submucosal oedema (Fig. 1) and congestion of submucosal blood vessels (Fig. 1). Section from groups BF2 and MIX revealed no histological changes (Fig. 1) expected congestion of blood vessels (Fig. 1).These results agree with Banerjee *et al.*, (2008) ;El-Demerdash *et al.*, (2010) and Shahin *et al.*,(2018) who reported that indomethacin caused marked damage to the gastric mucosa such as focal coagulative

necrosis, leukocytic infiltration, and blood vessels congestion (EL-Moselhy *et al.*, 2009), associated with a significant increase in lipid peroxidation and generation of oxygen free radicals (Kim *et al.*, 2011). The perfect recovery of gastric mucosa due to administration of Borago or ranitidine presumably relies upon vasodilating action. These action increments mucosal blood flow and promote angiogenesis, a key factor in ulcer recuperating (Konturek *et al.*, 1993).

Macroscopic examination of gastric ulcer showed that control groups showed no ulcer spots (Fig 2). In contrary, Indomethacin appeared several ulcer spots. Moreover, the ranitidine group detected some minor ulcer spots (Fig 2). In groups that received Borago extracts, particularly BF at the dose of 200mg/kg, a reduction in a number of ulcer spots.

Table 6. The severity of histological changes in gastric tissues

Groups	Control	IND	RAN+ IND	BL1+ IND	BL2+ IND	BF1+ IND	BF2+ IND	MIX+ IND
Necrosis of gastric mucosa	-	+++	-	-	-	-	-	-
Congestion of mucosal blood vessels	-	+++	-	++	-	+	+	+
Congestion of submucosal blood vessels	-	++	-	++	+	++	-	-
Submucosa oedema	-	+++	-	+	+	++	-	-
Submucosal inflammatory cells infiltration	-	++	-	-	++	-	-	-

(-) no change (+) mild change (++) moderate change (+++) severe change

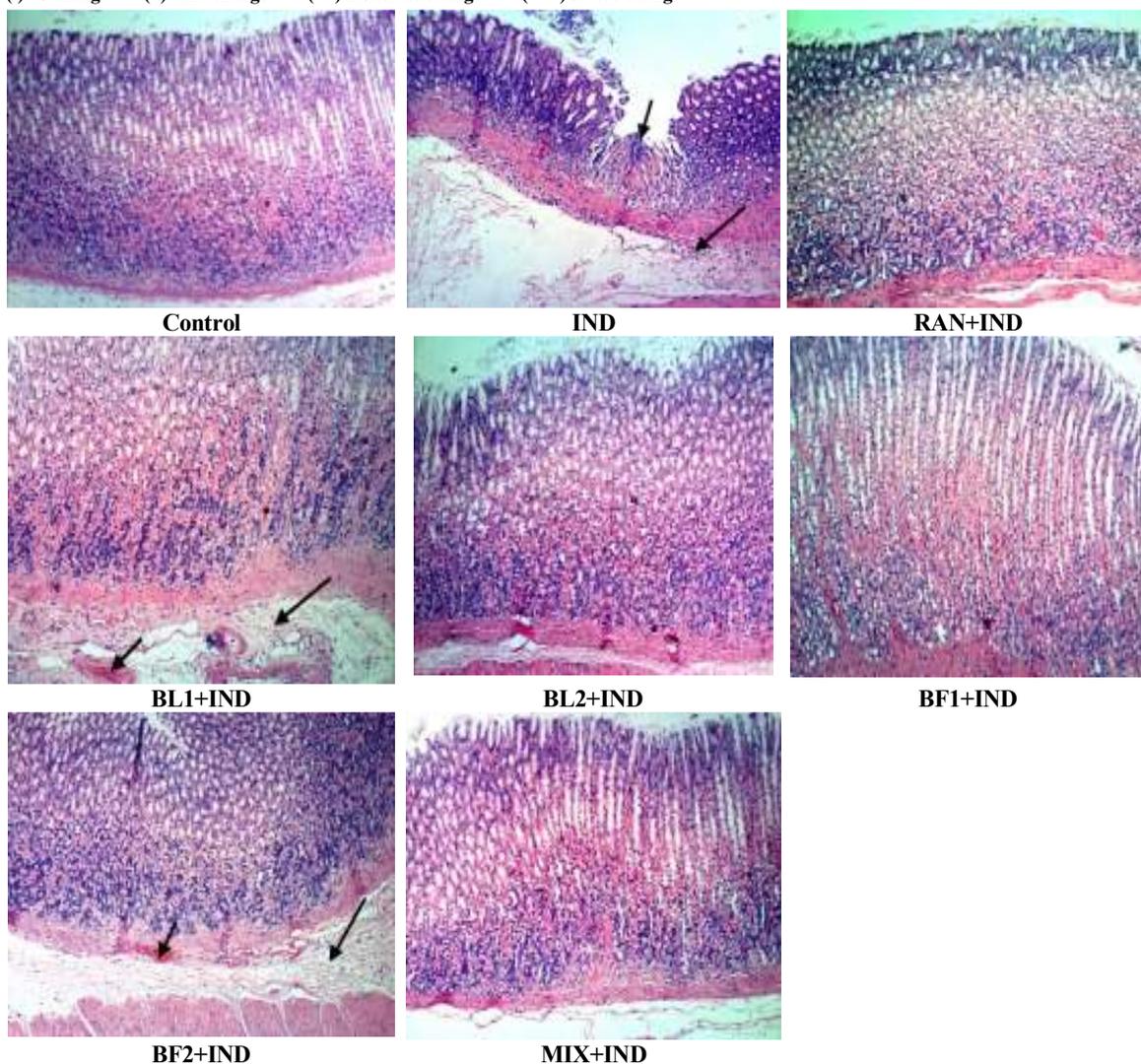


Fig. 1. Histological examination of gastric tissue

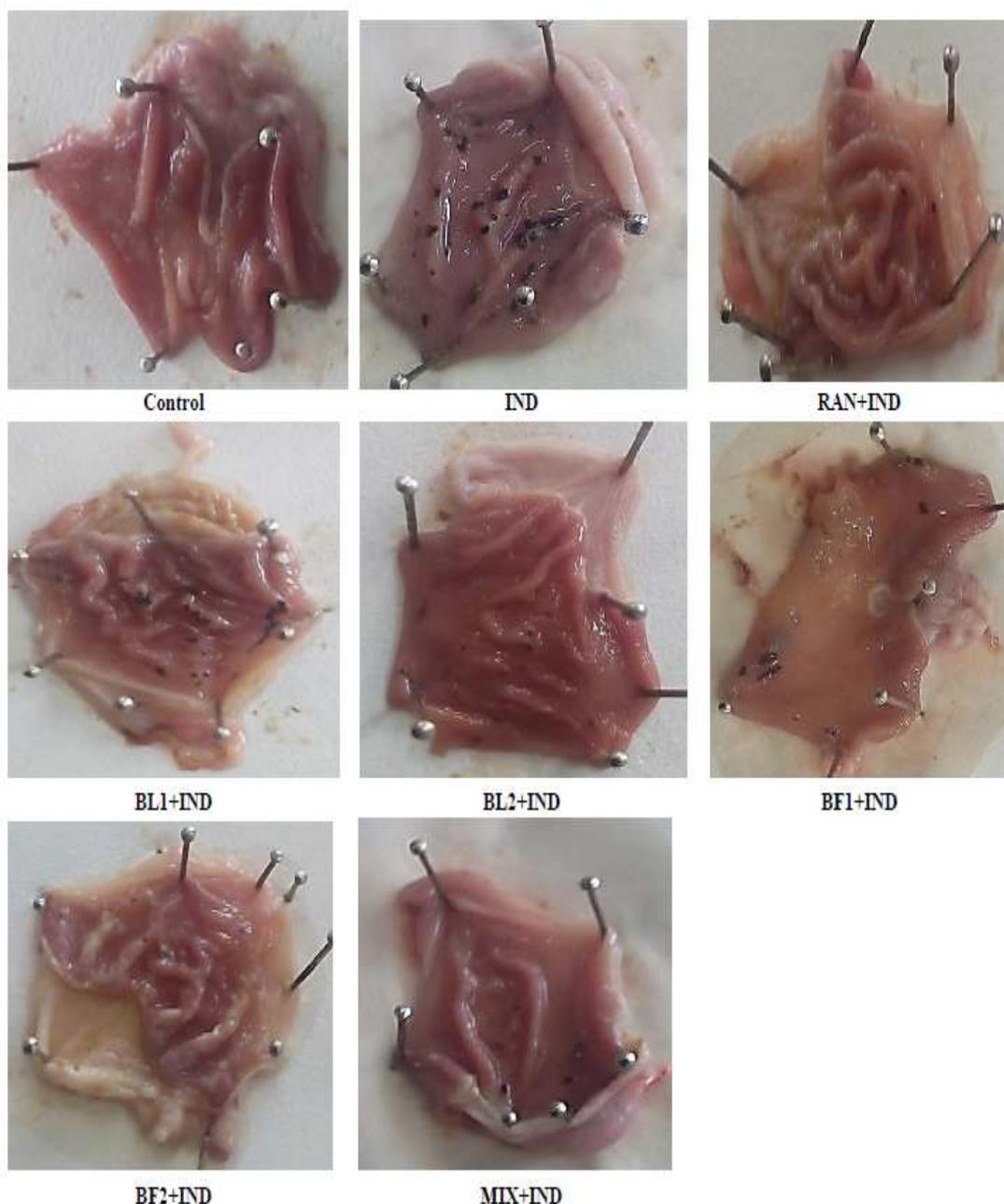


Fig. 2. Microscopic presentation of gastric tissue

In conclusion, our results showed that Borago extracts may have a gastroprotective effect against indomethacin induce gastric ulcers. These impacts may be due to the presence of glycosides phenolics, flavonoids, and tannins in the ethanolic extracts of Borago which it's due to inhibiting lipid peroxidation and enhancing enzymatic antioxidant defenses.

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التأثير الوقائي لمستخلصات خبز النحل علي قرحة المعدة الناتجة عن الحقن بالإندوميثاسين في الجرذان هناء سالم صالح جازوي و ماجدة عويس محمود قسم الكيمياء الزراعية - كلية الزراعة - جامعة المنيا - المنيا- مصر

قرحة المعدة تعتبر واحدة من أخطر الأمراض في العالم. وعلى الرغم من وجود العديد من الأدوية المستخدمة لعلاجها، إلا أن الغالبية العظمى منها تعطي بعض التأثيرات السلبية. والهدف من هذه الدراسة تقييم تأثير مستخلصات أوراق (BL) و أزهار (BF) خبز النحل (*Borago officinalis* L) والخليط منها (Mix) ضد قرحة المعدة التي يسببها الإندوميثاسين في الجرذان والمقارنة مع الرانيتيدين كعلاج مرجعي. تم حدوث قرحة المعدة عن طريق الإندوميثاسين بجرعة واحدة (٣٠ مجم / كجم من وزن الجسم). وتم إعطاء BL و BF عن طريق الفم بجرعتين (١٠٠ و ٢٠٠ مجم / كجم من وزن الجسم)، كما أعطى المخلوط بجرعة (٢٠٠ ملجم / كجم من وزن الجسم) والرانيتيدين بجرعة (٢٠ ملجم / كجم من وزن الجسم) لمدة ثلاثة أسابيع قبل حقن الإندوميثاسين. أظهرت النتائج أن الإندوميثاسين قلل قيمة الرقم الهيدروجيني بشكل كبير، محتوى الميوسين، نشاط الكاتالاز (CAT) وأكسيد النيتريك (NO)، بينما زاد ulcer index، الحموضة الحرة، الحموضة الكلية و MDA مقارنة مع مجموعة الكونترول. أظهرت المعالجة السابقة لمستخلصات خبز النحل انخفاض كبير في ulcer index، الحموضة الحرة، الحموضة الكلية، malondialdehyde (MDA)، وحدثت زيادة كبيرة في قيمة الرقم الهيدروجيني، محتوى الميوسين، نشاط الكاتالاز (CAT) وأكسيد النيتريك (NO) مقارنة بمجموعة الإندوميثاسين. تشبه التأثيرات الوقائية لمستخلصات خبز النحل العلاج بدواء الرانيتيدين. وأكد الفحص الهستولوجي للغشاء المخاطي للمعدة هذه النتائج. خبز النحل لديه تأثير وقائي ضد الإندوميثاسين الذي يسبب قرحة المعدة لأنه يحتوي على مضادات أكسدة. ونتائج هذه الدراسة تبين إمكانية استخدام خبز النحل ضد تأثيرات قرحة المعدة وكذلك في تخفيف الآثار الضارة للعقاقير المستخدمة في علاجها.