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Full Length Research Paper

Evaluation of anti-ulcer, anti-secretory and anti-*helicobacter pylori* effects of folkloric medicinal plant, *Fumaria vaillantii* L, in rats

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This paper evaluated anti-ulcer, anti-secretory and anti-*helicobacter pylori* effects of folkloric medicinal plant, *Fumaria vaillantii* L, in rats. Different toxic agents; ethanol (80%), NaOH (0.2 mol/L), NaCl (25%) and indomethacin (30 mg/kg, body weight) were used to produce acute gastric ulceration in rats. Anti-secretory studies were undertaken by using pylorus-ligation, Shay rat technique. *F. vaillantii* L aqueous extract (Aq-FV) was used in three doses (100, 200 and 300 mg/kg bodyweight). Aq-FV was further tested for anti-*H. pylori* activity. Extract significantly attenuated gastric mucosal damage induced by toxic agents and indomethacin in rats. Aq-FV restored partially mucus secretion in indomethacin model. In pylorus-ligated rats, Aq-FV significantly reduced the basal gastric acid secretion, acidity and ulceration. Aq-FV possesses significant and more potent anti- ulcer and cytoprotective activities against experimentally-induced gastric ulcers in comparison to Omeprazole. Extract showed significant but less potent anti-*H. pylori* activity in comparison to Clarithromycin. Evaluation agreed with the folkloric use of *F. vaillantii* L as anti-ulcer and anti-secretory tool.

Key words: *Fumaria vaillantii* L, cytoprotection, gastric ulcer, gastric secretion, gastric wall mucus, anti-*helicobacter pylori*.

INTRODUCTION

Peptic ulcer is one of the most common gastrointestinal diseases (Torab et al., 2009). Modern tools like proton pump inhibitors and H_2-receptor antagonists are widely used to treat peptic ulcer disease world over (Tsumura et al., 2007) . Despite the high prices, the use of these anti-secretory drugs may be associated with adverse events and ulcer relapses (Tzathas et al., 2008; Kwok et al., 2008; Van Leerdam, 2008; Kovacs et al., 2009). Therefore, the search for a more effective, safer/less toxic and cost-effective anti-ulcer agent is needed. In an effort to further search curative and safe agent for the treatment of peptic ulcers in our indigenous medicinal plants, the present study was undertaken and gastroprotective efficacy of aqueous extract of *Fumaria vaillantii* Linn. (Aq-FV) was evaluated in rats having experimentally-induced ulcers.

Further, *F. vaillantii* L. has commonly been used to treat the gastrointestinal disorders in the eastern/folk medicine in Pakistan and no scientific report, on potential gastro-protective claims of *F. vaillantii* L has been found in the reported literature to date, therefore, the present study was carried out to evaluate its effect on experimentally induced gastric ulcers in rats.

F. vaillantii L. is annual herb, sub-erect or diffuse, probably scarcely scandent. It is distributed up to 8000 feet on the Himalaya, Baluchistan-Pakistan, Afghanistan, Persia, and Magnolia. The plant has been used as diuretic, diaphoretic and aperients (Kirtikar and Basu, 1987). Hot water extract of the plant has been used for scrofulous skin diseases, dyspepsia, and liver complaints (Kapur and Sarin, 1984) and methanolic extract has been indicated for antibacterial activity (Sabahi et al., 1987). *F.*

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Abbreviation: ALT, Alanine aminotransferase; **AST,** aspartate aminotransferase; **ALP,** alkaline phosphatase.

vaillantii L. has been used as a remedy for constipation and diarrhea (Gilani et al., 2005).

MATERIALS AND METHODS

Materials

All materials/chemicals were of analytical grade which were used as received from Macter International Pvt. Ltd. Karachi, Pakistan (Omeprazole), Abbott Laboratories (Pakistan) Ltd., Landhi, Karachi, Pakistan (Clarithromycin), BDH Chemicals Ltd, Poole, UK, E-Merck, Germany and Fluka, Buchs, Switzerland (solvent and chemicals used).

Methods

Plant material and preparation of aqueous extract

Aerial parts of *F. vaillantii* L. (family, Papaveraceae) were purchased from local herb shops in Bahawalpur-Pakistan and identified by expert taxonomists. A sample was preserved (voucher # FV. 041-16-04-2007) at the herbarium of Pharmacognosy Section, Faculty of Pharmacy and Alternative Medicine, the Islamia University of Bahawalpur-Pakistan, for future reference. Shade-dried aerial parts of *F. vaillantii* L were ground to fine powder (75 micron). Finally, powdered drug (1.0 kg) was macerated in about 2.0 lit of distilled water and extracted for 24 h at room temperature, thrice. The combined filtrate was evaporated by a rotary evaporator (Laborota, Heidolph, Japan) at 37 °C. Dried aqueous extract (yield, 7.43 g/kg) was stored air-tight at -20 °C till used (Akhtar et al.,

Test animals

Adult healthy Wister male albino rats, same age (approximately), weighing 150-200 g were obtained from National Institute of Health-Islamabad, Pakistan and maintained under standard conditions of temperature, humidity and light (12 h dark, 12 h light) with free access to a standard feed, M/S Lever Brothers, Rahim Yar Khan, Pakistan and water *ad libitum*. Animals were fasted for 12 h prior to their use in the experiments. The conduct of experiments and the procedure of sacrifice (under ether) were approved by the Ethics Committee of Experimental Animal Care Society, Faculty of Pharmacy and Alternative Medicine, the Islamia University of Bahawalpur -Pakistan. Animals were divided randomly into different groups of 6 - 8 rats each (Akhtar et al., 2004).

Study design

Test substance was suspended in aqueous 2.5% gum tragacanth solution before its administration (Akhtar et al., 2004). 100, 200 and 300 mg/kg b.w. doses were used to determine the preliminary gastroprotective activity of Aq- FV. Accurately, measured extract (100 mg/mL) was administered intragastrically (ig) through gastric intubation, unless stated otherwise intraperitoneally (ip) that is, anti-secretory studies (Al Mofleh et al., 2007). Omeprazole (30 mg/kg, ig) was used as reference (positive control) (de Andrade et al., 2007; Agbaje, 2008; Oluwole et al., 2008). 1 mL of necrotizing agent, that is, ethanol (80%), NaOH (0.2 mol/L) or NaCl (25%) was administered (*ig*) in treated control, positive control and treated groups of rats, separately (Al Mofleh et al., 2007). Aq- FV was administered ig 30 min prior the toxic agent in the treated groups. Positive control rat-group received Omeprazole (30 mg/kg, ig). Control-group rats were given an equal amount of the vehicle. Three hour after the completion of treatments, the rats were sacrificed and examined for lesions in their stomachs. The length (mm) of each lesion was measured under dissection microscope and ulcer index was calculated by adding the length of all the lesions in the glandular regions of stomachs (Indran et al., 2008; Massignani et al., 2009).

Gastric lesions induced by indomethacin

Indomethacin (suspended in 1.0% carboxy-methylcellulose in water, 10 mg/mL) in a dose of 30 mg/kg, b.w. was administered ig to 12 h fasted, treated control-group and treated-group rats (Al Mofleh et al., 2008). Control rats were treated similarly with an equivalent amount of the vehicle. Stomachs of sacrificed rats wer e excised out of the body after 3 h and studied accordingly. The scoring of lesions and assay of gastric wall mucus were observed (Al Mofleh et al., 2008).

Pylorus-ligated rats (anti-secretory studies)

Five groups of 12 h fasted rats were pylorus-ligated under ether anesthesia with avoidance of bleeding and occlusion of blood vessels. Aq-FV (100 - 300 mg/kg) to the treated, Omeprazole (30 mg/kg) to positive treated control and equal volume of vehicle to control rats was given ip immediately following pylorus ligation (Shay). Rats were sacrificed after 3 h, stomachs were removed, with the contents collected, volumes measured, centrifuged and analyzed for titratable acidity against 0.01 mol/L NaOH at pH 7 (Shay et al., 1945; Alqasoumi et al., 2009).

Gastric wall mucus determination

The modified method of Corne et al. (1974) was used to determine gastric wall mucus. Glandular segments of the stomachs were separated from respective rumen, weighed, and transferred immediately to 10 mL of 0.1% w/v Alcian blue solution (0.16 mmol/L sucrose solution buffered with 0.05 mL sodium acetate at pH 5). Segments were stained for 2 h, and excess dye was removed by two successive rinses with 10 mL sucrose (0.25 mmol/L) solution, first for 15 min and then for 45 min. Alcian blue complexed with the gastric wall mucus was extracted with 10 mL of magnesium chloride (0.5 mmol/L) which was intermittently shaken for 1 min at 30 min intervals for 2 h. 4 mL of extract was then vigorously shaken with an equal volume of diethyl ether. The emulsion was centrifuged at 4000 Gm for 10 min. Absorbance of aqueous layer was observed at 580 nm. Alcian blue extracted per gram of wet glandular tissue was then calculated (Al Mofleh et al., 2008).

Bacterial strain

Helicobacter pylori (HP) was obtained from endoscopic samples of ulcer patients, BVH (Bahawal Victoria Hospital-Bahawalpur-Pakistan) and cultured on Ham's F-12 nutrient agar medium with 5% fetal bovine serum (FBS) at 37°C for 72 h in a microaerophelic condition (5% O_2, 15% CO_2 and 80% N_2). HP was characterized by specific tests such as urease, catalase, oxidase, gram staining, colony characteristics and morphological appearance by Micro-biologist and further confirmed by growth of culture in the presence of susceptible and resistant antibiotics (Nanjundaiah et al., 2009).

Agar diffusion assay

HP activity was tested by the standard agar diffusion method

(Siddaraju and Dharmesh, 2007). Petri plates were prepared with Ham's F-12 nutrient agar media containing 5% FBS inoculated with 100 µl of HP culture (10^5 cells/mL). Sterile discs of high-grade cellulose of diameter 5.5 mm were impregnated with 20 µl of known extract (0.25 - 1.0 mg/disc) of Aq-FV placed on the inoculated plates. Clarithromycin was used as positive reference standard and 0.9% saline as negative control. For comparative evaluation discs containing 10 µg each of clarithromycin, Aq-FV was performed in addition to the control. HP growth inhibition was determined as the diameter of the inhibition zones around the discs. Growth inhibition diameter was an average of four measurements taken at four different directions and all tests were performed in triplicates.

Determination of minimal inhibitory concentration

Minimal inhibitory concentrations (MIC) were determined by conventional broth dilution method (Siddaraju and Dharmesh, 2007). Serial dilutions (final volume of 1 ml) of Aq-FV (50 - 500 µg/ml) were prepared with 0.9% saline. 9 ml of Ham's F-12 nutrient medium with 5% FBS was added to each dilution. Broths were inoculated with 100 µl of HP suspension (5 x 10^4 CFU) and incubated for 24 h at 37°C. Clarithromycin was used as a positive control since HP is susceptible to clarithromycin and 0.9% saline as negative control. After 24 h, HP growth was assayed by measuring absorbance at 625 nm. MIC was defined as the lowest concentration in µg of Aq-FV to restrict the growth to <0.05 absorbance at 625 nm (no macroscopic visible growth).

Toxicity studies

Rats were fed once daily with Aq-FV (1 g/kg b.w.) in addition to normal feeding for 14 days. The control group received the vehicle only. 24 h after the last dose, number of animals survived were noted and sacrificed by cervical dislocation, blood was collected and serum was used for estimation of total protein and enzymes related to liver function tests; serum alanine aminotransferase (ALT), serum aspartate aminotransferase (AST) and alkaline phosphatase (ALP) using standard protocols (Nanjundaiah et al., 2009). Macroscopic inspection of liver, spleen, kidney, lungs and heart was done.

Statistical analysis

Data are expressed as Mean ± S.E.M. (n = 6). One-way ANOVA was performed to compare the means with control group. Statistically significant differences were accepted at $p<0.05$.

RESULTS

Effect of Aq-FV on ethanol, sodium hydroxide and sodium chloride-induced gastric ulcers

Ethanol (80%), NaOH (0.2mol/L) and NaCl (25%) produced extensive gastric lesions mainly in the glandular part of the stomachs. Ulcer index in ethanol, sodium hydroxide and sodium chloride treated-groups was observed 8.75 ± 0.84, 8.34 ± 0.95 and 7.84 ± 0.54, respectively. Pre-treatment of rats with Aq-FV antagonized this effect in a dose dependent manner and 300 mg/kg dose significantly prevented gastric mucosal lesions induced by necrotizing agents used. Omeprazole, a reference drug also caused a significant reduction in ulcer index (Figure 1).

Effect of Aq-FV on indomethacin-induced gastric ulcer

Indomethacin induced- gastric mucosal lesion formation was inhibited by Aq- FV in a dose dependent manner. 100 mg/kg dose showed 6.97 ± 0.70, 200 mg/kg dose, 6.70 ± 0.64, and 300 mg/kg dose, 4.21 ± 0.62 ($p < 0.001$) ulcer indices in the treated-group of animals (Table 1). Treatment with indomethacin significantly decreased the Alcian blue binding capacity of gastric wall mucus (335.65 ± 12.30 mg Alcian blue/g of tissue) as compared to control-group of rats (481.24 ± 14.56 mg Alcian blue/g of tissue).

Pre-treatment with Aq-FV at 100 mg/kg (337.63 ± 12.58 mg/g), 200 mg/kg (340.15 ± 12.86 mg/g), and 300 mg/kg (392.18 ± 12.47 mg/g) showed increasing Alcian blue binding capacity of gastric mucosa. Omepra-zole antagonized significantly indomethacin-induced gastric ulcer and mucus secretion effects (Table 1).

Effect of Aq-FV on pylorus-ligated gastric secretion and gastric ulcer index

In the treated control-group of rats, pylorus ligation for 3 hours resulted in an accumulation of 7.83 ± 0.38 mL of gastric secretions, titratable acidity; 172.21 ± 6.13 mEq/L and an ulcer index; 6.75 ± 0.42. Pre-treatment with Aq-FV and Omeprazole inhibited these effects. Highest dose (300 mg/kg of Aq-FV) tested, significantly ($p < 0.001$) decreased gastric secretion (4.13 ± 0.63), acidity (78.53 ± 4.21), and ulcer index (3.73 ± 0.52) in the treated-group of animals (Table 2).

Anti-*Helicobacter pylori* activity of Aq-FV

HP isolated from endoscopic samples was Gram-negative, motile and showed positive for urease, catalase and oxidase tests (Table 3). Further, it was confirmed by the response to antibiotics as it was resistant to antibiotics like erythromycin, nalidixic acid, polymixin B, amoxicillin and vancomycin and was susceptible to clarithromycin and metronidazole. The appearance of a characteristic white mucilaginous colony confirms the identity of bacteria as *H. pylori* (Table 3).

In the agar diffusion method, Aq-FV showed 41.2% inhibition zone around the disc at 10 mg/mL concentration while a susceptible antibiotic clarithromycin, 98.4% inhibition zone at 10 mg/mL. MIC values determined by broth dilution method were 500 µg and 100 µg for Aq-FV and clarithromycin, respectively (Table 4).

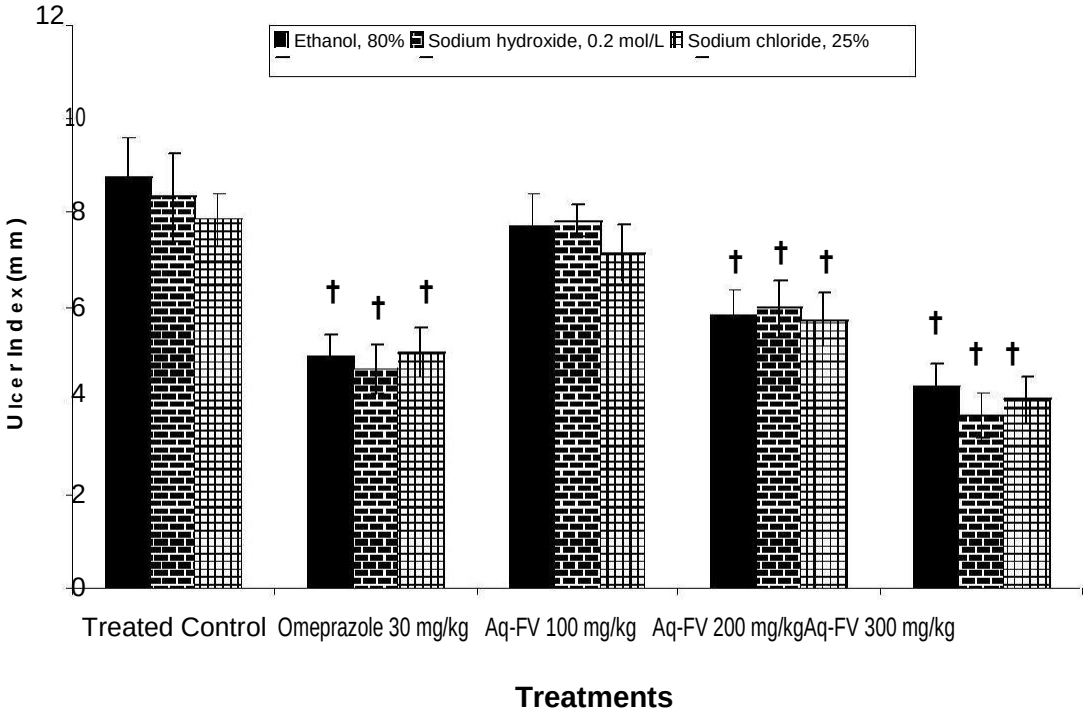

Figure 1. Effect of aqueous *Fumaria vaillantii* L. extract (Aq-FV) on gastric lesions induced by ethanol, sodium hydroxide and sodium chloride in rats.

Test drugs: significant from respective treated controls † $P < 0.05$. All other values are non-significant ($P > 0.05$) from respective treated control,
Mean values ± Standard error of means of six experiments.

Table 1. Effect of aqueous *Fumaria vaillantii* L extract (Aq-FV) on indomethacin induced-gastric mucosal lesions and gastric wall mucus concentration.

S. #	Treatment(s)	Dose (mg/kg, ig)	Ulcer index (mm)	Gastric wall mucus (µg Alcian blue of wet glandular tissue)
01	Vehicle (Control)	1 ml	0.46 ± 0.21	481.24 ± 14.56
02	Indomethacin (Treated control)	30	7.62 ± 0.54†	335.65 ± 9.30†
03	Omeprazole + Indomethacin (Positive control)	30+30	8.91 ± 1.35†	353.61 ± 6.82†
04	Aq-FV + Indomethacin	100 + 30	6.97 ± 0.70	337.63 ± 12.58
05	Aq -FV + Indomethacin	200 + 30	5.70 ± 0.64†	368.15 ± 9.86†
06	Aq -FV + Indomethacin	300 + 30	4.21 ± 0.62†	392.18 ± 10.47†

Indomethacin: significant from control (distilled water) † $p < 0.05$. Test drugs: significant from treated control (indomethacin) † $p < 0.05$. All other values are non-significant ($p > 0.05$) from treated control (indomethacin). Mean values ± Standard error of means of six experiments.

Toxicity studies with Aq-FV

Toxicity studies indicated no lethal effect up to 1 g/kg b.w. dose given orally for 14 days in the rats. No change was observed in the liver, spleen, kidney, lungs and heart of animals macroscopically. There were no significant differences in total protein, ALT, AST and ALP between normal and Aq-FV treated rats (Table 5) indicating no adverse effect on the major organs. Animals after above treatment schedule remained healthy as that of control animals with normal food and water intake, body weight gain and behaviour.

DISCUSSION

Gastric mucosa is normally well protected against aggressive/corrosive activities of gastric acid and pepsin

Table 2. Effect of aqueous *Fumaria vaillantii* L extract (Aq-FV) on gastric secretion, acidity and gastric ulcer index in pylorus ligated rats.

S. #	Treatment(s)	Dose (mg/kg, ip)	Volume of gastric content (mL)	Titratable acid	Ulcer index (mm)
01	Pylorus-ligated (control)	-	7.83 ± 0.38	172.21 ± 6.13	6.75 ± 0.42
02	Omeprazole (treated-control)	30	5.78 ± 0.77†	135.63 ± 4.54†	4.67 ± 0.62†
03	Aq-FV (treated)	100	6.45 ± 0.81	161.17 ± 4.76	6.62 ± 0.65
04	Aq-FV (treated)	200	6.02 ± 0.76‡	149.64 ± 4.81‡	5.11 ± 0.64‡
05	Aq-FV (treated)	300	4.13 ± 0.63†	78.53 ± 4.21†	3.73 ± 0.52†

Test drugs: significant from treated control (Shay Rats) † $P < 0.05$; ‡ $P < 0.001$. All other values are non-significant ($P > 0.05$) from treated control (Shay Rats).
Mean ± S.E.M = Mean values ± Standard error of means of six experiments.

Table 3. Characteristic biochemical tests for *H. pylori*.

S. #	Test	Result
01	Urease	Positive
02	Catalase	Positive
03	Oxidase	Positive
04	Gram staining negative	Gram
05	Motility	Motile
06	Colony characteristics	White mucilage
Antibiotic/antibacterial susceptibility of organism		
01	Erythromycin	Resistant
02	Nalidixic acid	Resistant
03	Polymixin B	Resistant
04	Vancomycin	Resistant
05	Amoxicillin	Susceptible (+)
06	Clarithromycin	Susceptible (+++)
07	Tetracycline	Susceptible (+)
08	Metronidazole	Susceptible (+++)

Helicobacter pylori obtained from endoscopic excision, was identified by Gram staining, enzyme analysis and morphological analysis in addition to antibiotic/antibacterial susceptibility.

Table 4. Anti-*H. pylori* activities of aqueous Fumaria vaillantii L extract (Aq-FV).

S. #	Treatment(s)	Inhibition (%)	MIC (µg/ml)
01	Saline (0.9%)	0.0	-
02	Clarithromycin	98.4	100
03	Aq-FV	41.2	500

Concentration (w/v) of all the test agents used; 10 mg/mL in 0.9% saline

Table 5. Toxicity studies with aqueous *Fumaria vaillantii* L extract (Aq-FV).

S. #	Parameters	Control	Aq-FV treated
01	Total protein	338 ± 36.71a	349 ± 35.61a
02	SGOT (U/dL)	18.12 ± 1.42a	15.61 ± 1.24a
03	SGPT (U/dL)	14.74 ± 1.06a	15.41 ± 1.05a
04	ALP (U/dL)	40.56 ±1.94a	42.04 ± 2.21a

SGPT: Serum glutamate pyruvate transaminase
SGOT: Serum glutamate oxaloacetate transaminase

by defensive/cytoprotective factors, that is, mucus, bicarbonate, prostaglandin secretions and blood flow. The mucosal concentration of prostaglandins has been found directly related to the gastric mucus, bicarbonate secretions and blood flow (Komoike et al., 2003).

Results of present study show that the Aq-FV possesses significant anti-secretory, anti-ulcer and cytoprotective properties in rats-models (Tables 1 and 2) in addition to the activity against *H. pylori* (Table 4). Pre-treatment with Aq-FV caused a dose-dependent (100 - 300 mg/kg, b.w.) reduction in the volume of basal gastric secretion, titratable acidity and lesions- formation in pylorus-ligated, Shay rats (Table 2). It has been found, anti-secretory agents e.g. H_2-receptor antagonists

ameliorate the decrease in gastric mucosal blood flow caused by factors that disturb the gastric mucosa such as indomethacin/NSAIDs and ethanol (Murashima et al., 2009). Gastric acid is an important factor in the genesis of ulceration in pylorus-ligated rats (Shay, 1945). Gastric acid secretions are believed to increase in the hyper-secretion model of pylorus ligature due to vagus-vagal reflux activation by the stimulation of pressure receptors in the antral gastric mucosa (Baggio et al., 2003). Since, Aq- FV markedly inhibited gastric acid secretion and luminal ulcers in pylorus-ligated rats (Table 2); this observed effect could be related, at least in part, to the ability of Aq-FV to reduce gastric acid secretion. It is believed that gastric acid secretion plays an important role in the progression from an erosive mucus layer to a gastric lesion.

On the other hand, substances which have the ability to suppress gastric acid secretion, such as proton pump inhibitors and histamine H_2-receptor antagonists are found to accelerate the healing process of the gastric ulcers or inhibit the formation of mucosal injury (Brzozowski et al., 2000). Aq-FV was observed to offer the gastric mucosa, a statistically significant and dose-dependent protection against ulceration caused by various necrotizing agents that is, ethanol and strong alkalis (Figure 1). Ethanol-induced gastric ulcers have been widely used in the evaluation of gastroprotective activity (Al Mofleh et al., 2008).

Ethanol is metabolized in the body and releases super-oxide anion and hydroperoxy free radicals. It has been found that oxygen- derived free radicals are implicated in the mechanism of acute and chronic ulceration in the stomach (Umamaheswari et al., 2007). The genesis of ethanol-induced gastric lesions is of multifactorial origin with a decrease in gastric mucus and is associated with the significant production of free radicals leading to increased lipid peroxidation which in turn causes damage to cells and cell membranes (Khazaei and Salehi, 2006). Cytoprotection caused by Aq-FV may be related to its ability to prevent gastric acid secretion and/or increase the mucosal defense such as prostaglandins and reduction in lipid peroxidation (Alqasoumi et al., 2008). Indomethacin, a non-selective cyclooxygenase inhibitor, treatment is known to induce gastric damage through multiple mechanisms, including suppression of prostaglandin generation, overproduction of leukotrienes, topical irritation and local blood-flow reduction (Whittle, 2003; Toma et al., 2005). Pre- treated rats with Aq- FV showed a significant protection in this model. Possibly, an enhanced level of gastric mucus, prostaglandins formation and leukotriene inhibition may contribute to the gastroprotective activity of Aq-FV.

The data revealed; Aq-FV significantly protected gastric mucosa against the depletion of gastric wall mucus. The mucus gel adhering to the gastric mucosal surface protects the underlying epithelium against acid, pepsin and necrotizing agents such as ethanol and indomethacin (Alqasoumi et al., 2008) . However gastric wall mucus, plays an important role in the defense of the gastric mucosa against aggression of chemical or mechanical factors than the soluble mucus in the lumen of the stomach (Allen and Flemström, 2005). Gastric wall mucus coating is believed to be important in facilitating the repair of the damaged gastric epithelium (Shih et al., 2005). Therefore, cytoprotection caused by Aq-FV might be due to, at least in part, from interaction with the adhering gastric mucus layer.

Furthermore, Aq-FV showed significant *in vitro* anti- *H. pylori* activity (Table 4). *H. pylori* have been reported to weaken the protective mucous coating of the stomach, which allows acid to get through to the sensitive lining beneath. Both the acid and the bacteria irritate the lining and cause ulcer formation (Brzozowski et al., 2006) . It has also been suggested that, infection caused by *H. pylori* is mediated largely through the generation of reactive oxygen species, especially the hydroxyl radicals (Nanjundaiah et al., 2009). It is speculated therefore, anti-H. *pylori* activity of Aq-FV may be responsible for its observed gastroprotective, anti-secretary and anti-ulcer effects.

Fumaria extracts in chloroform: medianol (1:1) displayed highly potent inhibition against acetylcholine-esterase and butyrylcholinesterase enzymes at 1 mg/ml concentration (Orhan et al., 2004), which may cause the stimulation of gastric acid secretion via cholinergic-parietal cell stimulation. Data clearly indicating the opposite effects caused by aqueous extract of *F. vaillantii* L that is, reduction in gastric acid secretion, acidity and ulcer formation. It seems likely the responsible entity for inhibition of acetylcholinesterase and butyrylcholineste-rase enzymes, is not water extractable rather chloroform: medianol (1:1) soluble. On the other hand, Gilani et al., (2005) indicated the possibility of atropine sensitive activities of Aq-FV that is in accord to our findings.

In conclusion, the data obtained, confirm the traditional indications for *F. vaillantii* L and present a new therapeutic option for the treatment of gastric ailments like gastric ulcer. The exact mechanism(s) underlying this anti-ulcerogenic effect remain unclear, but the extract contains substance(s), which might increase endogenous prostaglandins and mucus synthesis in addition anti-*H. pylori* activity. Furthermore, the anti-secretory mechanism can not, however, be dismissed. The detailed phytochemical studies followed by pharmacological investigations and toxicity evaluations are still required to isolate the pure active principle(s) of the Aq-FV and to elucidate their precise mode(s) of anti-ulcer actions.

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