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Anti-ulcer activity of the three different extracts of *Ferula lehmannii* Boiss leaf in rats

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Abstract: *Ferula lehmannii* Boiss (FLB) is a perennial plant that belongs to the family Apiaceae, which is a traditional remedy used to treat gastric ulcers in Xinjiang. The main purpose of the research is to investigate the possible antiulcer effect of three different extracts, water decoction (WD), fresh liquid (FL), and chloroform extract (CE), using a model of acetic acid-induced gastric ulcer. 56 rats were divided into seven groups (n=8) and treated ranitidine and extracts of FLB. After 12 days of treatment, the ulcer index and biochemical parameters were evaluated. In all tested groups, the results indicated that the chloroform extract and water decoction highly significantly decreased the mucosal damage index as compared to the model group, restoration of glutathione per oxidase (GSH-PX) levels and super oxide dismutase (SOD) activity, and reduction of malondialdehyde (MDA) levels. The ulcer inhibition rate of water decoction group, fresh liquid and chloroform extract group reached 25.30%, 4.96% and 30.87%, respectively. The macroscopic observations were supported by histological findings. 44, 31, 32 compounds were identified through GC-MS analysis of different extracts. In conclusion, FLB exhibits potential anti-ulcer activity attributed to its high content terpenoid, phytosterin and fatty acid, the underlying antiulcer mechanism might be relevant to the reduction in inflammation and oxidative stress.

Keywords: *Ferula lehmannii* Boiss, gastric ulcer, antioxidant, different extracts.

INTRODUCTION

Peptic ulcer disease, also known as peptic ulcer or stomach ulcer, the occurrence of it is related to the combined effects of various factors affecting millions of people worldwide (Li W *et al*., 2016). Gastric was regarded as a global health problem that are prevalent in many countries and regions (Thorsen *et al*., 2013). The development of gastric ulcers is caused by the destruction of the mucosal barrier through an imbalance between attack and defense factors that are existing in gastric mucosa (Choi *et al*., 2009). Gastric acid and *Helicobacter pylori* are the main reasons for damage to the gastric mucosa. Other factors that also can damage or destroy the defense mechanism of the gastric mucosa include physical and chemical factors, drug factors, alcohol, tea, and intense spices. At present, acid-suppressing drugs and gastric mucosal protective drugs are available methods for the treatment of gastric ulcers. However, many disadvantages have been reported such as osteoporosis, hypercalcemia, constipation and the deterioration of carcinoids in the gastric mucosa (Devault and Talley, 2009; Eom *et al*., 2011). Thus, natural products that can treat gastric ulcer and exhibit few side effects are necessary.

The genus *Ferula* (Apiaceae) consists of 170 species around the world (Pimenov and Leonov, 1994). In China, approximately 25 species are mainly distributed in Xinjiang province and grow on mountains and desert areas. Aromatic plants have been subjected to phytochemical analysis for their volatile components, and results unveiled these bioactive phytochemicals which mainly belong to the monoterpene and sesquiterpene classes of compounds exists in the essential oils and have valuable therapeutic potentials (Iranshahi, 2011). *Ferula* species has been confirmed the occurrence of terpenoids, sulfur-containing compounds and coumarins. Numerous investigations on essential oils of *Ferula* species have confirmed some valuable properties, such as antimycobacterial, anticonvulsant, antioxidant, antiulcer, digestive and sedative features (Sahebkar and Iranshahi, 2010; Bagheri *et al*., 2010; Alqasoumi *et al*, 2011). *Ferula lehmannii* Boiss is found to grow widely in Shihezi, Xinjiang, its leaves have a strong garlic odor. The aerial parts of FLB are traditionally used as a wild food plant to cure stomach diseases. In addition, many local herdsmen mix it in the food of sheep and cattle to cure poor digestion, and this practice has proven to be effective. However, no studies have reported the active role of FLB in the treatment of gastric ulcer.

This work aimed to investigate the volatile substances of three different extracts and gastroprotective effects of the aerial parts of *Ferula lehmannii* Boiss in acetic acid-induced gastric ulcer in rats, provide a theoretical basis and technical support for the utilization of FLB in Xinjiang.

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MATERIALS AND METHODS

Materials

Fresh aerial parts of *Ferula lehmannii* Boiss (FLB) were collected in April 26, 2016 from Nanshan Mountain, Shihezi City, Xinjiang, China. The plant was rolled out for more than a week and dried naturally. It was identified by Prof. Ping Yan from the Department of Botany, Shihezi University and several local botanists. A voucher specimen of the plant was deposited in the herbarium (number 12097) of Shihezi University of Xinjiang.

Assay kits and ranitidine were purchased from Jiancheng Biological Engineering Research Institute (Nanjing, China) and Taiyuan Shanxi Pharmaceutical Co., Ltd, respectively.

Preparation of different extracts

Fresh whole the aerial parts of FLB (100 g) were cut at an average length of 1-2 cm and watered with 100 mL of distilled water. The filtrate was placed in a bottle and stored at low temperature. This liquid was regarded as fresh liquid (FL).

The water decoction (WD) was prepared as follows. Ground powder (100 g) was mixed with 10 times volume of distilled water and soaked for 1h. The medicinal materials were extracted three times from leaves under reflux with water at boiling temperature for 30 min, and the decocted liquids were concentrated to 100mL.

The chloroform extract (CE) was prepared by soaking grass 30 min at room temperature, heating the leaves for one hour, and filtering the liquid. This process was repeated three times. The extract was concentrated at reduced pressure via rotary evaporation. After completely removing the organic solvent, the extract was dissolved with edible oil, the dose was 1 g of extract with 9 g of oil.

Experimental animal

Adult Sprague–Dawley rats (180-220g) were purchased from the Animal Research Center at Xinjiang Medical University [Animal center certificate: SYXK (XIN), XJ-001]. In the 50% humidity, 25°C±1°C animal room, adaptive feeding for 3 days, gave the basic diet, free drinking water, except for 12h prior to the experiment when they were deprived of food. These Experimental procedures followed the rules of guidelines for animal experiments of Shihezi University and regulations of Institutional Animal Ethics Committee.

Acetic acid-induced chronic gastric ulcers

A total of 56 rats were randomly divided into seven experimental groups, each containing eight rats: (1) model group (MG), (2) normal control group (NG), (3) sham-operated group (SG), (4) ranitidine group (RG, 0.03 g/mL, 1 mL/100 g), (5) water decoction group (WDG, 1 mL/100 g), (6) fresh liquid group (FLG, 1 mL/100 g), and (7) chloroform extract group (CEG, 1 mL/100 g).

Acetic acid induced gastric ulcers by treatment (Okabe and Pfeiffer, 1971) with few modifications. Except for NG, food was withheld for 24 h before modeling, whereas water was allowed. The rats were anaesthetized with 3% pentobarbital sodium. After laparotomy, the stomach was exposed and 50μL of 20% (v/v) acetic acid was injected into the submucosal layer between the gastric sinus muscular layer and serous membrane for 1 min. SG rats were injected with 50mL of sterile saline. The stomach was replaced and poured with some penicillin, sutured, and disinfected. A total of 48 routine feedings after ulcer induction was performed. Each group was administered through gavage for 12 days. MG, SG, and NG were given 1 mL/100 g normal saline.

Macroscopic assessment of gastric ulcer

The ulcer index was calculated by the following formula:
$S\ (mm^2) = 1/4 \times DL \times DS \times \pi\ (\pi = 3.14)$
where S, DL, and DS represent ulcer index, ulcer length, and ulcer width, respectively.
Inhibition (%) = {[(S of MG) – (S of EG)]/ S of MG} × 100
where S, MG, and EG represent the ulcer index, model group, and experimental group, respectively.

Histological examination

Parts of gastric tissue gained from each experimental groups were placed in 10% formalin solution 24 h, alcohol and xylene were used for dehydration, embedded in paraffin wax, before hematoxylin/eosin (H&E) staining sectioned at 4 μm for histological evaluation.

Determination of biochemical parameters

SPSS software (version 19.0) was used for statistical analysis. Results are expressed as the mean ± standard error of the mean. Differences between means were determined by one-way ANOVA. Super oxide dismutase (SOD), Malondialdehyde (MDA) and Glutathione per oxidase followed by Tukey multiple comparison test. A value of $p<0.05$ was considered statistically significant, whereas $p<0.01$ was defined as very significant.

Gas chromatography–mass spectrometry (GC–MS) analysis

Volatile components from different extracts were identified by GC-MS analysis. Using an Agilent GC-MS equipped with a DB-5 fused silica column (30 m × 0.250 mm, film thickness 0.25μm). The following operating conditions were applied: oven temperature of 60°C-280°C, heating rate of 4°C min^{-1} raised to 280°C and maintained for 20 min. The sample (1μL) was injected with a split ratio of 1:10. The ionization energy was 70 eV, and scan range was 40–550 U.

Table 1: Effects of different subjects on gastric ulcer induced by acetic acid in rats

Group	Ulcer index	Inhibition
MG	41.14±1.48	-
SG	-	-
NG	-	-
RG	27.78±2.78**	32.48%
WDG	30.73±4.19**	25.30%
FLG	39.10±1.98	4.96%
CEG	28.44±1.93**	30.87%

Values are mean ± SEM. (n=8). Statistical comparison was performed using ANOVA followed by Tukey′s test
* $p < 0.05$,significantly different from the MG (model group).
** $p < 0.01$, extremely significantly different from the MG.

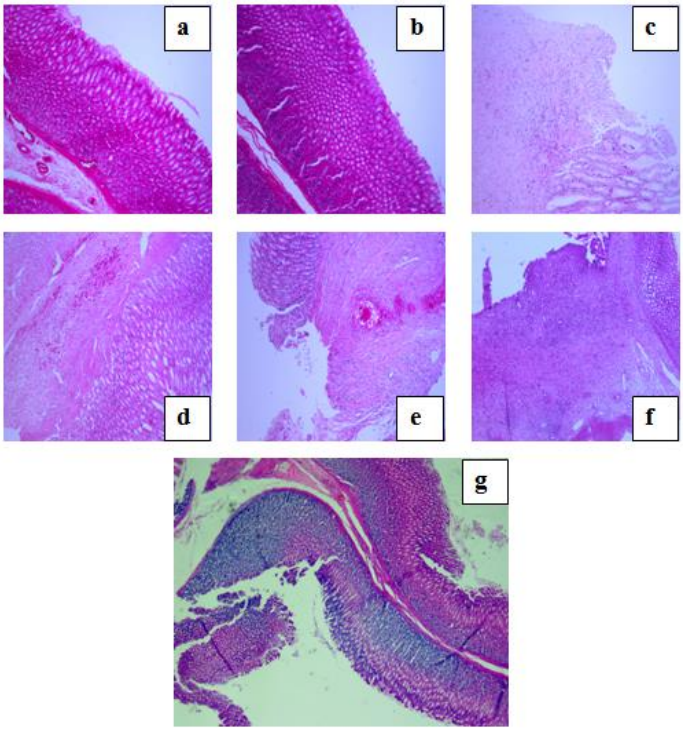

Fig. 1: Representative histological H&E analysis of acetic acid-induced experimental chronic gastric ulcers. Microscope magnification ×100. a sham-operated group (SG), b normal group (NG), c ranitidine group (RG), d water decoction group (WDG), e fresh liquid group (FLG), f chloroform extract group (CEG, 1 ml/100 g), g model group (MG).

Chemical compositions were identified by computer matching of their spectral patterns with WILEY and NIST and by comparing the fragmentation patterns of mass spectra and retention indices relative to *n*-alkanes (C_7-C_{40}) with those given in the literature. Percentages of compounds were calculated using the area normalization method without considering the response factor (Adams, 2007)

STATISTICAL ANALYSIS

SPSS software (version 19.0) was used for statistical analysis. Differences between means were determined by One-way analysis of variance (ANOVA) followed by Tukey multiple comparison tests.

RESULTS

Ulcer index and ulcer inhibition

The ulcer index and inhibition recorded after pre-treatment are shown in table 1. Ranitidine group (RG), water decoction group (WDG) and chloroform extract group (CEG) exhibited anti-ulcer effects and significantly reduced the ulcer area by 32.48, 25.30 and 30.87%, respectively. No difference was observed between CEG and RG based on their inhibition data. These results indicate that chloroform extract was effective for the treatment of gastric ulcer. However, fresh liquid group (FLG) showed few therapeutic effects, 4.96% inhibition and did not reach statistical significance.

Histological H&E analysis

Histological analysis of gastric tissues is shown in fig. 1. The normal architecture of stomach with intact gastric mucosa and neatly arranged glands were observed in sham-operated group (SG) and normal control group (NG). No evidence of inflammatory cells and edema was found. The injection of acetic acid caused severe disruption of gastric epithelia in model group (MG), in which the glands were completely destroyed and identical with the macroscopic appearance of chronic gastric erosion. Gastric tissue regeneration signals were not observed in the group treated with FL. However, moderate regeneration of the gastric mucosa and arrangement of columnar structures above the granulation were observed in WDG and CEG, similar to the group treated with ranitidine. WDG and CEG still suffered from mild inflammatory infiltration and edema. However, they exhibited visible effects of prevention and treatment of gastric ulcer compared with MG.

Effects of FLB on the levels of SOD, MDA and GSH-PX

In chronic ulcer, acetic acid stimulated the increase of Malondialdehyde (MDA) levels and decreased the Super oxide dismutase (SOD) and Glutathione per oxidase (GSH-PX) contents. The treatment of rats with WD, CE, and ranitidine led to a significant decrease in MDA when compared with the MG ($p<0.01$), whereas FLG did not change significantly (fig. 2). SOD activity in MG, RG, WDG, FLG, and CEG were lower than that in NG. In particular, WDG and CEG significantly improved when compared with MG ($p<0.05$), but their performance was inferior to RG (fig. 3). GSH-PX is one of the important enzymes that decompose hydrogen peroxide. As shown in fig. 4, besides NG, RG and CEG significantly increased ($p<0.05$) compared with MG. The results of other groups were not significantly different.

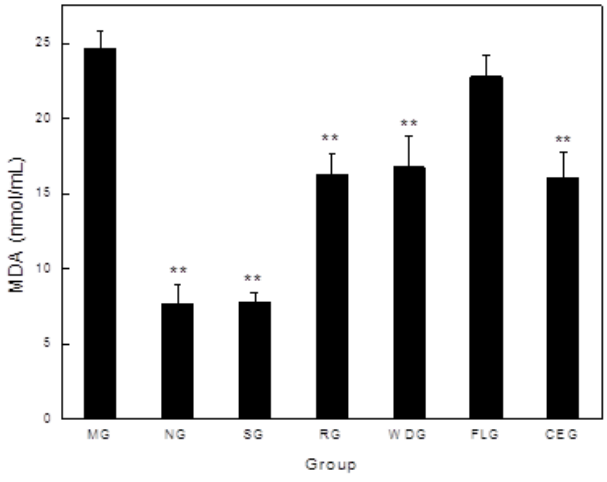

Fig. 2: MDA levels in serum.*p<0.05, significantly different from the MG (model group).**p<0.01, extremely significantly different from the MG.

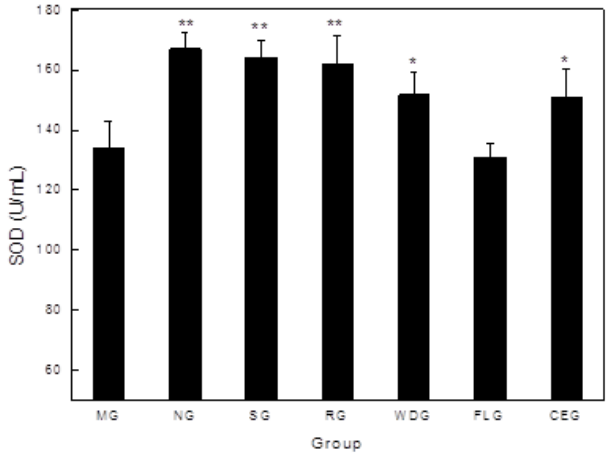

Fig. 3: SOD levels in serum. *p<0.05,significantly different from the MG (model group). **p<0.01, extremely significantly different from the MG.

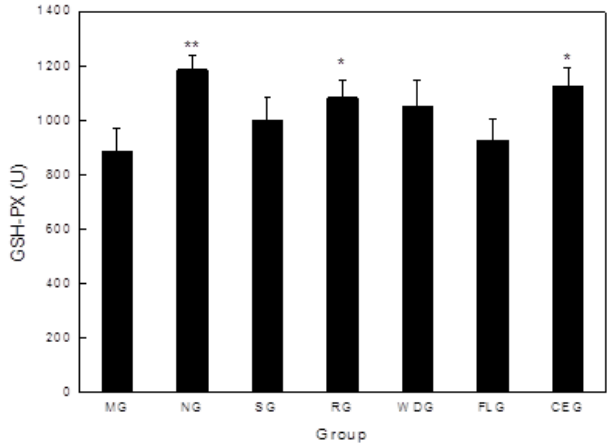

Fig. 4: GSH-PX levels in serum. *p<0.05, significantly different from the MG (model group). **p<0.01, extremely significantly different from the MG.

Chemical composition of water decoction (WD), fresh liquid (FL), and chloroform extract (CE)

Gas chromatography–mass spectrometry (GC-MS) analysis identified 44, 31, and 32 compounds from WD, FL, and CE, respectively. As shown in table 2, differences were observed among the three samples. In water decoction, the abundant compounds were aromatic compounds such as benzaldehyde (12.11%) and 2-phenylethanol (10.20%). In addition, components of the volatile oil were decocted out which mainly weres terpenoids, accounted for 36.38%. In fresh liquid, the major compounds were (Z)-sec-butyl propenyl disulfide (34.43%) and leaf alcohol (21.82%), it also contains a small amount of aromatic compounds and 15 terpenoids. In chloroform extract, the major components were linolenic acid (14.33%), 1-heptatriacotanol (12.54%), and β-sitosterol (11.54%), these substances do not exist in the other two extracts. The main volatile chemical constituents of *Ferula lehmannii* Boiss were monoterpenes, sesquiterpene, fatty acid and steroids.

Table 2: The volatile compounds of different extracts from the aerial parts of *Ferula Lehmannii* Boiss

Number	Composition	Molecular formula	ID[a]	Relative content(%)[b]		
				WD	FL	CE
1	Dimethyl sulfide	C_2H_6S	B		0.20±0.01	
2	3-Methyl-2-buten-1-ol	$C_5H_{10}O$	B	0.98±0.02		
3	(Z)-1-(methylthio)-1-Propene	C_4H_8S	A	0.44±0.01		
4	2-Methylcyclo pen tanone	$C_6H_{10}O$	B			0.39±0.02
5	2-Furanmethan ol	$C_5H_6O_2$	B	1.63±0.10		
6	2-Hexenal	$C_6H_{10}O$	B	0.34±0.01	1.34±0.06	
7	leaf alcohol	$C_6H_{12}O$	B	5.83±0.16	21.82±7.47	
8	1-Hexanol	$C_6H_{14}O$	B	1.20±0.03	2.82±0.21	
9	Styrene	C_8H_8	B	0.18±0.01		
10	Ethylbenzene	C_8H_{10}	B	0.13±0.01		
11	Benzaldehyde	C_7H_6O	B	12.11±4.35	1.29±0.20	4.51±1.60
12	Dimethyl trisulfide	$C_2H_6S_3$	B			1.58±0.32
13	Benzenemethanol	C_7H_8O	B	7.90±1.13	2.36±0.42	
14	Benzoic acid	$C_7H_6O_2$	B			0.56±0.04
15	Guaiacol	$C_7H_8O_2$	B	0.90±0.02		
16	Benzeneacetaldehyde	C_8H_8O	B	5.58±1.17	0.89±0.01	0.86±0.31
17	Acetophenone	C_8H_8O	B	1.71±0.42		
18	2-Phenylethanol	$C_8H_{10}O$	B	10.20±3.25	1.95±0.52	
19	Methyl heptenol	$C_8H_{16}O$	B	0.57±0.02		
20	Octanal	$C_8H_{16}O$	B			0.84±0.11
21	2-Pentylfuran	$C_9H_{14}O$	B		0.41±0.01	
22	Umbelliferone	$C_9H_6O_3$	A			0.34±0.31
23	Cosmene	$C_{10}H_{14}$	B		2.55±0.32	
24	(-)-β-Pinene	$C_{10}H_{16}$	A			0.19±0.01
25	Artemisia triene	$C_{10}H_{16}$	B	0.21±0.02		
26	α-Pinene	$C_{10}H_{16}$	B		0.33±0.04	
27	Camphene	$C_{10}H_{16}$	B		0.72±0.00	
28	β-Pinene	$C_{10}H_{16}$	B	0.37±0.03		
29	β-Myrcene	$C_{10}H_{16}$	B	6.09±2.52		
30	β-Terpinen	$C_{10}H_{16}$	A	0.27±0.30		
31	Limonene	$C_{10}H_{16}$	B	3.63±0.01	0.16±0.01	
32	β-Phellandrene	$C_{10}H_{16}$	B	0.27±0.02		
33	(E)-Ocimene	$C_{10}H_{16}$	B	0.94±0.04		
34	(Z)-Ocimene	$C_{10}H_{16}$	B		0.69±0.01	
35	Terpinolene	$C_{10}H_{16}$	B	0.25±0.00		
36	Methyl sec-butyl disulphide	$C_5H_{12}S_2$	A	0.48±0.02	0.30±0.02	
37	Benzeneacetaldehyde	$C_{10}H_{10}O$	B	0.98±0.01		
38	Myrtenol	$C_{10}H_{16}O$	B	0.94±0.01	0.50±0.02	
39	Perillaldehyde	$C_{10}H_{14}O$	B	1.90±0.41		
40	Cuminol	$C_{10}H_{14}O$	B	0.42±0.03		
41	Thymol	$C_{10}H_{14}O$	B	0.26±0.02		
42	β-cyclocitral	$C_{10}H_{16}O$	B	0.37±0.02	0.29±0.01	
43	Perilla alcohol	$C_{10}H_{16}O$	B	3.37±0.45	1.19±0.16	
44	δ-camphor	$C_{10}H_{16}O$	A	0.26±0.02		
45	Cis-Rose oxide	$C_{10}H_{18}O$	B	0.38±0.04		
46	Terpinen-4-ol	$C_{10}H_{18}O$	B	0.43±0.01		
47	7-methyl-3-methylene-6-Octen-1-ol	$C_{10}H_{18}O$	A		2.12±0.14	
48	γ-Isogeraniol	$C_{10}H_{18}O$	A	5.49±1.02		
49	Borneol	$C_{10}H_{18}O$	B	4.18±2.01	3.16±0.34	
50	α-Terpineol	$C_{10}H_{18}O$	B	1.98±0.14	0.26±0.01	
51	Geraniol	$C_{10}H_{18}O$	B		1.76±0.03	
52	(Z)-sec-Butyl propenyl disulfide	$C_7H_{14}S_2$	B	5.61±0.41	34.43±9.43	1.01±0.01
53	Jasmone	$C_{11}H_{16}O$	B	0.34±0.01	0.61±0.25	
54	(Z)-1-(But-1-en-1-yl)-2-(secBbu tyl) disulfane	$C_8H_{16}S_2$	A			0.24±0.01
55	3,6-Dimethyl-4,5-dithiaoctane	$C_8H_{18}S_2$	A		0.69±0.01	
56	β-Ionone	$C_{13}H_{20}O$	B	1.90±0.54	0.64±0.01	

Continue…

Number	Composition	Molecular formula	ID[a]	Relative content(%)[b]		
				WD	FL	CE
57	1-(1-(Methyl thio) propyl)-2-propyl disulfane	$C_7H_{16}S_3$	A			1.67±0.61
58	α-Gurjunene	$C_{15}H_{24}$	A		0.89±0.02	
59	(-)-Aristolene	$C_{15}H_{24}$	B			0.15±0.01
60	cis-β-Guaiene	$C_{15}H_{24}$	A	0.37±0.00		
61	β-Bisabolene	$C_{15}H_{24}$	B	0.16±0.01		
62	γ-Selinene	$C_{15}H_{24}$	B		0.10±0.01	
63	Elemicin	$C_{12}H_{16}O_3$	B	0.54±0.02	0.52±0.02	
64	Isoaromadendrene epoxide	$C_{15}H_{24}O$	B			5.75±1.63
65	β-Dihydroagaro furan	$C_{15}H_{26}O$	B			0.23±0.03
66	Hedycaryol	$C_{15}H_{26}O$	B			0.17±0.01
67	Guaiol	$C_{15}H_{26}O$	B	2.21±0.70	1.04±0.04	0.12±0.02
68	γ-Eudesmol	$C_{15}H_{26}O$	A		2.02±0.03	0.28±0.01
69	Agarospirol	$C_{15}H_{26}O$	A	1.63±0.14		
70	2-Hexyl-1-decanol	$C_{16}H_{34}O$	B			8.92±2.21
71	Hexadecanoic acid	$C_{16}H_{32}O_2$	B			2.34±0.62
72	Linolenic acid	$C_{18}H_{30}O_2$	B			14.33±7.20
73	Linoleic acid	$C_{18}H_{32}O_2$	B			2.69±0.20
74	Oleic Acid	$C_{18}H_{34}O_2$	B			0.23±0.01
75	1-Nonadecanol	$C_{19}H_{40}O$	A			4.29±1.30
76	Neophytadiene	$C_{20}H_{38}$	A			1.85±0.62
77	Phytol	$C_{20}H_{40}O$	B			2.43±0.16
78	cis-8,11,14-Eicosatrienoic acid	$C_{20}H_{34}O_2$	A			0.84±0.13
79	Ethyl linoleate	$C_{20}H_{36}O_2$	B			0.23±0.02
80	Methyl arachidonate	$C_{21}H_{34}O_2$	A			0.37±0.01
81	Stigmasterol	$C_{29}H_{48}O$	A			4.45±0.32
82	β-Sitosterol	$C_{29}H_{50}O$	B			11.54±3.34
83	Vitamin E	$C_{29}H_{50}O_2$	A			1.46±0.21
84	1-Heptatriacota nol	$C_{37}H_{76}O$	A			12.54±5.63
Sulfur-Containing Compounds				6.53%	35.62%	4.50%
Terpenoids				36.38%	15.23%	6.89%
Steroids						15.99%
Fatty acid						20.43%

[a]Identification method: A, identified by comparing of mass spectra with MS libraries. B, identified by retention index identical to bibliography.
[b]Relative content(%): peak area relative to total peak area.

DISCUSSION

The widely recognized medicinal component of the genus *Ferula* is oleo-gum-resin, numerous studies have investigated the medicinal chemical composition of this genus. The composition analysis of *Ferula* species suggested the presence of biologically active compounds, such as daucane sesquiterpenes, sulfur containing molecules, and coumarins (Dastan *et al*., 2012; Sahebkar *et al*., 2010; Ibraheim *et al*., 2012). In Iran, the *Ferula* genus has many applications in traditional medicine, such as preservation of meat and oil and ulcer treatment.

The acetic acid-induced rat gastric ulcer model is the classical model of gastric ulcer. It has good repeatability, especially in deep and large ulcers with long healing time, easy relapse after treatment, and are similar to human chronic gastric ulcers (Okabe and Amagase, 2005; Okabe and Pfeiffer, 1972). The origin of acetic acid-induced gastric lesions is a multi-factorial process that starts mainly with the depletion of gastric wall mucous content (Amagase *et al*., 2003). Such a depletion is frequently related to the remarkable production of free radicals, resulting in mucosal damage, including ulceration, erosion, and hemorrhage (Verma and Kumar, 2016). The harmful substances that cause gastric ulcers are oxygen-derived free radicals, primarily hydroxyl radicals, super-oxide anions, and lipid peroxides, (Da *et al*., 2013). SOD and GSH-PX both decreased, which indicated the process of oxidative impairment and ulcer expand. The data revealed that FLB interfered with the oxidative proceeding by reducing free radical levels MDA and increasing SOD and GSH-PX activity. Thus, FLB exerted a bio-protective effect to scavenge free radicals and reduce the harmful effect of acetic acid.

From the macro-analysis, the healings of the ulcer surface in the drug groups were different from the model group. Especially the ranitidine group, chloroform extract group and water decoction group, they had no perforation and less ulcer exudation, serous adhesion was not serious. Analysis from the pathological observation, the gland morphology of chloroform extract group and water decoction group were basically repaired, even there were

a few inflammatory cells. No obvious pathological state was found in submucosal microcirculation, and the recovery was similar to ranitidine group. In conclusion, chloroform extract and water decoction can effectively repair damaged gastric tissue, improve structure of gastric tissue, the effect was similar to ranitidine.

The GC-MS analysis of different extracts showed the presence of 84 chemical constituents. Water decoction is the main form of traditional Chinese Medicine, the leakage of ingredients in the extraction process using organic solvents can be ensured by direct injection. The result showed there were a large amount of volatile oil components in the soup, 24 terpenoids comprised the largest group. Rozza investigated gastroprotective mechanisms of Citrus lemon (Rutaceae) essential oil and showed that its majority compound limonene had anti-ulcer activity which was involved with increasing in mucus secretion (Rozza *et al*., 2011), a study indicated that the oral administration of β-myrcene had significantly decreased gastric and duodenal lesions as well as increased gastric mucus production (Bonamin *et al*., 2014), Terpinen-4-ol was a mixture of optical isomers and each possessed potent antiulcer activity (Matsunaga *et al*., 2000). The presence of these terpenes compounds can be correlated with the gastroprotective activity. Chloroform extract could promote healing and recovery of chronic experimental gastric ulcer in rats, it produced remarkable therapeutic effects and contained fatty acids, sterols and a small amount of terpenoids, especially the high content of linolenic acid (14.33%) and β-sitosterol (11.54%), they have strong antioxidant effects which can increase the activity of SOD and GSH-PX, reduce the generation of MDA (Marques *et al* 2013; Lagarda *et al* 2006), thus protective activity of CE against experimental gastric mucosal lesions could be due to prevent or scavenge free radicals generated during initiation of ulcer pathogenicity.

In this study, 44, 31, and 32 compounds were identified via GC–MS of different samples. The gastric ulcer model in rats induced by acetic acid was successfully implemented. The aerial parts of *Ferula lehmannii* Boiss, particularly chloroform extract and water decoction, could effectively cure gastric ulcer. The underlying mechanism might be associated with the reduction in oxidative stress by decreasing lipid peroxidation and promoting the synthesis of oxygen free radical scavengers. Therefore, *Ferula lehmannii* Boiss may be a potential drug in the treatment of gastric ulcer and future studies are necessary to confirm the protective mechanism.

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