

ANTI-ULCEROGENIC ACTIVITY OF *FERULAGO ISAUURICA* AND *F. SYRIACA* GROWING IN TURKEY

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Abstract

In order to evaluate the claimed folkloric utilisation of Ferulago species, the anti-ulcerogenic activities of lyophilised aqueous extracts obtained from the aerial parts and roots of Ferulago isaurica Peşmen and F. syriaca Boiss. (Apiaceae) have been studied using EtOH-induced ulcerogenesis model in rats. All plant parts exhibited statistically significant gastroprotective activity against in vivo model employed in the present study however the highest activity was observed for the roots of F. isaurica (100%).

Key Words: Anti-ulcerogenic activity, Apiaceae, Ethanol-induced ulcerogenesis, *Ferulago isaurica*, *Ferulago syriaca*, Peptic ulcer.

Türkiye’de Yetişen *Ferulago isaurica* ve *F. syriaca* Türlerinin Antiülserojenik Aktivitesi

Ferulago türlerinin halk arasındaki kullanımını değerlendirmek üzere, Ferulago isaurica Peşmen ve F. syriaca Boiss.’in (Apiaceae) toprak üstü kısımları ve köklerinden ayrı ayrı hazırlanan liyofilize sulu ekstrelerin antiülserojenik etkisi sıçanlarda EtOH ile oluşturulan ülser modeli ile çalışılmıştır. Tüm ekstreler uygulanan modele karşı istatistiksel olarak belirgin bir gastroprotektif aktivite gösterirken, en yüksek aktivite F. isaurica köklerinde görülmüştür (%100).

Anahtar Kelimeler: Antiülserojenik aktivite, Apiaceae, Etanolle oluşturulan ülser, *Ferulago isaurica*, *Ferulago syriaca*, Peptik ülser.

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Introduction

For the discovery of new leading drug molecules which would be used for the benefit of mankind nature offers unlimited resources. In order to evaluate these sources it is logical to give priority to the folk remedies used in traditional medicine. There have been quite a high number of traditional remedies worldwide used to treat various gastric disorders such as stomach ache and peptic ulcers for thousands of years (1).

The plants of the genus *Ferulago* have been used since antiquity in folk medicine against ulcer, snake bites, as well as against headache and spleen disturbances (2). *Ferulago* species, as well as *Ferula* and *Prangos* species are known as a common name of “Çakşır” or “Çağşır” in Turkey and the roots have mostly been used as aphrodisiacs (3). Their aerial parts are especially used for the rutting of the sheep, and the decoction of the roots is also probably used as aphrodisiac in men, though nobody admits that they are using it themselves. Moreover, these species are also reported to be used as sedative, digestive, tonic, to heal hemorrhoids and against intestinal worms (4). On the other hand, *Ferula foetida*, not found in Turkey, is also reported to be used for chronic gastritis, dyspepsia and irritable colon, though unproven scientifically. In homeopathy, this plant is also suggested to treat symptoms of low gastric acid levels, feeling of stomach pressure, flatulence and loose stools (5). Since *Ferulago* and *Ferula* species are closely allied and both have the same local name in Anatolia, *Ferulago* species might also have a similar gastro-intestinal activity as cited in PDR for *Ferula* species (5).

F. isaurica Peşmen is a narrow endemic species of Turkey which is reported to locate only in Alanya, South Anatolia. *F. syriaca* Boiss. is not an endemic species, but it has a limited distribution in Turkey, Syria, Palestine and Cyprus. Both species are perennial plants, reaching up to 270 cm in height.

The aim of the present study is to evaluate the anti-ulcerogenic activity of two Turkish *Ferulago* species, *F. isaurica* and *F. syriaca*, to prove the folkloric claim on *Ferulago* species against gastric complaints using *in vivo* EtOH-induced ulcerogenesis model in rats.

Experimental

Plant Materials

The collection sites of the plants are given below:

- *F. isaurica* Peşmen: Antalya, Alanya, 6 km after Derince turn, rocky slopes facing north, 990-1040 m, 16/7/2000, AEF 22956.

- *F. syriaca* Boiss: Hatay, Yayladağ Road, on the way to Ziyaret Mountain, rocky slopes, 480 m, 23/6/2001, AEF 22951.

Both of the species were identified by C. S. Erdurak (Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Botany). Voucher specimens are deposited in AEF, the Herbarium of Ankara University, Faculty of Pharmacy Ankara, Turkey.

Preparation of the test samples

Although decoction of the root is described as remedy in folk medicine, the aqueous extracts obtained from either aerial parts or roots were administered in rats. For the extraction procedure 10 g of material was extracted by boiling in 150 ml of distilled water for 20 minutes, filtered and lyophilised using Labconco Freeze Dry System/Freezone® 4.5 device. Doses of the extracts were estimated as the amount of extract (mg) obtained from 10 g of plant part with water as described above and administered as per kg of body weight in 5 ml/kg volume as suspension in 0.5% carboxymethylcellulose (CMC)/distilled water (6).

Animals

Sprague-Dawley rats of either sex (125-170 g) purchased from Gülhane Military Academy of Medicine (Ankara) were used in biological tests. The animals were left 48 hours for acclimatisation to animal room conditions and were maintained on standard pellet diet and tap water ad libidum. The food was withdrawn 24 hours before the experiment, but free access of water was allowed. To avoid coprophagy the rats were fasted in wire-

bottomed cages. For each group 6 rats were used. The test samples were administered to animals in 5 ml/kg body weight dosage as a suspension in 0.5% CMC/distilled water. The control group animals were given vehicle and received the same experimental handling as those of the test group.

Effects on ethanol-induced ulcerogenesis

Test sample was administered orally 15 min before the oral application of EtOH 96% (1 ml) to a group of six rats (7). 60 min later, the animals were sacrificed with an over-dose of ether. The stomachs were removed and inflated with 10 ml of formalin solution and immersed in the same solution to fix the outer layer of stomach. Each stomach was then opened along the greater curvature, rinsed with tap water to remove gastric contents and blood clots and examined under dissecting microscope (20 x 6.3 x) to assess the formation of ulcers. The sum of length (mm) of all lesions for each stomach was used as the ulcer index (UI), and the percentage of inhibition was calculated by the following formula;

$$[(UI \text{ control} - UI \text{ treated}) / UI \text{ control}] \times 100.$$

Statistical analysis of data

Results were expressed as mean \pm S.E.M. The statistical difference between the mean ulcer index of the treated group and that of the control was calculated by using ANOVA and Student Newman-Keuls multiple comparison test.

Results and Discussion

The results of the *in vivo* experiments are shown in Table 1. Lyophilised water extracts of the aerial parts and roots of both plants showed significant anti-ulcerogenic activity in rats. Aqueous extract of the roots of *F. isaurica* was shown to possess the highest protective effect (100% inhibition) against EtOH-induced ulcerogenesis. All stomachs which were treated with the root decoction of this plant were completely protected from any damage. Though the weakest anti-ulcerogenic effect was observed for the roots of *F. syriaca*, it was again found to be significantly potent (94.1%). Yet the roots are reported to

be used as remedy for ulcer therapy, it was also shown that the aerial parts to possess significant protective activity on ethanol-induced gastric lesions.

TABLE 1. Effects of the plant extracts against gastric lesions induced by EtOH in rats.

Plant material	Dose (mg/kg)	Ulcer Index (mean±S.E.M.)	Prevention from ulcer ^a	Inhibition (%)
Control	---	182.8±19.2	---	---
<i>Ferulago isaurica</i> (aerial parts)	1080	8.9±6.5 ***	4/6	95.1
<i>Ferulago isaurica</i> (roots)	1220	0.0±0.0 ***	6/6	100.0
<i>Ferulago syriaca</i> (aerial parts)	1240	4.1±2.9 ***	5/6	97.8
<i>Ferulago syriaca</i> (roots)	1140	10.7±9.5 ***	4/6	94.1

*** P<0.001 significant from control; S.E.M., mean standard error.

^a: Number of stomachs completely prevented from any bleeding or lesion.

The anti-ulcerogenic activities of any *Ferulago* species has not been reported previously elsewhere (1). The species investigated in the present study *F. isaurica*'s being a narrow endemic for Turkey, and *F. syriaca*'s having limited distribution throughout the world outlines the importance of these plants.

There are 30 *Ferulago* species in Turkey and 16 of which are reported as endemic. The aerial parts are reported to contain monoterpenes and sesquiterpenes and recently investigated the volatile oil composition of 12 Turkish species from Western Anatolia (4). Coumarins and several other types of nonpolar components were isolated from the aerial parts or roots of other *Ferulago* species as well (8). However, the polar components which might be found in the aqueous extracts have not been reported so far. Our studies on the anti-ulcerogenic activity of the afore-mentioned plant remedies are in progress for the isolation of active constituents and to elucidate their mode of action.

Conclusion

Ferulago isaurica and *F. syriaca*, have been claimed to possess anti-ulcerogenic activity. Since these plants are mostly used as aqueous extracts in folk medicine for different purposes, we prepared their lyophilised water extracts for this study. It has been shown that, the aerial parts and roots of both of the species possess statistically significant gastroprotective activity (95.1% and 100% for *F. isaurica*; 97.8% and 94.1% for *F. syriaca*, aerial parts and roots, respectively). Since we have used lyophilised water extracts, we assume that polar components might demonstrate this activity. Further studies need to be conducted to isolate the active substances that are responsible for this activity.

References

1. **Yeşilada E., Gürbüz İ.**, A compilation of the studies on the anti-ulcerogenic effects of medicinal plants. In "Recent Progress in Medicinal Plants" Vol.II. "Phytochemistry and Pharmacology" Eds. Surender Singh, V.K. Singh, J.N. Govil, pp. 111-174, SCI Tech Publishing LLC, Houston, Texas, **2003**.
2. **Öndersev, D.V., Kabasakal, L., Gürkan, E., Tuzlacı, E.**, Analgesic, antipyretic and antiinflammatory activities of *Ferulago confusa* fruit extract. 7th International Symposium on Pharmaceutical Sciences, Proceedings and Abstracts, Ankara, Turkey, pp. 209, **2003**.
3. **Baytop, T.**, Therapy with medicinal plants in Turkey, Past and Present, pp. 348-349, Nobel Tıp Kitapevi, Istanbul, **1999**.
4. **Başer, K.H.C., Demirci, B., Özek, T, Akalın, E., Özhatay, N.**, "Micro-distilled volatile compounds from *Ferulago* species growing in Western Turkey", *Pharm. Biol.* 40(6), 466-471, **2002**.
5. **Gruenwald, J., Brendler, T., Jaenicke, C.**, PDR for Herbal Medicines, pp. 47-48, Medical Economics Company Inc., NJ, **2000**.

6. Yeşilada, E., Sezik, E., Fujita, T., Tanaka, S., Tabata, M., "Screening of some Turkish Medicinal Plants for their anti-ulcerogenic activities", *J. Ethnopharmacol.*, 7, 263-265, 1993.
7. Robert, A., Nezamis, J.E., Lancaster, C., Hanchar, A.J. "Cytoprotection by prostaglandins in rats", *Gastroenterol.*, 77, 433-443, 1979.
8. Jiménez, B., Grande, M.C., Anaya, J., Torres, P., Grande M., "Coumarins from *Ferulago capillaris* and *F. brachyloba*", *Phytochemistry* 53, 1025-31, 2000.

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