



Phenolic Content, Antioxidant and Antimicrobial Potential of Endemic *Ferulago platycarpa*

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Highlights

- In this study, biological activities of endemic *Ferulago platycarpa* were determined.
- In this study, TAS, TOS and OSI values of *Ferulago platycarpa* were determined for the first time.
- In this study, Phenolic contents of *Ferulago platycarpa* were determined.

Article Info

Received: 22/03/2020

Accepted: 31/05/2020

Keywords

Ferulago platycarpa

Endemic

Antioxidant

Antimicrobial

Phenolic content

Abstract

In this study, biological activities and phenolic contents of endemic *Ferulago platycarpa* Boiss. & Bal. were determined. Within the scope of biological activity, antimicrobial activity, antioxidant and oxidant status of plant extracts were determined. Phenolic contents were determined by using HPLC. Antimicrobial activity was determined against bacteria and fungus strains using the modified agar method. Antioxidant and oxidant status were calculated with Rel Assay kits. Gallic, chlorogenic, cinnamic, syringic acids, epicatechin, catechin and quercetin were found in the plant. It was also determined that the plant has antioxidant and antimicrobial potential. But, because of higher TOS value, it was considered that the plants, which were collected from region suitable for OSI value, could be a natural antioxidant source.

1. INTRODUCTION

Throughout human history, plants have always been a natural resource for humans [1]. Plants were used initially by instinct or by imitating animals. Over time, it became a more rational use as a result of discoveries made through trial and error [2,3]. All these discoveries made through trial and error, combined with beliefs and practices, have been transferred from generation to generation throughout the ages and have formed great information [4,5]. Today, the fact that 75% of the natural herbal compounds used in the treatment have been discovered as a result of researches on traditional folk medicine reveals how valuable this information [6].

In recent years, the use of many natural herbs has increased due to the decreased reliability of synthetic drugs. In addition, the food and cosmetics industry has also turned to natural products. Therefore, studies on secondary metabolites synthesized by plants are increasing. [7].

Apiaceae, a very cosmopolitan family throughout the world, is one of the families known to contain essential oils. It is known that most of the family-related species are concentrated in Asia [8,9]. *Ferulago*

genus, belonging to the family Apiaceae, contains many bioactive components. It is represented in the world by about 50 taxa. The countries in which the *Ferulago* species has the greatest biodiversity are Asian countries such as China, Turkey, Iran, Russia and Kazakhstan. In Turkey, *Ferulago* species are commonly known as 'Çakşır' or 'Çağşır', represented by 35 taxa and 18 of them are endemics. This situation shows that Turkey may be the gene center of *Ferulago* [8,10].

Ferulago species are consumed as food in the form of pickles in Turkey. They are also known as odorant and preservative in dairy products, especially in cheese [11]. The genus is used in the treatment of hemorrhoids, intestinal worms, ulcers, snake bites, digestive problems and headaches. It is also known that the genus has sedative and stimulant effects [8,12]. Because of these wide uses, studies on the biological activities of the genus have accelerated in recent years and the results obtained from these studies have revealed that *Ferulago* has anti-cancer, immunomodulatory, anti-proliferative, anti-apoptotic, antibacterial, anti-fungal, anti-viral, anti-oxidant and anti-coagulant effects [7,8,10].

In this study, endemic *Ferulago platycarpa* Boiss. & Bal. was used as material. The antioxidant, oxidant and antimicrobial activities of the plant extracts were determined. In addition, phenolic compounds were screened.

2. MATERIAL AND METHOD

Plant samples were collected from Gaziantep province. Herbarium specimens of the plants collected from field studies were kept in the herbarium at Department of Biology, Gaziantep University. Plant samples were dried under suitable conditions. After drying, methanol, ethanol and dichloromethane extracts of plant samples were extracted in a Soxhlet (Gerhardt EV 14) extractor. The extracts were then concentrated on Heidolph Laborator 4000 Rotary Evaporator and then, they were stored at +4 °C before experiments.

2.1. Determination of Phenolic Contents

Phenolic compounds in the plant were screened using HPLC (SHIMADZU) device [13]. The injection volume was adjusted to be 20 µL. Mobile phase: A: 3% acetic acid, B: methanol. The flow rate was regulated to be 0.8 mL per minute. Chromatographic separation was carried out with an Agilent Eclipse XDB-C18 column (250x4.6 mm; id 5 µm) at 30 °C.

2.2. TAS, TOS and OSI

The antioxidant (TAS/mmol Trolox equiv./L) and oxidant status (TOS/µmol H₂O₂ equiv./L) of plant extracts were calculated with Rel Assay kits. Trolox and hydrogen peroxide were used as the calibrator. OSI value (arbitrary unit: AU) was determined by the ratio of TOS values to TAS values [14,15].

2.3. Antimicrobial activity

Antimicrobial activities of plant extracts were determined using the agar dilution method (CLSI, EUCAST). MIC (Minimal inhibitor concentrations) values were determined against bacteria and fungus strains. Gram positive bacteria strains: *Staphylococcus aureus* ATCC 29213, *S. aureus* MRSA ATCC 43300 and *Enterococcus faecalis* ATCC 29212. Gram negative bacteria strains: *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853 and *Acinetobacter baumannii* ATCC 19606. Fungus strains: *Candida albicans* ATCC 10231, *C. krusei* ATCC 34135 ATCC 13803 and *C. glabrata* ATCC 90030. Pre-cultured studies were done Mueller Hinton Broth medium (Bacteria) and RPMI 1640 Broth medium (Fungus). The standard inoculum yield of bacteria and fungi were prepared according to McFarland 0.5 equivalence. All tests were done at 800-12.5 µg/mL concentrations. Concentrations were made with distilled water. Reference drugs were used as fluconazole and amphotericin B (Fungus), amikacin, ampicillin and ciprofloxacin (Bacteria). Mueller Hinton Agar was dissolved by using water bath and sterilized by putting 9 mL in 15 mL sterile tubes. 1 mL of sample extracts were added to these tubes, mixed and poured into Petri dishes. Seven dilutions were prepared for each extract by this way. Standard inoculum

of bacteria and fungi (106 CFUs/mL) were seeded on agar plates with a disposable inoculating loops (0.01 mL).

All plates were evaluated at 35 °C for 16-20 hours for the bacterium and 48 hours for the fungi. The presence of colony formation was assessed growth, and the absence of colony was assessed as inhibition. Control plates were also used for each working series. The minimum concentration of dilution to prevent the growth of bacteria and fungi were determined as the minimal inhibitor concentration (MIC) [16-21].

3. THE RESEARCH FINDINGS AND DISCUSSION

3.1. Phenolic Content

The phenolic contents of *F. platycarpa* were determined using the HPLC method and the results and chromatograms were given in Table 1.

Table 1. Phenolic Contents of *F. platycarpa*

	Phenolic Contents (ppm)
Gallic acid	14.63
Clorogenic acid	19.71
Epicatechin	20.22
Cinnamic acid	33.105
Sringic acid	0.39
Catechin	84.92
Quercetin	14.33

As a result of HPLC screening seven phenolic compounds were identified in *F. platycarpa*. The highest concentration in detected phenolic compounds was Catechin with 84.92 ppm. The other compounds from the highest to the lowest concentrations were 20.22 ppm epicatechin, 197.07 ppm chlorogenic acid, 33.11 ppm cinnamic acid, 14.63 ppm gallic acid, 14.33 ppm quercetin and 0.39 ppm syringic acid respectively. In previous studies, it has been reported that gallic acid has antimicrobial, anti-inflammatory, anti-depressant, anti-parkinson, anti-diabetic, anti-malarial, diuretic, cardioprotective, anti-viral, antifungal, wound healing, anthelmintic and anxiolytic effects [22-30]. Chlorogenic acid has been reported to have anticancer, antioxidant, anti-inflammatory, cardiovascular, hepatoprotective, reno-protective, anti-diabetic and anti-lipidemic properties [31,32]. Epicatechin and catechin were determined to have antioxidant, antimicrobial, anti-inflammatory, anticancer effects [33-35]. Cinnamic acid has been reported as anti-inflammatory, anti-oxidative, anti-tumor, anti-microbial, anti-hypertensive and anti-hyperlipidemic [36]. Syringic acid has been found to have antioxidant, antiproliferative, antiendotoxic, antimicrobial, anti-inflammatory and anti-cancer effects [37]. Quercetin has been reported to have antioxidant, anti-inflammation, antimicrobial and anti-apoptotic effects [38,39]. In this study, it was found that *F. platycarpa* contains high amounts of catechin, epicatechin chlorogenic acid. In this context, it has been determined that *F. platycarpa* may be a source for these phenolic compounds.

3.2. TAS, TOS and OSI Results

Oxidative stress can result in lipid peroxidation and oxidative DNA damage. It can also cause effects that can damage the cellular loop such as physiological adaptation mechanisms and imbalance of intracellular signal transduction [40,41]. Antioxidant compounds play an active role in reducing the effects of oxidative stress [42]. In this context, determination of the antioxidant capacities of plants is very important in terms of determination of new natural antioxidant sources. There are no studies in the literature that determine TAS, TOS and OSI values of *F. platycarpa*. According to our studies on *F. platycarpa* 6 different plant samples were taken and these samples were run in 5 replicates. When our studies, it is seen that the endogenous antioxidant compound capacity that the plant produces is 5.688 ± 0.024 mmol/L. The oxidant compound level of the plant, which was produced as a result of environmental effects and metabolic

activities, was determined as $15.552 \pm 0.109 \mu\text{mol/L}$. It is determined that the oxidative stress level indicating how much the oxidant compounds were tolerated with the endogenous antioxidant compounds in percentage was 0.273 ± 0.001 . According to the studies oxidative stress on plants, the TAS value of *Mentha longifolia* subsp. *longifolia* was reported as $3.628 \pm 0.234 \text{ mmol/L}$, the TOS value was $4.046 \pm 0.615 \mu\text{mol/L}$ and the OSI value was 0.112 ± 0.025 [43]. In another study, the TAS value of *Thermopsis turcica* was reported as $2.06 \pm 0.09 \mu\text{mol/g}$ [44]. In another study, the TAS value of *Brassica rapa* was reported as 1.25 mmol/L [45]. The TAS, TOS and OSI values of *F. platycarpa* used in our study compared to these studies were found to be higher. In this context, it was determined that *F. platycarpa* has antioxidant potential and could be used as a natural antioxidant source. However, in terms of the TOS value, the higher levels indicate that the oxidant compounds in the plant are produced more by the environmental factors. Therefore, it was considered that the samples collected from more suitable regions for the oxidative stress condition of the plant could be used as an antioxidant source.

3.3. Antimicrobial Activity Results

In spite of the technological developments that have been experienced in recent years, the spread of infectious diseases cannot be controlled. Microorganisms are the leading cause of infectious diseases [46]. They are one of the oldest living things on the planet that existed on Earth for millions of years. Recently, the resistance of bacteria to synthetic antibiotics has become a global problem [47]. For this reason, researchers have considered the use of natural products such as medicinal plants for the production of new antibiotic drugs [48]. In this study EtOH, MeOH and DCM extracts of *F. platycarpa* were used and their activities on test microorganisms were determined. The results of the study were given in the Table 2.

Table 2. Antimicrobial Activities of *F. platycarpa*

	<i>S. aureus</i>	<i>S. aureus</i> MRSA	<i>E. faecalis</i>	<i>E. coli</i>	<i>P. aeruginosa</i>	<i>A. baumannii</i>	<i>C. albicans</i>	<i>C. glabrata</i>	<i>C. krusei</i>
EtOH	800	800	800	800	400	400	800	400	400
MeOH	200	200	200	400	200	200	400	200	200
DCM	400	400	400	800	400	200	800	400	200
Ampicillin	1.56	3.12	1.56	3.12	3.12	-	-	-	-
Amikacin	-	-	-	1.56	3.12	3.12	-	-	-
Ciprofloksasin	1.56	3.12	1.56	1.56	3.12	3.12	-	-	-
Flukanazol	-	-	-	-	-	-	3.12	3.12	-
Amfoterisin B	-	-	-	-	-	-	3.12	3.12	3.12

200, 400 and 800 ($\mu\text{g/mL}$) extract concentrations

According to Table 2 was examined, it was seen that the highest activity was determined as MeOH extract of the plant. When other extracts were compared, it was determined that DCM extract was higher than EtOH extract activity. In this study, the highest activity on *S. aureus*, *S. aureus* MRSA and *E. faecalis* were seen with at 200 $\mu\text{g/mL}$ concentration of MeOH extract, then 400 $\mu\text{g/mL}$ concentration of DCM extract and 800 $\mu\text{g/mL}$ concentration of EtOH extract, respectively. Moreover, the highest activity on *E. coli* and *C. albicans* were seen at 400 $\mu\text{g/mL}$ concentration of MeOH extract, then 800 $\mu\text{g/mL}$ concentration of DCM and EtOH extracts. On the other hand, the highest activity on *P. aeruginosa* and *C. glabrata* were seen at 200 $\mu\text{g/mL}$ concentration of MeOH extract, then 400 $\mu\text{g/mL}$ concentration of DCM and EtOH extracts. Finally, the highest activity on *A. baumannii* and *C. krusei* were seen at 200 $\mu\text{g/mL}$ concentration of MeOH and DCM extracts, then 400 $\mu\text{g/mL}$ concentration of EtOH extract. Previous studies have reported that methanol, chloroform, ethyl acetate and hexane extracts of *F. platycarpa* are effective at different concentrations on *Staphylococcus aureus*, *Enterococcus faecalis* and *Candida albicans* [49]. In comparison to this study, it was determined that EtOH, MeOH and DCM extracts of *F. platycarpa* were effective against *E. coli*, *P. aeruginosa*, *A. baumannii*, *C. glabrata* and *C. krusei* at 200-800 $\mu\text{g/mL}$ concentrations. In this context, it was determined that *F. platycarpa* can be used as a natural antimicrobial source for the tested microorganisms.

4. CONCLUSION

In this study, phenolic contents, antioxidant and antimicrobial activities of endemic *F. platycarpa* plant, collected from Gaziantep (Turkey) were determined. As a result of the studies, it was determined that the plant contains gallic acid, chlorogenic acid, epicatechin, cinnamic acid, syringic acid, catechin and quercetin. It was also determined that the plant could be a rich natural source for these identified compounds. On the other hand, it is observed that the plant has antioxidant potential. As a result, biological activity of the plant was determined for the first time and it could be used as a pharmacological agent.

CONFLICTS OF INTEREST

No conflict of interest was declared by the authors.

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