

Investigation of resveratrol and phenolic compounds of ethnomedicinal plant *Polygonum cognatum* Meissn. collected from Sivas

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ABSTRACT: *Polygonum cognatum* Meissn., which is also known as “madımak, solucanotu” has been used in the Turkish folk medicine for the treatment of various diseases and has also been consumed in the dishes and salads by local people. It has even been the subject of a folk song, sung among the people in Sivas. In this study, it was aimed to examine the resveratrol and phenolic compounds that are valuable for health industry, in leaf and root extracts obtained from *P. cognatum*, which is widely distributed in Sivas. While resveratrol was investigated by using HPLC-PDA, the phenolic compounds were determined by using LC-HRMS. Results of analyses showed that resveratrol could not be detected in both leaf and root extracts, but both root and leaf extracts were quite rich in following phenolic compounds. While chlorogenic acid, hyperoside, rutin, and fumaric acid were the most abundant phenolic compounds detected from the leaf extract, the (+)-catechin, fumaric acid, chlorogenic acid and p-coumaric acid were the most abundant phenolic compounds in the root extract. As a conclusion, *P. cognatum* with its rich phenolic compounds content of the root and leaf parts are good candidates in terms of using in dietary supplements, health care and cosmetic products.

KEYWORDS: *Polygonum cognatum* Meissn., phytochemicals, resveratrol, phenolic compounds, HPLC, LC-MS.

1. INTRODUCTION

The genus *Polygonum* belongs to the family Polygonaceae. The species in this genus which are used in the traditional folk medicine and cuisine, mainly distributed in North and South America, Asia, Europe and North Africa. There are approximately more than 300 species all over the world, 41 of them exist in Türkiye and the 8 of them are endemic species [1,2]. The *Polygonum* species occur as a perennial, annual or suffrutescent herbs and usually only the upper part of the perianth seen as colored. The lower parts of the perianth being green generally [3]. In the Turkish folk medicine, *Polygonum* species are used in the eczema, wounds and rheumatic pain by decoction [4,5].

The knotweed (*Polygonum cognatum* Meissn.) which also called as “madımak, solucanotu” in Türkiye, is a perennial herb with pinkish perianth and petiole, oblong-elliptic leaves [3,6]. The plant is consumed in the salads with yoghurt and in the dishes as soup, appetizer with egg and main course by local people especially in the Central and Eastern Anatolian regions in Türkiye [7,8]. It has even been the subject of a folk song, sung among the people in Sivas region [9]. *P. cognatum* has been used as a diuretic agent and also treatment for diabetes and gastrointestinal diseases in the Turkish folk medicine [10]. Previous studies

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reported that the plant had antimicrobial, antifungal, antidiabetic, diuretic, antioxidant, antimicrobial, insecticidal, cytotoxic, anthelmintic and anti-inflammatory activities [6,7,11-13]. Also, an *in-vivo* clinical study has been revealed that *P. cognatum* aqueous extract showed a protective effect against colitis in the rat model due to the anti-inflammatory and antioxidant activities [13]. The plant was previously reported to contain sterols, triterpenes, saponins, tannins, polyuronides and phenolic compounds which were attributed to the aforementioned activities [13, 14]. In a recent study *P. cognatum* samples that were collected from Cumra and Manisa provinces were found rich in different phenolic compounds: rutin, isorhamnetin, chlorogenic acid and resveratrol levels were determined to be the highest [14].

The present study was carried out to examine the phytoactive compounds of the *P. cognatum* in terms of public health and health care industry, due to the presence of many species of *P. cognatum* in Türkiye that are used as folk medicine and are consumed widely as food by the local people. The contribution of the study to the field is the comparison of the leaf and root parts of *P. cognatum* separately in terms of resveratrol and other phenolic components, which have pharmaceutical value. For this aim, the leaves and roots of *Polygonum cognatum* Meissn. were collected from Sivas (Haydarlı, which is the central village of Sivas, has 1.349 m altitude.) and analyzed by both HPLC-PDA and LC-HRMS to determine their phenolic compounds.

2. RESULTS

2.1. Qualitative analysis of resveratrol using HPLC-PDA

Resveratrol is a polyphenolic compound, which has many benefits and usages in the health care, cosmetic and pharmaceutical industries. Because of its antiproliferative, anti-angiogenic, anti-inflammatory, antioxidant, and antimicrobial properties, it is thought to be a promising compound in the treatment of diseases such as diabetes mellitus, obesity, cardiovascular diseases, multiple myelomas, metabolic syndrome, hypertension, Alzheimer's disease, inflammatory diseases, rhinopharyngitis and types of cancer. Also the antiaging and crossing skin barrier activities have been proven by some researchers [15, 16]. *Polygonum cuspidatum* Sieb.et Zucc., which is a member of the *Polygonum* genus and known as Japanese knotweed contains resveratrol as a major compound and it has been stated that the amount of resveratrol contained in *P. cuspidatum* is higher than that of grapes and other plants [17]. In this study, we first investigate the resveratrol content in the *Polygonum cognatum* Meissn. leaf and root extracts by using HPLC-PDA to compare the other members of *Polygonum* species which contain resveratrol. As a result of analysis, resveratrol was not determined in the *P. cognatum* collected from the Sivas conversely to the *P. cognatum* collected from Cumra and Manisa provinces [14]. And this result was attributed to the level of resveratrol which was probably under the limit of detection.

2.2. Quantitative analysis of phenolic compounds using LC-HRMS

Phenolic compounds are secondary metabolites of the plants and they have many promising usages in the prevention and treatment of the diseases. They can be used as a preservative agent, natural dye etc. in food, cosmetic and pharmaceutical products. Phenolic compounds are also important with their antioxidant properties [18]. The extracts of the roots and the leaves of *P. cognatum* were analyzed using LC-HRMS. As a result of the analysis, it was observed that the amounts of chemical components of the leaf and root extracts were different. Only fumaric acid values were found to be close to each other, but the amounts of other major components were determined to be different. The detailed mass parameters of each target compound are given in Table 1.

Table 1. Constituents of the ethanol extracts of *Polygonum cognatum* Meissn leaves and roots ^a.

No	Analyte	RT ^b	Quantification (mg/L) ^c		Polarity (ESI)	m/z
			Leaves	Roots		
1	Fumaric acid	2,18	124,137 ± 3,5774	138,543 ± 3,9925	Negative	115,0037
2	Ascorbic acid	2,24	2,431 ± 0,0958	0,87 ± 0,0343	Negative	175,0248
3	(+)-Catechin	2,38	6,311 ± 0,2086	172,255 ± 5,6945	Negative	289,0718
4	Chlorogenic acid	2,47	556,157 ± 19,8864	59,234 ± 2,1180	Negative	353,0878
5	Pyrogallol	2,32	0,168 ± 0,0076	0,287 ± 0,0129	Negative	125,02442
6	(-)-Epicatechin gallate	2,63	0,25 ± 0,0076	21,759 ± 0,6644	Negative	441,0827
7	Caffeic acid	3,1	5,511 ± 0,2063	1,037 ± 0,0388	Negative	179,0350
8	Luteolin 7-glucoside	3,95	0,633 ± 0,0262	0,22 ± 0,0091	Negative	447,0933
9	p-Coumaric acid	3,95	26,81 ± 0,8870	38,373 ± 1,2696	Negative	163,0401
10	Rutin	4,29	164,136 ± 5,0356	22,082 ± 0,6775	Negative	609,1461
11	Hyperoside	4,33	449,01 ± 15,5350	34,205 ± 1,1834	Negative	463,0882
12	Apigenin 7-glucoside	4,85	0,26 ± 0,0093	0,033 ± 0,0012	Negative	431,0984
13	Orientin	4,98	0,536 ± 0,0197	*	Negative	447,0933
14	Quercitrin	4,99	10,602 ± 0,4008	0,526 ± 0,0199	Negative	447,0933
15	Ellagic acid	5,05	0,156 ± 0,0065	0,847 ± 0,0356	Negative	300,9990
16	Myricetin	5,07	0,056 ± 0,0023	0,074 ± 0,0031	Negative	317,0303
17	Quercetin	5,61	2,899 ± 0,0855	0,565 ± 0,0167	Negative	301,0354
18	Naringenin	5,66	0,11 ± 0,0046	0,242 ± 0,0102	Negative	271,0612
19	Luteolin	5,75	0,069 ± 0,0024	0,401 ± 0,0137	Negative	285,0405
20	Apigenin	6,07	0,008 ± 0,0002	0,019 ± 0,0005	Negative	269,0456
21	Chrysoeriol	6,09	0,045 ± 0,0009	0,049 ± 0,0010	Negative	299,05611
22	(-)-Epigallocatechin	2,21	*	24,095 ± 0,7446	Positive	307,0812
23	(-)-Epigallocatechin gallate	2,33	*	3,97 ± 0,1494	Positive	459,0922

^a The values represent the mean ± S.E.M. of three parallel measurements ($p < 0.05$).

^b RT: Retention time.

^c Values in mg/L (w/v) of extract

*: None detected

3. DISCUSSION

According to the results presented in Table 1, chlorogenic acid (556.157 ± 19.8864 mg/L), hyperoside (449.010 ± 15.5350 mg/L), rutin (164.136 ± 5.0356 mg/L) and fumaric acid (124.137 ± 3.5774 mg/L) was determined as the major compounds of the leaf extract of the *P. cognatum*. Between them chlorogenic acid has been indicated as a promising phytoactive agent in prevention and treatment of cardiovascular diseases, type of cancers, diabetes and the other chronic diseases due to the antioxidant, anti-inflammatory, anti-bacterial, anti-viral, hypoglycemic, lipid lowering, anti-cardiovascular, anti-mutagenic, anti-cancer and immunomodulatory activities [19]. On the other hand, hyperoside and rutin compounds show strong antioxidant, anti-inflammatory, hypoglycemic and anti-cancer activities. In an *in vivo* study, it was shown that the hyperoside might be beneficial in diabetic complications and atherosclerosis. And also, rutin promotes cardiovascular system health by supporting the capillary veins and alleviates the LDL cholesterol. [20,21]. The results of the root extract of the *P. cognatum* showed that (+)-catechin (172.255 ± 5.6945 mg/L), fumaric acid (138.543 ± 3.9925 mg/L), chlorogenic acid (59.234 ± 2.1180 mg/L), p-coumaric acid (38.73 ± 1.2696 mg/L) was found as major compounds. Between them, catechins are very powerful antioxidant, anti-aging and anti-inflammatory compounds which prevent cancer and infectious diseases and support cardiovascular system health. It is also used generally in the cosmetic industry owing to the anti-aging, photoprotective and antioxidant properties and benefits to the skin and hair health [22-24]. And fumaric acid is a strong antioxidant molecule which promises treatment of moderate to severe psoriasis. It has a variety of applications in the food and pharmaceutical industries [25-26]. As presented in Table 1, (-)-epigallocatechin and (-)-epigallocatechin gallate could not be detected in the leaf extract and also, orientin could not be detected in the root extract of *P. cognatum*. There is only one study in the literature in which the phenolic compounds of *P. cognatum* were detected and they were studied with HPLC. The highest amount of compound detected in the extracts obtained by using whole parts of the *P. cognatum* plant collected from

both Manisa and Cumra provinces was rutin. Also, the other highest compound in the Cumra's sample is catechin [14].

4. CONCLUSION

The present study revealed that resveratrol could not be detected in the root and leaf extracts of *Polygonum cognatum* Meissn., but they were both quite rich in terms of other phenolic compounds. While the chlorogenic acid, hyperoside, rutin, and fumaric acid were obtained as the major compounds of the leaf extract, the (+)-catechin, fumaric acid, chlorogenic acid and p-coumaric acid were the detected as the major compounds of the root extract of the *Polygonum cognatum* Meissn. In our LC-MS study, it was determined that especially the aerial parts of *P. cognatum* is richer in phenolic substances. In line with these promising results of phenolic content of the leaf and root extracts the *P. cognatum* can be a valuable source for the food. Also, considering the beneficial effects of *P. cognatum* plant grown naturally or in small-scale agricultural lands, further studies should be conducted and its cultivation should be encouraged. Using new technologies and production processes this plant which is rich in phenolic compounds could be developed as dietary supplement, cosmetic and herbal medicinal products and brought into the economy.

5. MATERIALS AND METHODS

5.1. Plant collection and extraction

Leaves and roots of *Polygonum cognatum* Meissn. were collected from Sivas (Center, Haydarlı village), on May 2022 and was identified by Professor Murat Kartal, Bezmialem Vakıf University, Türkiye. Herbarium specimen of the plant was deposited in the Altınbaş University Herbarium (Herbarium number: HERA1060).

Air-dried and powdered leaves (10 g) and roots (10 g) extracted with 100 mL ethanol (96%) for 24 hours at room temperature in a reflux condenser. Then the extracts were filtered (Whatman paper) and evaporated (Heidolph Hei-VAP HL, Germany). 77 mg dry ethanolic leaf extract and 93 mg dry ethanolic root extract were weighed and solved in 2 mL %100 MeOH and then filtered with 0.22µm PTFE before HPLC analysis. 1 mg of resveratrol was solved in 100 mL and then filtered with 0.22µm PTFE for the HPLC analysis. 50 mg dry ethanolic leaves and root extracts weighed carefully and solved in 1.5 mL %100 MeOH and then filtered with 0.22µm PTFE before LC-MS analysis.

5.2. Chemicals and instruments

Leaves and roots of *P. cognatum* were analyzed qualitatively using HPLC-PDA (PerkinElmer, Massachusetts, United States). Chemical compositions of leaves and roots of *P. cognatum* were determined by using LC-HRMS (Thermo, Bremen, Germany). Formic acid (98-100%), ethanol (96%), methanol were obtained from Merck (Darmstadt, Germany). Ascorbic acid (≥99%), fumaric acid (≥99%), caffeic acid (≥98%), p-coumaric acid (≥98%), rutin (≥94%), quercetin (≥95%), naringenin (≥95%), luteolin (95%), pyrogallol (≥98%), chlorogenic acid (≥95%) and resveratrol (≥99%) were from Sigma-Aldrich (Germany); (-)-epigallocatechin (>97%), (-)-epigallocatechin gallate (>97%), (+)-catechin (>97%), (-)-epicatechin gallate (>97%), orientin (>97%), luteolin 7-glucoside (>97%), hyperoside (>97%), ellagic acid (>97%), quercitrin (>97%), apigenin (>97%) were from TRC Canada; apigenin 7-glucoside (>97%) was from EDQM CS; myricetin (>95%) was from Carl Roth GmbH + Co and chrysoeriol (≥98%) was from ChemFaces, as certified reference materials.

5.3. Qualitative analysis of resveratrol using HPLC-PDA

The high-performance liquid chromatographic apparatus (PerkinElmer Flexar HPLC) with a degasser, pump (PerkinElmer Quaternary LC Pump) and a controller coupled to a PerkinElmer PDA Plus photodiode-array detector equipped with an automatic injector interfaced to Chromera® chromatography manager software. Separation was performed using a liquid chromatography method for *Polygoni multiflori radix* of European Pharmacopeia 10.0 with slight modifications [27]. C18 column (4.6 × 250 mm, 5 µm, PerkinElmer) was used, column temperature was 30°C, with a flow rate of 1 mL/min. The detection

wavelength was set at 320 nm. The mobile phase consisted of 0.1% anhydrous formic acid in water (v/v) (A) and acetonitrile (B). The following gradient was used for separation: 0-15 min: 10% B-30% B, 15-16 min: 30% B-80% B, 16-21 min: 80% B. The injection volume was 10 µL. A 15 min equilibrium time was allowed between injections and sample solutions were injected three times.

5.4. Quantitative analysis of phenolic compounds using LC-HRMS

LC-HRMS measurements were carried out on a Thermo ORBITRAP Q-EXACTIVE (Bremen, Germany) mass spectrometry-equipped ESI ion source and with Dionex LC system. Scan range was set to m/z 100-900 amu and other mass parameters are used as following: gas flow rate: 45, aux gas flow rate: 10, spray voltage: 3.80 kV, capillary temperature: 320 °C, aux gas heater temperature: 320 °C and Slens RF is 50. A Troyasil C18 column (150 x 3 mm i.d., 5 µm particle size, Istanbul, Türkiye) was for separation of compounds. The mobile phases A and B were composed of 1% formic acid-water and 1% formic acid-methanol, respectively. The gradient program was 0-1.00 min 50% A and 50% B, 1.01-6.00 min 100% B, and finally 6.01-15 min 50% A and 50% B. The flow rate of the mobile phase was 0.35 mL/min, and the column temperature was set to 22°C. Environmental conditions were set as temperature 22.0 ± 5.0 °C and relative humidity (50 ± 15) % rh.

Identification of compounds was performed by comparison of retention time of standard compounds (in the range of purity 95-99% see section chemicals) and HRMS data of Bezmialem Vakıf University, Drug Application and Research Center Library-ILMER. Dihydrocapsaicin (purity 95%) was used as an internal standard for LC-HRMS measurements in order to reduce the repeatability problem caused by external effects, such as ionization repeatability, in mass spectrometry measurements [28]. The detailed mass parameters of each target compound are given in Table 1.

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