Letters in Applied NanoBioScience
Open-Access Journal (ISSN: 2284-6808)

Article
Volume 13, Issue 1, 2024, 3
https://doi.org/10.33263/LIANBS131.003

Ultra-HPLC Analysis of Phenolics Compounds in *Fraxinus uhdei* and *Taxodium mucronatum* Tree Extracts

Braulio Edgar Herrera-Cabrera [1], Adriana Delgado Alvarado [1], Rafael Salgado Garciglia [2], Jorge Montiel Montoya [3], Maribel Valdez Morales [3], Alejandra Hernández García [2], Luis Germán López Valdez [4], José Lorenzo Laureano [5], Victor Manuel Ocaño Higuera[6], Hebert Jair Barrales-Cureño [7,*]

1 Colegio de Postgraduados, Campus Puebla. Boulevard Forjadores No 205 Santiago Momoxpan, Puebla. C.P. 72760
2 Universidad Michoacana de San Nicolás de Hidalgo. Instituto de Investigaciones Químico Biológicas, Edificio B-3, Ciudad Universitaria, 58030, Morelia, Michoacán, México
3 Centro Interdisciplinario de Investigación para el Desarrollo Integral Regional, Instituto Politécnico Nacional, Unidad Sinaloa, Boulevard Juan de Dios Bátiz 250, Col. San Joachín, Guasave, Sinaloa, México
4 Universidad Autónoma Chapingo. Laboratorio de Productos Naturales, Área de Química. AP74 Oficina de correos Chapingo. Km 38.5 Carretera México-Texcoco, 56230, Texcoco, Estado de México, México
5 Universidad Intercultural del Estado de Puebla. Maestría en Ciencias en Manejo Sustentable de Recursos Naturales. Calle Principal a Lipuntuahuaca S/N, C.P. 73475, Lipuntahuaca, Huehuetla, Puebla, México
6 Universidad de Sonora. Blvd. Luis Encinas J, Calle Av. Rosales &, Centro, 83000 Hermosillo, Sonora, México
7 Instituto Tecnológico de Estudios Superiores de Zamora. Carrera en Ingeniería en Innovación Agrícola Sustentable. Km No. 7; Carretera Zamora-La Piedad, Comunidad El Sáuz de Abajo. Zamora, Michoacán, México
* Correspondence: hebert.bc@zamora.tecnm.mx (H.J.B.C.)

Scopus Author ID 57197733909
Received: 14.08.2022; Accepted: 4.10.2022; Published: 25.02.2023

Abstract: This research aimed to quantify and identify, by high-performance liquid chromatography, phenolics compounds from stems and leaf's tree extracts of *Fraxinus uhdei* and *Taxodium mucronatum*. Ethanolic extracts of *Fraxinus uhdei* and *Taxodium mucronatum* were analyzed with high-performance liquid chromatography to identify and quantify their major phenolics compounds (antioxidant majority flavonoids). Rutin, catechin, and quercetin were identified in foliar extracts of *Fraxinus uhdei*. Rutin, caffeic acid, catechin, and quercetin were identified in stem extracts of *Fraxinus uhdei*. Ferulic acid, quercetin, naringenin, and kaempferol were identified in foliar extracts of *Taxodium mucronatum*. Quercetin naringenin and kaempferol were identified in stem extracts of *Taxodium mucronatum*. Some phenolic compounds type flavonoids have been identified in other *Fraxinus* and *Taxodium* species but have not been identified and quantified in *Fraxinus uhdei* and *Taxodium mucronatum*, a Mexican species. For the first time, we report this secondary metabolite in *Fraxinus uhdei* and *Taxodium mucronatum* leaves and stem extracts. This analytical method can be standardized to serve as a quality analysis of *Fraxinus* and *Taxodium* trees products.

Keywords: flavonoids; naringenin; phenolics compounds; quercetin.

1. Introduction

The biological activity of a medicinal plant or tree resides in one or a set of chemical compounds found in the plant's tissues. These include essential oils, terpenes, and flavonoids. Flavonoids, derived from the Latin "flavus", meaning "yellow", are the most abundant subclass of polyphenols in the plant kingdom. Flavonoids are a group of secondary metabolites widely present in plants and are attributed to anti-inflammatory and antioxidant properties. They include many pigments and are also present in the epidermis of plants. Biosynthetically they

have a mixed origin from shikimic acid and acetylcoenzyme A via malonylcoenzyme A [1]. From the structural point of view, Flavonoids correspond to a 3-ring system fused in a carbon sequence that presents a central heterocycle in a C6C3C6 structure, which has been widely discussed for its stability and reactivity [2]. These compounds usually present at least three phenolic hydroxyls, facilitating their classification and reactivity. Flavonoids are compounds of phenolic nature. They are characterized by their strong antioxidant activity [3], an important property exploited by plants to protect organisms from free radicals, which have a physiological function in cell signaling mechanisms, and germ elimination, among other actions [4]. The antioxidant activity of flavonoids results from a combination of their chelating properties from a combination of their iron chelating and free radical scavenger iron chelating and free radical scavenging properties, as well as inhibition of oxidases: lipooxygenase, cyclooxygenase, myeloperoxidase, and xanthine oxidase, thus preventing the formation of reactive oxygen species and organic hydroxyperoxides [5]. In addition, it has been seen that they also inhibit enzymes indirectly involved in oxidative processes, such as in oxidative processes, such as phospholipase A2, while they stimulate A2; at the same time, they stimulate others with recognized antioxidant properties, such as catalase and superoxide dismutase [6]. Flavonoids remove reactive oxygen, especially in the form of superoxide anions, hydroxyl radicals, hydroxyl radicals, and in the form of superoxide anions, hydroxyl radicals hydroperoxides, and lipid peroxides, by blocking the harmful action of these substances on cells. The antioxidant protection of flavonoids has been corroborated in: keratinocytes, fibroblasts, fibroblasts in keratinocytes, dermal fibroblasts, sensory ganglions, endothelium, endothelial endothelium, nervous tissue, and low-density lipoproteins [7]. Quercetin is the flavonoid that meets the requirements to exert an effective antioxidant function, as it is five times antioxidant function, since it is five times greater than that of vitamins C and E, in than vitamins C and E, as well as having a similar water solubility to the latter [8]. That is why rutin (quercetin-3-b-D-ruthinoside) is, up to now, the only flavonoid in pharmacological flavonoid in pharmacological presentation (combined) [9]. There is a synergic effect with the mentioned vitamins. Ascorbic acid reduces the oxidation of quercetin, so that combined with it that, combined with it, it allows the flavonoid to maintain its functions for a longer period of time. For its part, quercetin protects vitamin E from oxidation [10]. Various chemical constituents, including coumarins, lignans, phenylethanoids, secoiridois, and flavonoids, have been isolated from *Fraxinus* plant.

Research on diverse sources of natural antioxidants contributes to the knowledge and reasonable use of the producing species, as is the case of the species at risk of extinction of the genus *Fraxinus* and *Taxodium* because their phenolic components, particularly flavonoids, have been described in the minority. Therefore, the objectives of the present work were to characterize by HPLC the analytical screening of the profile of flavonoids biosynthesized *in situ* plant tissues of *Fraxinus uhdei* and *Taxodium mucronatum.*

2. Materials and Methods

Reagents and Standards. The solvents used for the extraction and high-performance liquid chromatography analytical method were HPLC and analytical grade, respectively, obtained from Sigma-Aldrich (St Louis, MO, USA, 2022). All reagents, solvents, samples, standards, and stock solutions were filtered through 0.20 µm PTFE membrane filters (Phenomenex, USA) before injection or separating into the analytical instrument.

Sample plant collection. Stem and whole leaves of *Fraxinus uhdei* and *Taxodium mucronatum* were collected during spring (January-February) 2022 in the vicinity of the city of Zamora (Figure 1), State of Michoacán, Mexico (19° 59' 32" N 102° 15' 47" W, 102º 15' 47" O, 1580 masl). Tree samples were herborized.

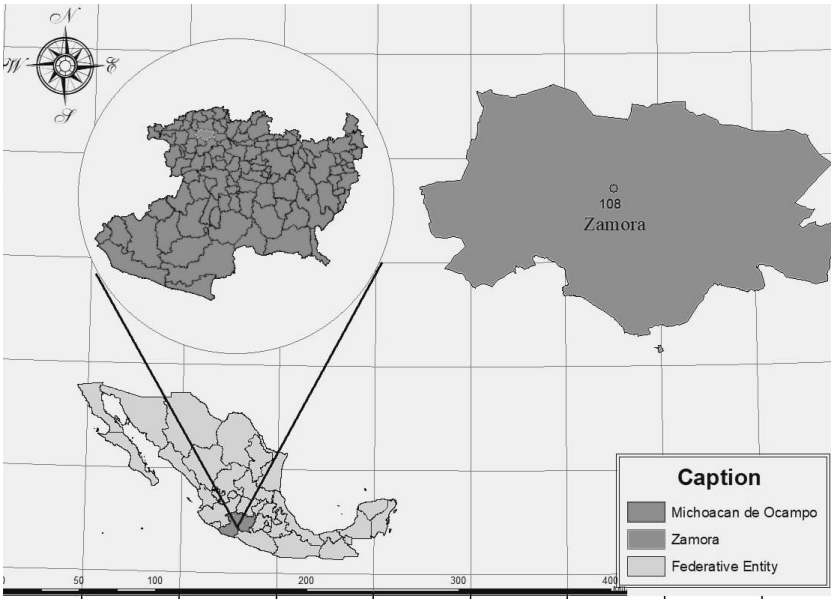

Figure 1. Geographical location of sampling sites of *Fraxinus uhdei* and *Taxodium mucronatum.*

Obtaining the extracts plant. Hundred mg samples of dried leaves and 100 mg of dried stems of *Fraxinus uhdei* and *Taxodium mucronatum* were taken by quadruplicate; these organs are renewable sources so as not to damage the trees. The leaves and stems of *Fraxinus uhdei* and *Taxodium mucronatum* were macerated in a mortar with a pistil. In a 250 mL flask, 100 mL of 80% ethanol was added to each sample, the mouth of the flask was covered with aluminum foil, and each sample was allowed to rest for 48 h. The samples were then filtered on filter paper. Finally, a rotary evaporator (Buchi brand-Germany) was used to evaporate the solvent from each extract. The crude extracts were placed in amber bottles for further analysis.

HPLC analysis. The profile of phenolic compounds was determined from the methods modified by Valdez-Morales *et al*. (2014), with some brief modifications. Flavonoids and phenolic compounds were identified and quantified on an automatic injection chromatograph, Ultimate 3000, Dionex brand, equipped with a quaternary pump and a diode array detector. An Acclaim 120, C18 column (4.6 mm, 250 mm, 5 microns, Thermo Sci brand) was used. The mobile phase used consisted of A acidified water to pH 2.8 with acetic acid and B acetonitrile, a gradient was used starting with 90% A and 10% B up to 2.5 min, gradually increasing the percentage of B: 12% at 6 min, 23% at 18 min, 35% at 24 min, 95% at 30 min and returning to the initial conditions of 90% A in a final time of 40 min.

The rest of the chromatographic conditions are summarized: flow rate of 0.3 mL/min, injection volume of 10 µL, and the recorded wavelengths were 260, 280, 300, 320, 350, and 375 nm. The compounds were identified by comparing their retention times and absorption spectra with the previous run standards and with which the calibration curves were made. The Chromeleon 7.0 software was used for chromatographic analysis. The concentration values of each phenolic compound (flavonoid) were calculated from the area under the signal curve observed in the chromatogram.

Compounds were identified as a function of their retention time and absorption spectra. Identity was only assigned to signals with a purity greater than 980 (1000 being the maximum value). The areas at the wavelength of maximum absorption of each compound were captured, as was the corresponding standard curve used. Data were analyzed with ANOVA (two ways) in the statistical package SAS Statistics version 17 for Windows.

3. Results and Discussion

Flavonoids are low molecular weight compounds with a common diphenylpyran (C6-C3-C6) skeleton, composed of two phenyl rings (A and B) linked through a heterocyclic pyran C-ring. The individual carbon atoms of the A, B, and C rings are numbered by a system using ordinary numbers for the A and C rings and prime numbers for the B ring. Of the three rings, the A ring is biosynthesized via the polyacetoacetate route, and the B ring, along with the C3 unit, comes from the sialic acid route. All flavonoids are hydroxylated structures in their aromatic rings and are polyphenolic structures [11].

Flavonoids are mostly found as glycosides but can also occur in free form (also called flavonoid aglycones). In addition, they can occur as sulfates, dimers, or polymers. Glycosides can be found in two forms: O-glycosides with the carbohydrates linked through oxygen atoms (hemiacetal bond) or C-glycosides with the carbohydrates linked through carbon-carbon bonds. Of all these natural forms, O-glycosides are the major ones. There are several subgroups of flavonoids [12].

The classification of these compounds is based on the oxidation state of the heterocyclic ring (C-ring) and the position of the B-ring. Within each family, there is a great variety of compounds, which differ from each other by the number and position of the hydroxyl groups, and by the different functional groups, they may have (methyl, sugars, organic acids). The main subgroups of flavonoid compounds are flavonols, flavones, flavanones (dihydroflavones), isoflavones, anthocyanidins, and flavonols [13].

Several authors have analyzed the concentration of flavonoids in different tree species extracts due to their useful function as antioxidants. Guevara-Fefer *et al*. (2017) found flavonoids in extracts of thirteen tree species of the genus *Bursera*. *Bursera* contains variety of flavonoids depending on the species, those identified have been: quercetin (flavonol), rutin (flavonol glucoside), naringenin (flavanone), naringin (flavanone glucoside), apigenin (flavone) and apiin (flavone glucoside) [14].

Trees of the genus *Bursera* produce resins and exudates, the chemical profile of the genus being the biosynthesis of triterpenes, sesquiterpenes, lignans, and flavonoids [14]. In our research, we found that *Fraxinus uhdei* in leaves and stems extracts had high concentrations of caffeic acid (11.56 µg/mL) and quercetin (24.02 and 23.94 µg/mL), respectively, and low concentrations of catechin (3.68 and 0.45 µg/mL) in both ethanolic extracts. *Taxodium mucronatum* in leaves and stems extracts had high concentrations of quercetin (14.74 and 13.9 µg/mL), respectively, and low concentrations of kaempferol (1.56 and 0.97 µg/mL) in both ethanolic extracts (Table 1).

Table 1. Concentrations of phenolic compounds identified in *Fraxinus uhdei* and *Taxodium mucronatum* tree extracts.

Extract Sample	Retention time (min)	Secondary metabolite (flavonoid)	Concentration (µg/mL)
Leaves of *Fraxinus uhdei*	26.01	Rutin	5.49 c
	28.55	Catequin	3.68 d
	31.9	Quercetin	24.02 a[1]

Extract Sample	Retention time (min)	Secondary metabolite (flavonoid)	Concentration (µg/mL)
Stems of *Fraxinus uhdei*	26.02	Rutine	3.72 d
	27.41	Caffeic acid	11.56 b
	28.54	Catequin	0.45 e
	31.9	Quercetin	23.94 a
Leaves of *Taxodium mucronatum*	30.04	Ferulic acid	10.05 b
	31.91	Quercetin	14.74 b
	32.98	Naringenin	11.25 b
	34.23	Kaempferol	1.56 e
Stems of *Taxodium mucronatum*	31.9	Quercetin	13.9 b
	32.98	Naringenin	4.50 c
	34.23	Kaempferol	0.97 e

[1]means that the same letter is not statistically different (Tukey, $p \leq 0.05$).

Rutin, catechin, and quercetin were identified in foliar extracts of *Fraxinus uhdei* (Figure 1). rutin, caffeic acid, catechin, and quercetin were identified in stem extracts of *Fraxinus uhdei* (Figure 2). ferulic acid, quercetin, naringenin, and kaempferol were identified in foliar extracts of *Taxodium mucronatum* (Figure 3). quercetin, naringenin, and kaempferol were identified in stem extracts of *Taxodium mucronatum* (Figure 4, Figure 5, and Figure 6).

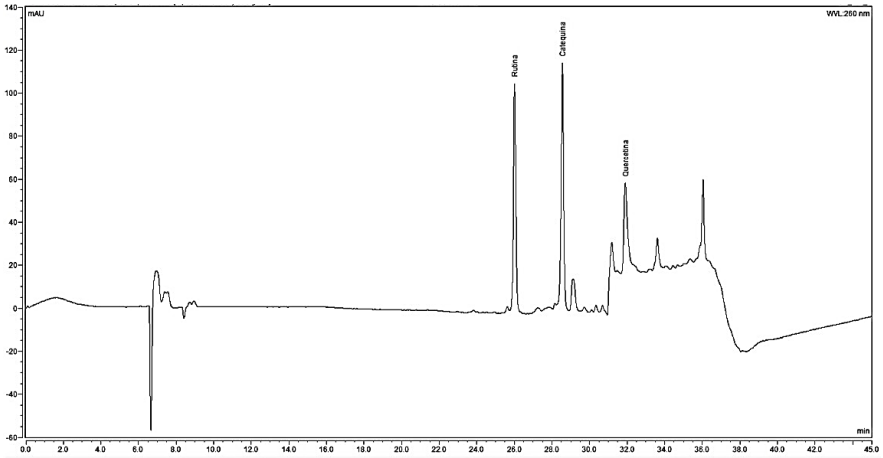

Figure 2. Phenolic compounds identification by HPLC from leaves of *Fraxinus uhdei*. Chromatograms of flavonoids were obtained from ethanol extract of *F. uhdei* by column chromatography. Rutin ($C_{27}H_{30}O_{16}$), catechin ($C_{15}H_{14}O_6$), and quercetin ($C_{21}H_{20}O_{12}$).

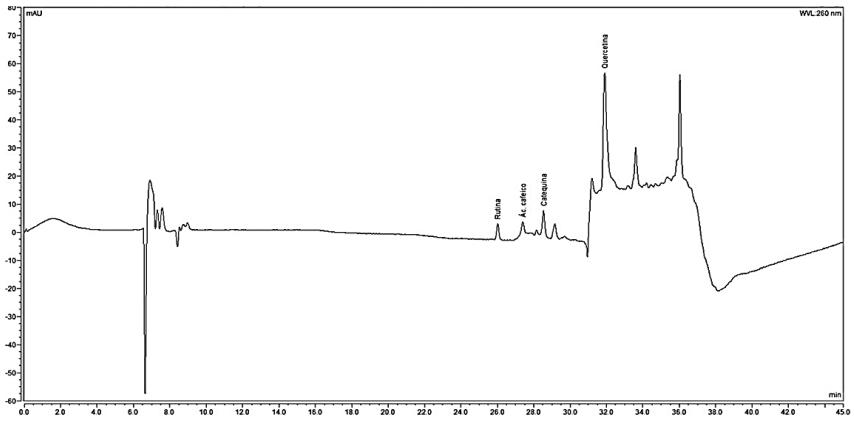

Figure 3. Compound identification by HPLC from stems of *Fraxinus uhdei*. Chromatograms of flavonoids were obtained from ethanol extract of *F. uhdei* by column chromatography. Rutin ($C_{27}H_{30}O_{16}$), caffeic acid ($C_9H_8O_4$), catechin ($C_{15}H_{14}O6$), and quercetin ($C_{21}H_{20}O_{12}$).

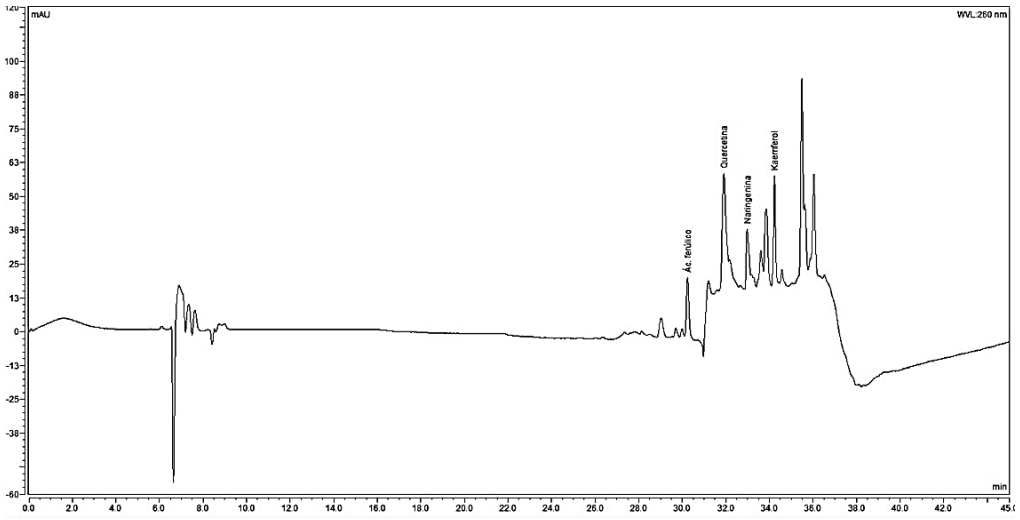

Figure 4. Compound identification by HPLC from leaves of *Taxodium mucronatum*. Chromatograms of flavonoids were obtained from ethanol extract of *T. mucronatum* by column chromatography. ferulic acid ($C_{10}H_{10}O_4$), quercetin ($C_{21}H_{20}O_{12}$), naringenin ($C_{15}H_{12}O$ 272.257 g/mol), and kaempferol ($C_{15}H_{10}O_6$ 286.23 g/mol).

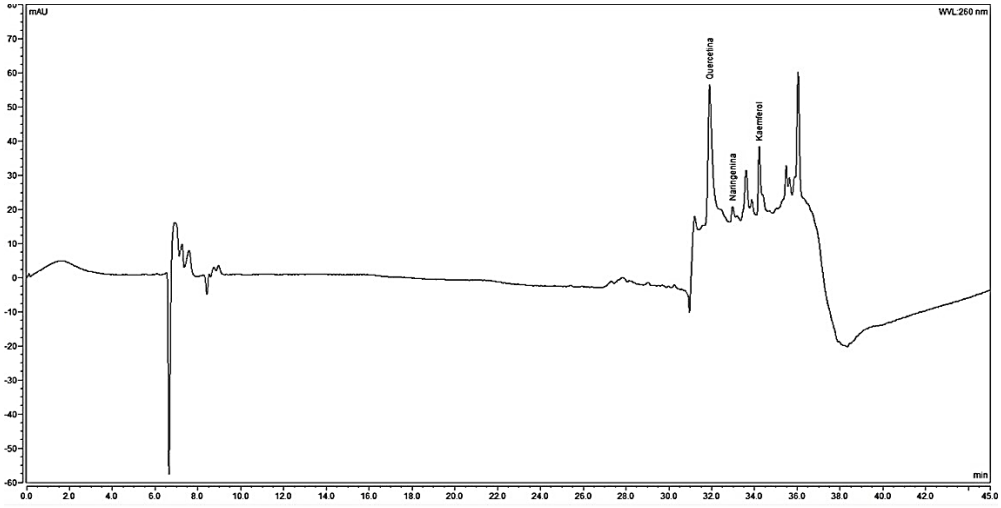

Figure 5. Compound identification by HPLC from stems of *Taxodium mucronatum*. Chromatograms of flavonoids were obtained from ethanol extract of *T. mucronatum* by column chromatography. quercetin ($C_{21}H_{20}O_{12}$), naringenin ($C_{15}H_{12}O$ 272.257 g/mol), and kaempferol ($C_{15}H_{10}O_6$ 286.23 g/mol).

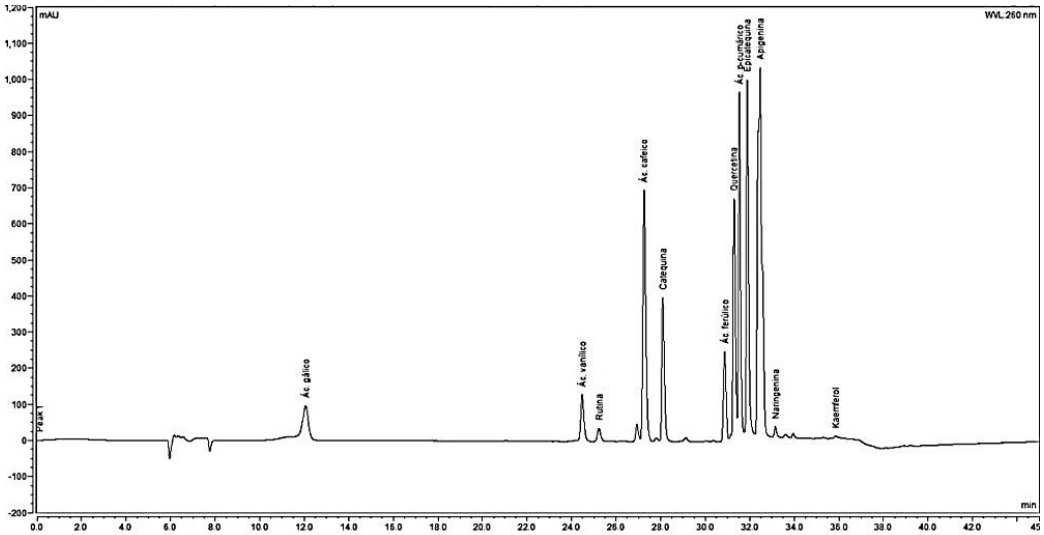

Figure 6. Chromatogram of the retention time of phenolics compounds standards.

Figure 7 shows the chemical structures of the phenolic compounds found in the present work (Figure 7).

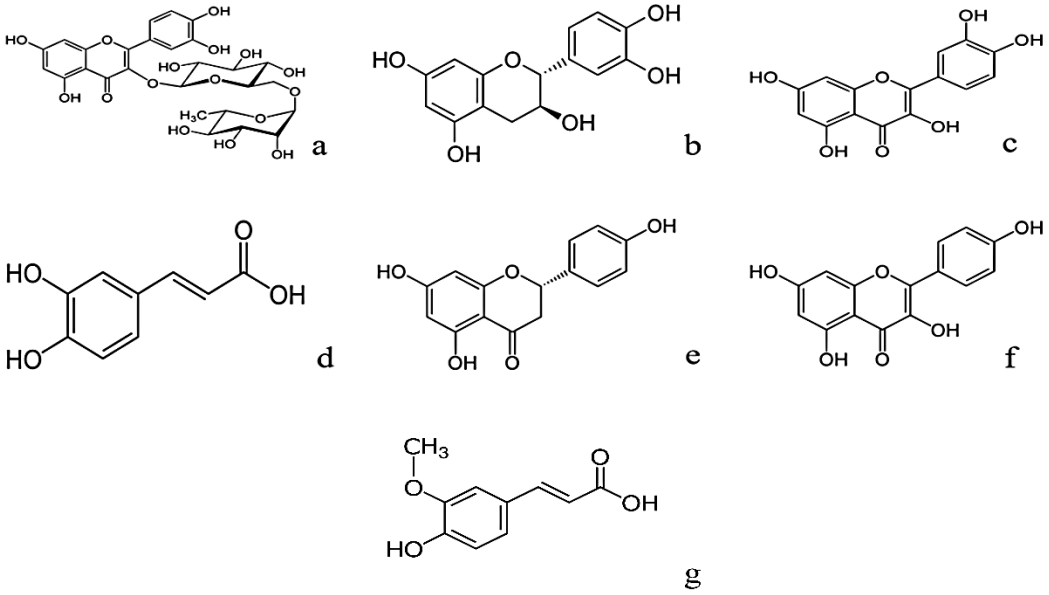

Figure 7. Secondary metabolites biosynthesized in *Fraxinus uhdei* and *Taxodium mucronatum* tree extracts. a) rutin, b) catequin, c) quercetin, d) caffeic acid, e) naringenin, f) Kaempferol, and g.) ferulic acid.

3.1. Rutin.

Rutin is a flavonoid obtained from various plant species, in this case, from the fruits of *Dimorphandra mollis*. It has a venotonic and protective action on the vascular endothelium, anti-inflammatory, anti-edematous, anti-varicose, and anti-cellulite. It treats pathological conditions characterized by capillary hemorrhages associated with increased capillary fragility, such as vascular accidents of hypertension, hematuric nephritis, and diabetic vasculopathy. It is also used in cases of venous insufficiencies such as varicose veins, hemorrhoids, tired legs, phlebitis, thrombophlebitis, and night cramps. It is usually administered orally in the form of capsules or tablets or topically in the form of creams, gels, and lotions-creams. In serums and creams, it is used as a revitalizing agent to reduce dark circles under the eyes [15,16]. The highest rutin concentration was found in the *Fraxinus uhdei* leaf extract (5.49 µg/mL).

3.2. Catechin.

The term catechin is commonly used to refer to the flavonoid family and the flavan-3-ols (or simply flavanols) subgroup. Flavanols possess the saturated C-ring and a hydroxyl group on the C3 carbon. They can occur as monomers or as polymers with varying degrees of polymerization. Unlike other flavonoid groups, their heterosidic-type combinations (between the reducing sugar group and a thiol group) are rare. The most representative flavanols in foods are of the flavan-3-ol type, and these can appear as monomers (catechin), as dimers condensed together, and as oligomers (procyanidins), or they can appear as polymers (proanthocyanidins or condensed tannins). Epicatechin and catechin are the major compounds in fruits. The most available data on the characterization of these compounds refer mainly to dimers and trimers of catechin, which represent the major forms. However, new analytical techniques have been developed in recent years, leading to a better characterization of all these compounds [17,18]. The highest catechin concentration was found in the extract of *Fraxinus uhdei* leaves (3.68 µg/mL).

3.3. Quercetin.

Quercetin is the most representative flavonol compound. Flavonols are characterized by having a keto group on carbon C4 and an unsaturation between carbons C2 and C3. They also have an additional hydroxyl group on the C3 carbon. They represent the most ubiquitous group of polyphenols present in foods. Quercetin inhibits the oxidation of low-density lipoproteins (LDLs) directly or through vitamin E, preventing it from oxidizing or regenerating once it has fulfilled its function. Likewise, quercetin reduces oxidative damage in the neurovascular structures of the skin and inhibits neuronal damage caused by experimental glutathione depletion [19,20]. The highest quercetin concentration was found in the *Fraxinus uhdei* leaf extract (24.02 µg/mL).

3.4. Caffeic acid.

Caffeic acid as well as ferulic acid are natural antioxidants and are structurally very similar, their only difference being the presence of a methoxyl group in ferulic acid in place of the hydroxyl group located at the 3-position of the phenyl radical. Several reports have documented that the antioxidant activity of this family of compounds (caffeic acid and ferulic acid) is directly related to the number of units (hydroxycinnamic) compounds is directly related to the number of guaiacol or catechol units present in the guaiacol or catechol units present in these systems, their ability to transfer electrons and/or protons, as well as their oxidized and/or protons, as well as with the stability of their oxidized radical type species [21,22]. The highest concentration of caffeic acid was found in the extract of *Fraxinus uhdei* stems (11.56 µg/mL).

3.5. Ferulic acid.

Ferulic acid is a hydroxycinnamic acid. It has been documented that the salt of ferulic acid, ferulic acid salt, and sodium ferulate prevents the oxidation of low-density lipoproteins (LDL) [23,24]. Both caffeic acid and ferulic acid have other biological activities, such as: antibacterial, antifungal, and antiviral. Another study approach has also considered the prooxidant activity, and in this sense, it has been found that both compounds can act as prooxidants in the presence of Fe^{+3} if they are at a concentration above 5 µM. The highest concentration of ferulic acid was found in *Taxodium mucronatum* leaf extract (10.05 µg/mL).

3.6. Naringenin.

Naringenin is a flavanone. Flavanones are flavone analogs with a saturated C-ring. They are glycosylated mainly by the attachment of a disaccharide at the C7 carbon. (7-O-neohesperidose), has antioxidant, anti-apoptotic, and anti-hyperlipidemic properties. It has been reported to be a useful nutraceutical in managing diabetes and its complications [25,26]. The highest concentration of naringenin was found in *Taxodium mucronatum* leaf extract (11.25 µg/mL).

3.7. Kaempferol.

Kaempferol is a Flavonol. Flavonols are characterized by having a keto group on the C4 carbon and an unsaturation between the C2 and C3 carbons. They also have an additional hydroxyl group on the C3 carbon. They represent the most ubiquitous group of polyphenols present in foods. It is a flavonol very soluble in water and ethanol. It provides the smell of

flowers and has antidepressant properties. It also functions as an agent in pancreatic cancer prevention. Some foods with kaempferol are apples, brussels sprouts, leek, and broccoli [27,28]. The highest concentration of kaempferol was present in the *Taxodium mucronatum* leaf extract (1.56 µg/mL).

4. Conclusions

The antioxidant flavonoids found in higher concentrations by Ultra-HPLC from leaf extracts of *Fraxinus uhdei* were: quercetin and rutin (72.37% y 16.54%, respectively). The antioxidant flavonoids found in the highest concentration by HPLC from foliar extracts of *Taxodium mucronatum* were: quercetin and naringenin (39.20% and 29.92%, respectively). The antioxidant flavonoids found in higher concentrations by HPLC from stem extracts of *Fraxinus uhdei* were: quercetin and caffeic acid (60.34% and 29.14%, respectively). The antioxidant flavonoids found in higher concentrations by HPLC from *Taxodium mucronatum* stem extracts were: quercetin and naringenin (71.76% and 23.23%, respectively). This is the first research in which the presence of this secondary metabolite in *Taxodium mucronatum* leaves and stem extracts are reported.

Funding

This research received no external funding.

Acknowledgments

The authors are grateful to Consejo Nacional de Ciencia y Tecnología (CONACyT, Mexico) and Instituto Tecnológico de Estudios Superiores de Zamora in Michoacan, Mexico.

Conflicts of Interest

The authors declare no conflict of interest.

References

1. Laoué, J.; Fernandez, C.; Ormeño, E. Plant Flavonoids in Mediterranean Species: A Focus on Flavonols as Protective Metabolites under Climate Stress. *Plants* **2022**, *11*, https://doi.org/10.3390/plants11020172.
2. Ribaudo, G. Synthesis of Flavonoids or Other Nature-Inspired Small Molecules. *Molbank* **2022**, *2022*, https://doi.org/10.3390/M1313.
3. Dias, M.C.; Pinto, D.C.G.A.; Silva, A.M.S. Plant Flavonoids: Chemical Characteristics and Biological Activity. *Molecules* **2021**, *26*, https://doi.org/10.3390/molecules26175377.
4. Albert, N.W.; Lafferty, D.J.; Moss, S.M.A.; Davies, K.M. Flavonoids – flowers, fruit, forage and the future. *Journal of the Royal Society of New Zealand* **2022**, 1-28, https://doi.org/10.1080/03036758.2022.2034654.
5. Speisky, H.; Shahidi, F.; Costa de Camargo, A.; Fuentes, J. Revisiting the Oxidation of Flavonoids: Loss, Conservation or Enhancement of Their Antioxidant Properties. *Antioxidants* **2022**, *11*, https://doi.org/10.3390/antiox11010133.
6. Kiani, R.; Arzani, A.; Mirmohammady Maibody, S.A.M. Polyphenols, Flavonoids, and Antioxidant Activity Involved in Salt Tolerance in Wheat, Aegilops cylindrica and Their Amphidiploids. *Front. Plant Sci.* **2021**, *12*, https://doi.org/10.3389/fpls.2021.646221.
7. Al-Khayri, J.M.; Sahana, G.R.; Nagella, P.; Joseph, B.V.; Alessa, F.M.; Al-Mssallem, M.Q. Flavonoids as Potential Anti-Inflammatory Molecules: A Review. *Molecules* **2022**, *27*, https://doi.org/10.3390/molecules27092901.
8. Drețcanu, G.; Știrbu, I.; Leoplold, N.; Cruceriu, D.; Danciu, C.; Stănilă, A.; Fărcaș, A.; Borda, I.M.; Iuhas, C.; Diaconeasa, Z. Chemical Structure, Sources and Role of Bioactive Flavonoids in Cancer Prevention: A Review. *Plants* **2022**, *11*, https://doi.org/10.3390/plants11091117.

9. Xi, X.;Wang, J.; Qin, Y.; You, Y.; Huang,W.; Zhan, J. The Biphasic Effect of Flavonoids on Oxidative Stress and Cell Proliferation in Breast Cancer Cells. *Antioxidants* **2022**, *11*, https://doi.org/10.3390/antiox11040622.
10. Bibi, N.; Shah, M.H.; Khan, N.; Al-Hashimi, A.; Elshikh, M.S.; Iqbal, A.; Ahmad, S.; Abbasi, A.M. Variations in Total Phenolic, Total Flavonoid Contents, and Free Radicals' Scavenging Potential of Onion Varieties Planted under Diverse Environmental Conditions. *Plants* **2022**, *11*, https://doi.org/10.3390/plants11070950.
11. Goufo, P.; Singh, R.K.; Cortez, I. A Reference List of Phenolic Compounds (Including Stilbenes) in Grapevine (Vitis vinifera L.) Roots, Woods, Canes, Stems, and Leaves. *Antioxidants* **2020**, *9*, https://doi.org/10.3390/antiox9050398.
12. Wang, W.; Zhang, X.; Liu, Q.; Lin, Y.; Zhang, Z.; Li, S. Study on Extraction and Antioxidant Activity of Flavonoids from Hemerocallis fulva (Daylily) Leaves. *Molecules* **2022**, *27*, https://doi.org/10.3390/molecules27092916.
13. Xie, L.; Deng, Z.; Zhang, J.; Dong, H.; Wang, W.; Xing, B.; Liu, X. Comparison of Flavonoid O-Glycoside, C-Glycoside and Their Aglycones on Antioxidant Capacity and Metabolism during In Vitro Digestion and In Vivo. *Foods* **2022**, *11*, https://doi.org/10.3390/foods11060882.
14. Guevara-Fefer, P.; Muñoz-Ocotero, V.; Llanos-Romero, R.E.; Zúñiga-Ruiz, B.; Cárdenas-Vázquez, R.J.; Contreras-Jiménez, J.L.; Ocampo-Bautista, F. Flavonoides de trece especies del género Bursera con potencial antioxidante. *Polibotánica* **2017**, *44*, 185-193, https://doi.org/10.18387/polibotanica.44.14.
15. Kreft, I.; Germ, M.; Golob, A.; Vombergar, B.; Bonafaccia, F.; Luthar, Z. Impact of Rutin and Other Phenolic Substances on the Digestibility of Buckwheat Grain Metabolites. *Int. J. Mol. Sci.* **2022**, *23*, https://doi.org/10.3390/ijms23073923.
16. Kianersi, F.; Abdollahi, M.R.; Mirzaie-asl, A.; Dastan, D.; Rasheed, F. Identification and tissue-specific expression of rutin biosynthetic pathway genes in Capparis spinosa elicited with salicylic acid and methyl jasmonate. *Scientific Reports* **2020**, *10*, https://doi.org/10.1038/s41598-020-65815-2.
17. Noll, C.; Kandiah, J.; Moroy, G.; Gu, Y.; Dairou, J.; Janel, N. Catechins as a Potential Dietary Supplementation in Prevention of Comorbidities Linked with Down Syndrome. *Nutrients* **2022**, *14*, https://doi.org/10.3390/nu14102039.
18. Munteanu, I.G.; Apetrei, C. Assessment of the Antioxidant Activity of Catechin in Nutraceuticals: Comparison between a Newly Developed Electrochemical Method and Spectrophotometric Methods. *International Journal of Molecular Sciences* **2022**, *23*, https://doi.org/10.3390/ijms23158110.
19. Salehi, B.; Machin, L.; Monzote, L.; Sharifi-Rad, J.; Ezzat, S.M.; Salem, M.A.; Merghany, R.M.; El Mahdy, N.M.; Kılıç, C.S.; Sytar, O.; Sharifi-Rad, M.; Sharopov, F.; Martins, N.; Martorell, M.; Cho, W.C. Therapeutic Potential of Quercetin: New Insights and Perspectives for Human Health. *ACS Omega* **2020**, *5*, 11849-11872, https://doi.org/10.1021/acsomega.0c01818.
20. Deepika; Maurya, P.K. Health Benefits of Quercetin in Age-Related Diseases. *Molecules* **2022**, *27*, https://doi.org/10.3390/molecules27082498.
21. Anaya, J.A.; Lizama, V.; García, M.J.; Álvarez, I. Applying rosemary extract and caffeic acid to modify the composition of Monastrell wines. *European Food Research and Technology* **2022**, *248*, 1787-1802, https://doi.org/10.1007/s00217-022-04005-y.
22. Liang, S.; Xu, S.; Qu, D.; Yang, L.;Wang, J.; Liu, H.; Xin, W.; Zou, D.; Zheng, H. Identification and Functional Analysis of the Caffeic Acid O-Methyltransferase (COMT) Gene Family in Rice (Oryza sativa L.). *Int. J. Mol. Sci.* **2022**, *23*, https://doi.org/10.3390/ijms23158491.
23. Kurasiak-Popowska, D.; Graczyk, M.; Przybylska-Balcerek, A.; Stuper-Szablewska, K.; Szwajkowska-Michałek, L. An Analysis of Variability in the Content of Phenolic Acids and Flavonoids in Camelina Seeds Depending on Weather Conditions, Functional Form, and Genotypes. *Molecules* **2022**, *27*, https://doi.org/10.3390/molecules27113364.
24. Villanueva, M.P.; Gioia, C.; Sisti, L.; Martí, L.; Llorens-Chiralt, R.; Verstichel, S.; Celli, A. Valorization of Ferulic Acid from Agro-Industrial by-Products for Application in Agriculture. *Polymers* **2022**, *14*, https://doi.org/10.3390/polym14142874.
25. Stabrauskiene, J.; Kopustinskiene, D.M.; Lazauskas, R.; Bernatoniene, J. Naringin and Naringenin: Their Mechanisms of Action and the Potential Anticancer Activities. *Biomedicines* **2022**, *10*, https://doi.org/10.3390/biomedicines10071686.
26. Stabrauskiene, J.; Marksa,M.; Ivanauskas, L.; Bernatoniene, J. Optimization of Naringin and Naringenin Extraction from Citrus _ paradisi L. Using Hydrolysis and Excipients as Adsorbent. *Pharmaceutics* **2022**, *14*, https://doi.org/10.3390/pharmaceutics14050890.
27. Bangar, S.P.; Chaudhary, V.; Sharma, N.; Bansal, V.; Ozogul, F.; Lorenzo, J.M. Kaempferol: A flavonoid with wider biological activities and its applications. *Critical reviews in food science and nutrition* **2022**, 1-25, https://doi.org/10.1080/10408398.2022.2067121.
28. Kluska, M.; Juszczak, M.; Żuchowski, J.; Stochmal, A.; Woźniak, K. Effect of Kaempferol and Its Glycoside Derivatives on Antioxidant Status of HL-60 Cells Treated with Etoposide. *Molecules* **2022**, *27*, https://doi.org/10.3390/molecules27020333.