Biochemical Systematics and Ecology 103 (2022) 104430

Contents lists available at ScienceDirect

Biochemical Systematics and Ecology

journal homepage: www.elsevier.com/locate/biochemsyseco

Non-volatile compounds from *Araucaria columnaris* (G.Forst.) Hook leaves

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ARTICLE INFO

Keywords:
Araucaria columnaris (G.Forst.) Hook.
Araucariaceae
Leaves
Phytochemical analysis
Chemophenetics

ABSTRACT

The phytochemical analysis on the leaves of a new population of *Araucaria columnaris* (G.Forst.) Hook. was reported. Seven compounds were identified i.e., 15-agathic acid methyl ester (**1**), ladanein (**2**), 7,4′,7″,4‴-tetra-*O*-methyl-robustaflavone (**3**), 3-*O*-*trans*-*p*-coumaroyl-quinic acid (**4**), 4-*O*-*trans*-*p*-coumaroyl-quinic acid (**5**), 5-*O*-*trans*-*p*-coumaroyl-quinic acid (**6**) and shikimic acid (**7**). Chromatographic and spectroscopic techniques were utilized for this. Their presence is important from the chemophenetic point of view, but further research is necessary to make final conclusions on this species.

1. Subject and source

Araucaria columnaris (G.Forst.) Hook., also known with the common names of Cook Pine and Columnar Araucaria, is a conifer belonging to the Araucariaceae family.

This species is morphologically characterized by a narrow and conical trunk which can grow up to 60 m, a rough, grey and resinous bark, short and whorled branches full of horizontal branchlets, small leaves spirally arranged and overlapped on the branchlets, big, scaly and egg-shaped female cones, smaller male cones located at the tips of the branchlets having the shape of a foxtail (Medeiros et al., 2008; Johns et al., 2017).

A. columnaris is mainly known as an ornamental tree and can be found in private and public gardens as well as along the streets of Southern Australia, New Caledonia, Northern New Zealand, Puerto Rico, Mexico, India, Philippines and Hawaii (Medeiros et al., 2008; Johns et al., 2017).

In this work, the first phytochemical analysis on the leaves of a European population of this species was reported. The leaves (19.7 g) were collected in the Botanical Garden of Rome (geographical coordinates 41°53′32″ N, 12°27′57″ E) in late May 2019. The botanical identification was directly performed by the botanists of the garden. A sample of this collection is kept in our laboratory for further reference under the voucher code AC25052019. The main other aim of this study was to provide a more general overview on the chemophentic characteristics of the species.

2. Previous work

Only a few works are present in literature about this species focusing mainly on the non-volatile phytochemical pattern. In fact, the three studies of Patial and Cannoo (2019, 2020, 2021) were about the essential oil composition and the presence of volatile diterpenes, sesquiterpenes and hydrocarbons as well as specific phenolic acids and flavonoids in different organs of an exemplar from India. The composition in volatile compounds was also studied by Saranja Devi et al., (2013), in the resin of this species collected, again, in India. Indeed, Aslam et al., 2014 performed a phytochemical screening on the aerial parts of this species purchased from a local market in Pakistan identifying cardiac glycosides and tannins. General flavonoids and tannins, without specifying the exact compounds, were found during the study of Tintu and Mannancheril (2020) in the barks of another exemplar from India. Several labdane and abietane diterpenoids were found by Cox et al. (2007) in the external resin of this species obtained from the Royal Melbourne Botanical Garden, instead. Brophy et al., (2000) studied only the essential oil composition of this species obtained from the Royal Sidney Botanical Garden. The presence of some specific phospholipids in *A. columnaris* collected in Russia was observed by Rozentsvet et al., (2000). The biflavonoid 4′,4‴,7,7″-tetra-*O*-methyl-cupressuflavone was isolated and identified by De Forest et al., (2014) in an exemplar from

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https://doi.org/10.1016/j.bse.2022.104430
Received 31 March 2022; Received in revised form 17 May 2022; Accepted 22 May 2022
Available online 30 May 2022
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Hawaii. Several biflavonoids were also isolated and identified by Ilyas et al. (1978) in the leaves of this species collected in India whereas some flavonoids, both aglycone and glycosylated, were observed in the shoots of this species from Egypt (Michael et al., 2010). Lastly, several alkanes were identified in the leaf vax of *A. columnaris* from Mount Tomah Botanic Gardens, Australia (Maffei et al., 2004) as well as several acidic polysaccharides were identified in the resinous exudates of *A. columnaris* from East Africa (Anderson and Munro 1969).

3. Present study

The phytochemical analysis on the leaves of *A. columnaris* evidenced the presence of seven compounds namely 15-agathic acid methyl ester (**1**), ladanein (**2**), 7,4′,7″,4‴-tetra-*O*-methyl-robustaflavone (**3**), 3-*O*-*trans*-*p*-coumaroyl-quinic acid (**4**) (IUPAC, 1976), 4-*O*-*trans*-*p*-coumaroyl-quinic acid (**5**) (IUPAC, 1976), 5-*O*-*trans*-*p*-coumaroyl-quinic acid (**6**) (IUPAC, 1976) and shikimic acid (**7**) (Fig. 1). All these compounds were identified by means of column chromatography together with NMR spectroscopy and mass spectrometry.

Compound (**1**) is a diterpene, compound (**2**) is a flavonoid, compound (**3**) is a biflavonoid, compounds (**4**–**6**) are quinic acid derivatives and compound (**7**) is an organic acid.

3.1. General experimental procedure

The following materials and solvents were used during this study: ethanol 96% for the extraction procedure; *n*-butanol and distilled water in mixture as eluting system for the column chromatography separation on silica gel (40–63 μm) as stationary phase; 2N sulphuric acid for the developments of the TLCs; deuterated solvents ($CDCl_3$, CD_3OD and D_2O) for the identification of metabolites by means of NMR spectroscopy; HPLC-grade methanol in mixture with 5 mM formic acid for the identification of metabolites by means of mass spectrometry.

All the solvents having RPE purity grade, if not differently specified, together with the deuterated solvents and the TLCs were purchased from

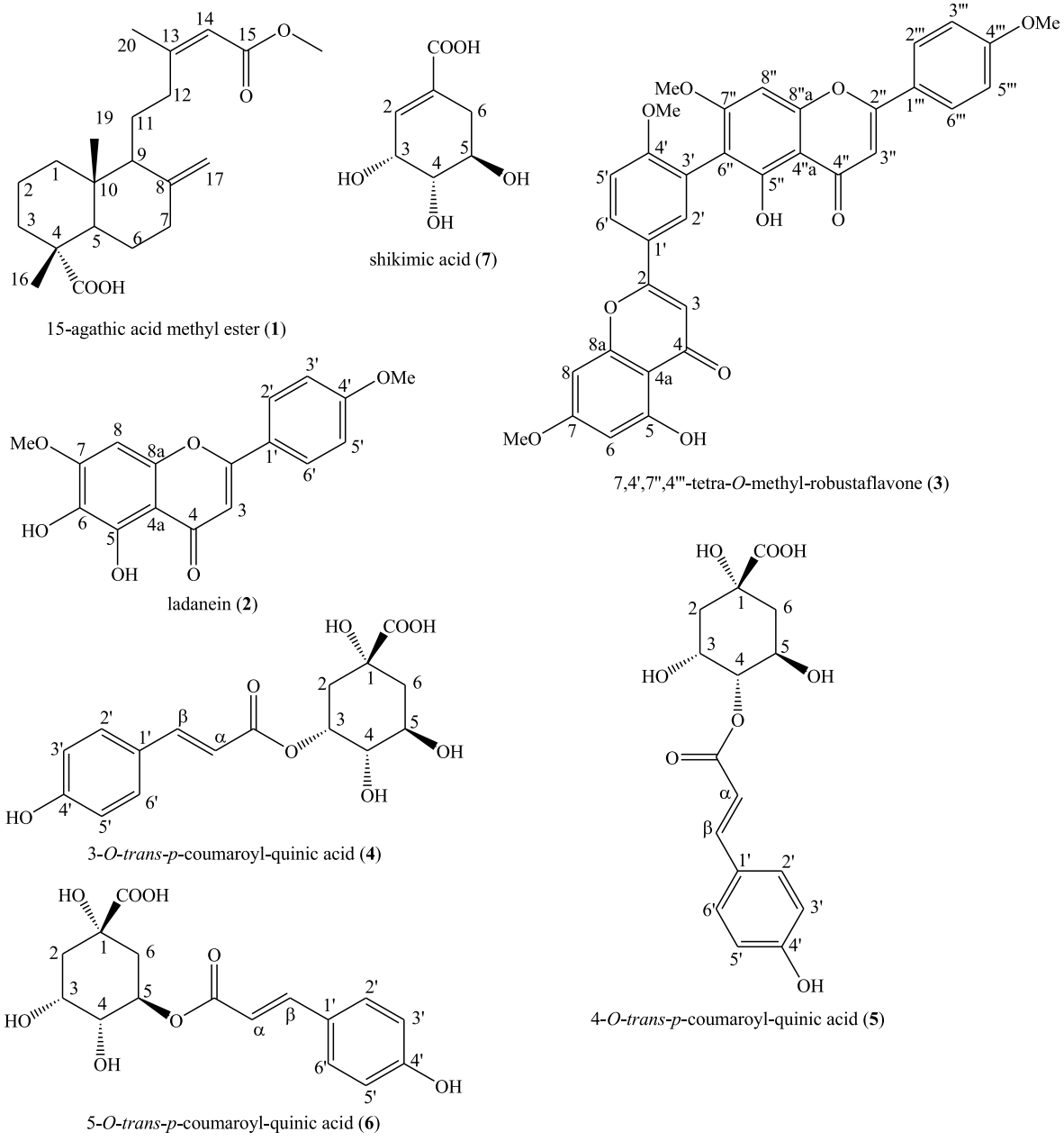


Fig. 1. Structures of the identified compounds in the leaves of *A. columnaris*.

Sigma-Aldrich. HPLC-grade methanol was purchased from Carlo Erba whereas silica gel was purchased from Fluka Analytical.

NMR spectra were recorded at 298 K on a Jeol JNM-ECZ 600R spectrometer with a magnet operating at 14.09 T corresponding to a proton resonance frequency of 600.19 MHz and equipped with a Jeol multinuclear z-gradient inverse probehead. ^{1}H NMR spectra were acquired with 32 transients, a spectral width of 9013.7 Hz (corresponding to 15 ppm) and 64K data points for an acquisition time of 7.3 s. The recycle delay was set to 7.7 s to achieve complete resonance relaxation between successive scans. The chemical shifts were referenced to TMS (s, 0 ppm) for spectra in $CDCl_3$, the internal solvent signal of CD_2HOD (m5, 3.31 ppm) was the reference for spectra in CD_3OD while the HDO signal (s, 4.79 ppm) was set as reference for spectra in D_2O.

Mass spectral data were acquired by a Quattro Micro Tandem MS/MS with a Waters ESI source (Micromass, Manchester U.K.). The infusion experiments were carried out using a flow rate of 5 μL/min, acquiring data in scan mode for 2 min, in the mass range 80–700 Da, with the following source parameters: compound (**1**), capillary 2.7 kV in ESI(−) and 2.5 kV in ESI(+), cone 22 V, source temperature 100 °C, desolvation temperature 150 °C; compound (**2**), ESI(+), capillary 2.5 kV, cone 22 V, source temperature 100 °C, desolvation temperature 150 °C; compound (**3**), ESI(+), capillary 2.7 kV, cone 25 V, source temperature 120 °C, desolvation temperature 350 °C; compounds (**4**–**6**), ESI(−) and ESI(+), capillary 2.7 kV, cone 30 V, source temperature 120 °C, desolvation temperature 350 °C; compound (**7**), ESI(−), capillary 2.7 kV, cone 30 V, source temperature 120 °C, desolvation temperature 350 °C. Cone gas flow was 40 L/h and desolvation gas flow was 400 L/h. Data acquisition, data handling, and instrument control were performed by MassLynx Software 4.1 v (Data Handling System for Windows, Micromass, U.K.).

3.2. Extraction, separation and identification procedures

The dried leaves of *A. columnaris* (19.7 g) were extracted with ethanol 96% (about 300 mL) three times after a maceration of 96 h, each. The ethanol was evaporated at reduced pressure at 50 °C until a water suspension was obtained. Throughout the concentration procedure, pH was checked on litmus paper in order to verify that pH was not too acid or basic (meaning between the range 5.5–8.5) because an extreme acidity or alkalinity might cause secondary reactions in the extract such as the hydrolysis of ester and glycosidic bonds. In this case, pH was about 7.5. The obtained dried dark green extract weighed 835.7 mg. An aliquot of this (700.0 mg) was subjected to chromatographic separation on silica gel (24.2 g, ratio about 1:35 *w/w*). The eluting system consisted of a mixture of *n*-butanol and distilled water at the concentration ratio of 82:18 *v/v*. From this first chromatographic separation all the compounds were identified by comparison with data reported in literature and standard compounds present in our laboratory: 15-agathic acid methyl ester (**1**) (Richomme et al., 1991) and ladanein (**2**) (Çitoglu et al., 1999) in mixture with fatty acids (ratio 1:5 *w/w* between them) from the combined fractions 4–9 (15.5 mg); ladanein (**2**) (Çitoglu et al., 1999) in mixture with 7,4′,7″,4‴-tetra-*O*-methyl-robustaflavone (**3**) (Venditti et al., 2017a) in ratio 25:1 *w/w* from the combined fractions 10–20 (21.9 mg); 3-*O*-*trans*-*p*-coumaroyl-quinic acid (**4**), 4-*O*-*trans*-*p*-coumaroyl-quinic acid (**5**) and 5-*O*-*trans*-*p*-coumaroyl-quinic acid (**6**) (Will et al., 2007; Gutiérrez Ortiz et al., 2017) in mixture with saccharides (ratio 2:5:1 *w/w/w* among them) from the combined fractions 31–38 (13.2 mg); shikimic acid (**7**) (Venditti et al., 2017a) in mixture with saccharides (ratio not calculable) from the combined fractions 80–98 (11.2 mg).

3.3. NMR and MS data of the identified metabolites

15-agathic acid methyl ester (**1**): ^{1}H NMR (600 MHz, $CDCl_3$) δ: 5.64 (1H, d, $J = 1.0$ Hz, H-14), 4.86 (1H, br. s, H-17a), 4.52 (1H, br. s, H-17b), 3.68 (3H, s, COOMe), 2.15 (3H, s, Me-16), 1.12 (3H, s, Me-19), 0.73 (3H, s, Me-20).

ESI-MS: *m/z* 371.30 $[M+Na]^+$, *m/z* 387.24 $[M+K]^+$, *m/z* 347.31 $[M-H]^-$.

Ladanein (**2**): ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.42 (1H, d, $J = 9.0$ Hz, H-2', H-6'), 6.86 (2H, d, $J = 9.0$ Hz, H-3', H-5'), 6.60 (1H, s, H-3), 6.58 (1H, s, H-8), 3.81 (3H, s, 4′-CH_3O), 3.79 (3H, s, 7-CH_3O).

ESI-MS: *m/z* 337.24 $[M+Na]^+$, *m/z* 353.25 $[M+K]^+$.

7,4′,7″,4‴-tetra-*O*-methyl-robustaflavone (**3**): ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.97 (1H, dd, $J = 8.8$, 2.4 Hz, H-6′), 7.87 (1H, d, $J = 2.4$ Hz, H-2′), 7.46 (2H, d, $J = 8.9$ Hz, H-2‴, H-6‴), 7.16 (1H, d, $J = 8.8$ Hz, H-5′), 6.82 (2H, d, $J = 8.9$ Hz, H-3‴, H-5‴), 6.64 (1H, s, H-3″), 6.62 (1H, s, H-3), 6.53 (1H, s, H-8″), 6.43 (1H, d, $J = 2.2$ Hz, H-8), 6.35 (1H, d, $J = 2.2$ Hz, H-6), 3.85 (3H, s, 4‴-CH_3O), 3.82 (3H, s, 7-CH_3O), 3.80 (3H, s, 4′-CH_3O), 3.77 (3H, s, 7″-CH_3O).

ESI-MS: *m/z* 595.49 $[M+H]^+$.

3-*O*-*trans*-*p*-coumaroyl-quinic acid (**4**): ^{1}H NMR (600 MHz, CD_3OD) δ: 7.65 (1H, d, $J = 16.0$ Hz, H-β), 7.45 (2H, d, $J = 8.5$ Hz, H-2′, H-6′), 6.80 (2H, d, $J = 8.5$ Hz, H-3′, H-5′), 6.36 (1H, d, $J = 16.0$ Hz, H-α), 5.42–5.38 (1H, m, H-3), 4.11–4.08 (1H, m, H-5), 2.25–2.00 (4H, overlapped signals, H-2, H-6).

ESI-MS: *m/z* 339.38 $[M+H]^+$, *m/z* 337.41 $[M-H]^-$.

4-*O*-*trans*-*p*-coumaroyl-quinic acid (**5**): ^{1}H NMR (600 MHz, CD_3OD) δ: 7.71 (1H, d, $J = 15.9$ Hz, H-β), 7.48 (2H, d, $J = 8.7$ Hz, H-2′, H-6′), 6.82 (2H, d, $J = 8.7$ Hz, H-3′, H-5′), 6.44 (1H, d, $J = 15.9$ Hz, H-α), 4.29–4.22 (2H, overlapped signals, H-3, H-5), 2.25–2.00 (4H, overlapped signals, H-2, H-6).

ESI-MS: *m/z* 339.38 $[M+H]^+$, *m/z* 337.41 $[M-H]^-$.

5-*O*-*trans*-*p*-coumaroyl-quinic acid (**6**): ^{1}H NMR (600 MHz, CD_3OD) δ: 7.67 (1H, d, $J = 16.2$ Hz, H-β), 7.46 (2H, d, $J = 8.6$ Hz, H-2′, H-6′), 6.81 (2H, d, $J = 8.6$ Hz, H-3′, H-5′), 6.39 (1H, d, $J = 16.2$ Hz, H-α), 4.29–4.22 (2H, overlapped signals, H-3, H-5),2.25–2.00 (4H, overlapped signals, H-2, H-6).

ESI-MS: *m/z* 339.38 $[M+H]^+$, *m/z* 337.41 $[M-H]^-$.

Shikimic acid (**7**): ^{1}H NMR (600 MHz, D_2O): 6.46–6.42 (1H, m, H-2), 4.42 (1H, t, $J = 4.4$ Hz, H-3); 4.03–3.97 (1H, m, H-5), 3.74–3.68 (1H, m, H-4), 2.78 (1H, dd, $J = 18.1$, 5.5 Hz, H-6a), 2.21 (1H, dd, $J = 18.1$, 6.8 Hz, H-6b).

ESI-MS: *m/z* 173.21 $[M-H]^-$.

4. Chemophenetic significance

To the best of our knowledge, during this study, compounds (**2, 4-6**) were identified in the Auracariaceae family for the first time whereas compounds (**3, 7**) were identified in the *Araucaria* genus for the first time and compound (**1**) was identified in the species for the first time.

In fact, compound (**1**) has been already observed in some *Araucaria* species collected in Australia (Kimura et al., 2012) as well as in one of its taxonomically related genera i.e., *Agathis* Salisb. and especially in the species *A. macrophylla* (Lindl.) Mast., *A. lanceolata* Warb. and *A. microstachya* J.F.Bailey & C.T.White (Cambie et al., 1989; Smith et al., 1981; Carman and Marty, 1966). By the way, labdane diterpenoids are considered as some of the main chemophenetic markers of the Auracariaceae family (Frezza et al., 2020). Nevertheless, this compound has been also isolated in *Juniperus brevifolia* (Seub.) Antoine comprised in Cupressaceae, a family which is taxonomically very close to Araucariaceae (Seca et al., 2008).

7,4′,7″,4‴-tetra-*O*-methyl-robustaflavone (**3**) has been previously reported only in the male reproduction organs of *Wollemia nobilis* W.G. Jones, K.D. Hill & J.M. Allen (Venditti et al., 2019a) which belongs to the Araucariaceae family, too. By the way, also biflavonoids are considered as important chemophenetic markers of the Auracariaceae family (Frezza et al., 2020) even if, during this study, only one of these compounds was evidenced.

Compound (**2**) has been previously isolated especially from Lamiaceae species (Tomás-Barberán et al., 1988; Bruno et al., 2007) but also from some Asteraceae (Seo et al., 2003) and Plantaginaceae species

(Ferhat et al., 2010). All these families are chemosystematically quite distant from Araucariaceae and this demonstrates the real ubiquitous occurrence of flavonoids in plants.

The identification of compounds (**4**–**6**) was fully confirmed after visualization of the relative ^{1}H NMR spectrum due to the presence of three different sets of signals associated to three different *p-trans*-coumaroyl and quinic moieties as reported in the literature (Will et al., 2007; Gutiérrez Ortiz et al., 2017). Their occurrence in plants is quite common. For example, all the three compounds have been identified in several *Chrysanthemum* spp. (Clifford et al., 2007) as well as in stone and pome fruits (Möller and Herrmann 1983). In addition, 3-*O-trans*-*p*-coumaroyl-quinic acid (**4**) has been also isolated, for example, from the leaves of *Vaccinium macrocarpon* Aiton (Ericaceae) (Neto et al., 2010) and from the leaves of two *Betula* species (Betulaceae) (Ossipov et al., 1996). 4-*O-trans-p*-coumaroyl-quinic acid (**5**) has been also isolated, for example, from the fruits of *Litchi chinensis* Sonn. (Sapindaceae) (Tang et al., 2018) and in the leaves from different varieties of *Camellia sinensis* (L.) Kuntze (Theaceae) (Wen et al., 2022).

Lastly, 5-*O-trans-p*-coumaroyl-quinic acid (**6**) has been also isolated, for example, from the immature fruits of *Pyrus pyrifolia* (Burm.f.) Nakai (Rosaceae) (Lee et al., 2013), the aerial parts of *Lactuca indica* L. (Asteraceae) (Kim et al., 2007) and the leaves of *Vaccinium macrocarpon* Aiton (Ericaceae) (Neto et al., 2010). All these families are also chemosystematically quite distant from Araucariaceae family and this also confirms the huge occurrence of this kind of compounds. Nevertheless, one point must be further highlighted *i.e.*, the non-presence of also the *cis*-isomers of these coumaroyl-quinic acids. This fact is extremely rare even though the interconversion *cis/trans* is quite rapid and common due to the highest stability of the *trans* isomer as reported in previous studies (Gutiérrez Ortiz et al., 2017; Clifford et al., 2006). This situation may depend on several intrinsic and extrinsic factors, but at the moment no serious hypothesis can be made because more in-depth studies are necessary. It is also important to highlight that 4-*O-trans*-*p*-coumaroyl-quinic acid (**5**) was found as the most abundant compound of its kind in this species. This fact is quite strange since the 5 and 3 isomers are usually the major ones (Clifford et al., 2006; Christensen et al., 2008; Park, 2010; Gutiérrez Ortiz et al., 2019). Yet, this peculiarity is not new having been already observed in some varieties of apple (Möller and Herrmann, 1983). This second evidence actually urges to perform further phytochemical studies to verify if there are other exceptions like these in nature.

Shikimic acid (**7**) has been previously isolated in the family only from *W. nobilis* (Venditti et al., 2017a, 2019a, 2019b, 2021; Frezza et al., 2017, 2018) and *Agathis robusta* (C. Moore ex F. Muell.) FM Bailey (Venditti et al., 2017b). Yet, it has no chemophenetic importance since it is quite ubiquitous in plants having been isolated also in other families like Arecaeae with *Phoenix dactylifera* L., Pinaceae with *Picea glauca* (Moench) Voss, Rosaceae with *Malus baccata* Loisel. and Iridaceae with *Iris pseudacorus* L. (Bochkov et al., 2012).

In conclusion, the presence of compounds like the labdane diterpenoid and the biflavonoid confirms the correct identification of the species as a member of the Araucariaceae family since they are some of its most important chemophenetic markers. Yet, other compounds were also identified and even particular ones. For this reason, further phytochemical studies are necessary in order to establish if this phytochemical pattern is typical of this population and of the species or it is only due to environmental factors.

Authors contribution

CF and DDV performed the separation procedure and elucidated the chemical structures; FS performed the NMR experiments and elucidated the chemical structures; RP performed the MS experiments; CT, SF, LT helped in elucidating the chemical structures; AB and MS supervised the entire work. All the authors wrote and edited the manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors wish to thank the Director of the Botanical Garden of Rome (Prof. Fabio Attorre) for providing us with the plant material and giving us the opportunity to study this species.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bse.2022.104430.

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