PHARMACIA

Pharmacia 72: 1–8
DOI 10.3897/pharmacia.72.e151142

Research Article

Metabolomics approach for geographical origin discrimination of *Cecropia peltata* by untargeted UHPLC-Q-Orbitrap-HRMS

Yancho Zarev[1], Anzhelika Dakovska[1], Yuliana Christopher[2], Orlando O. Ortiz[3,4,5], Yostin Añino[4,6], Iliana Ionkova[1], Andrés Rivera Mondragón[7,8]

1 *Department of Pharmacognosy, Faculty of Pharmacy, Medical University of Sofia, 2 Dunav str., 1000 Sofia, Bulgaria*
2 *Facultad de Biociencias y Salud Pública, Universidad Especializada de las Américas (UDELAS), Panama City, Panama*
3 *Botanischer Garten und Botanisches Museum Berlin, Freie Universität Berlin, Königin-Luise-Straße6-8, D-14195 Berlin, Germany*
4 *Coiba Scientific Station (Coiba AIP), Gustavo Lara Street, City of Knowledge, Clayton 0843-01853, Panama*
5 *Universidad de Panamá, Herbario PMA, Estafeta Universitaria, Apdo. 3366, Panamá City, Panama*
6 *Museo de Invertebrados G. B. Fairchild, Universidad de Panamá, P.O. Box 00017, Panama City, Panama*
7 *Universidad de Panamá, Instituto Especializado de Análisis (IEA), Panama City P.O. Box 3366, Panama*
8 *Universidad de Panamá, Facultad de Farmacia, Departamento de Química Medicinal y Farmacognosia, Centro de Investigaciones Farmacognósticas de la Flora Panameña (CIFLORPAN), Panama City P.O. Box 3366, Panama*

Corresponding authors: Yancho Zarev (yzarev@pharmfac.mu-sofia.bg); Andrés Rivera Mondragón (andres.riveraa@up.ac.pa)

Received 23 February 2025 ♦ **Accepted** 24 March 2025 ♦ **Published** 23 April 2025

Citation: Zarev Y, Dakovska A, Christopher Y, Ortiz OO, Añino Y, Ionkova I, Mondragón AR (2025) Metabolomics approach for geographical origin discrimination of *Cecropia peltata* by untargeted UHPLC-Q-Orbitrap-HRMS. Pharmacia 72: 1–8. https://doi.org/10.3897/pharmacia.72.e151142

Abstract

This study employed an untargeted metabolomic approach combined with chemometrics to investigate differences in the phytochemical composition of *Cecropia peltata* samples collected on the mainland and islands of the Panamanian Pacific. Twenty-three samples of *C. peltata* leaves were collected and analyzed using liquid chromatography-high resolution mass spectrometry analysis (LC-HRESI-MS). The results revealed a significant diversity of secondary metabolites. A supervised chemometric analysis model (OPLS-DA) was applied to differentiate specimens collected on the mainland from those collected on the islands. Among the metabolites identified as potential chemical markers in the studied specimens, five belong to the group of triterpenoid saponins. These compounds showed a significantly higher relative abundance in samples collected on the mainland than those collected on islands. In conclusion, this study highlights the chemical variability within *C. peltata* based on its geographic location. The findings suggest the importance of considering geographic origin when evaluating the therapeutic potential of this plant species in traditional and pharmaceutical medicine.

Keywords

Cecropia peltata, metabolomic analysis, triterpenoid saponins, chemometrics, geographic origin

Introduction

Plant chemosystematics studies identify and describe the range of chemicals found within a specific taxonomic group. Chemotaxonomy attempts to avoid replacing or supplanting phylogenetic research and analysis of the DNA sequence. However, its data could be utilized to support species through chemical characterization (Zidorn 2019). In this sense, chemotaxonomy can be a valuable tool to tackle challenging matters that could affect the formation of natural plant classifications in general (Fairbrothers et al. 1975; Reynolds 2007).

The *Cecropia* genus consists of more than 60 species that are widely distributed in Mexico, Panama, Argentina, Brazil, and Paraguay. *Cecropia* was first described as part of the Moraceae family, later classified as a new independent family, *Cecropiaceae*, and more recently, researchers have approached it as part of the Urticaceae family (Berg 1978). Most well-known and studied species include *C. pachystachya*, *C. peltata*, *C. lyratiloba*, *C. obtusifolia*, *C. palmata*, *C. glaziovii*, and *C. hololeuca*. The chemical compounds found in the *Cecropia* genus are most commonly terpenoids, flavonoids, and proanthocyanidins. *β*-sitosterol and ursolic acid have been isolated from *C. palmata* and *C. obtusa*. Orientin, isoorientin, and isovitexin were identified in *C. glaziovii* and *C. lyratiloba*. On the other hand, pomolic and oleanolic acids were found in *C. pachystachya* (Costa et al. 2011).

Plants of the *Cecropia* genus, commonly known as "guarumo," "yarumo," "embaúba," imbaúba, and "ambay," which means hollow trunk in the Tupí language, are plants used in Latin American countries to treat various diseases or conditions (Berg 1978). In folk medicine, desiccated leaves of this plant were commonly consumed in infusion primarily to treat diabetes mellitus but were also taken as an inflammation-reducing remedy. A study comparing *C. obtusifolia* and *C. peltata* showed that *C. peltata* has an exceedingly better hypoglycemic effect than *C. obtusifolia* (Nicasio et al. 2005). *C. pachystachya* is another species with traditional use in the antidiabetic treatment in folk medicine (Salam et al. 2023). In the Mexican culture, the plant parts (stem, root, bark, and leaves) are commonly applied in the treatment of blood sugar disorders in diabetic patients. In addition, leaf decoctions of the *Cecropia* plant are used in the Republic of El Salvador as a tranquilizer and for treating rheumatic diseases, among which are arthritis and gout. In another Central American country – Costa Rica – the *Cecropia* plant is widely used in the standard of care for high blood pressure and as a diuresis-increasing remedy (Rivera-Mondragón et al. 2021). *C. glaziovii* was discovered to have an intriguing antiviral action, and its activity was studied on the type 1 and type 2 herpes simplex viruses. The mechanism of action was found to be the inhibition of cell entry for both types, which reduces viral virulence (Silva et al. 2010). However, the lack of knowledge about the chemical composition and mechanism of action related to its therapeutic properties represents a significant challenge to validate the medicinal use of these medicinal plants. Since the current taxonomic research on the *Cecropia* genus particularly relies on anatomical and morphological data (Berg 1978), a detailed examination of the phytochemical profile of *Cecropia* could help distinguish between species, offering valuable insights for a more comprehensive taxonomic understanding of this genus.

In earlier research conducted by our team, the chemical composition of various *Cecropia* species was analyzed. These species were chosen because they are abundantly found in accessible areas in the provinces of Panama, West Panama, Chiriquí, and Darién (Rivera-Mondragón et al. 2017; Rivera-Mondragón et al. 2019a). An interesting finding was the variation in the phytochemical components found in various species of this genus (Ortiz et al. 2019; Rivera-Mondragón et al. 2019a). Our research group identified several issues that are worth covering within the present research study. One of them involves the existence of two morphotypes in *C. obtusifolia* with different chemical compositions depending on their origin. This species suggests the potential for chemical differences between specimens growing on the mainland and those in insular areas, resulting in two distinct entities from a chemical perspective. Specifically, in the case of medicinal plants, such as the *C. peltata* species, the use of these plants with inappropriate phytochemical profiles could lead to erroneous interpretations in pharmaceutical research on medicinal products.

Considering that *C. peltata* is a plant widely used in traditional medicine and ethnopharmacology, this research project seeks to differentiate *C. peltata* species found on land and in the Pacific islands of Panama through a non-targeted metabolomic approach as an innovative strategy. To achieve this purpose, we propose to use a metabolomic analysis of the specimens under study using modern chromatographic techniques coupled with mass spectrometry, together with chemometric (multivariate) analyses.

Materials and methods

General experimental procedures

For the purposes of our study, the leaves of twenty-three samples of *C. peltata* on land and on the largest island in the Central American region – Coiba Island, located in the Gulf of Chiriquí, Panamanian province of Veraguas – were collected manually. This study focused on qualitative metabolomic analysis to compare the phytochemical composition of *C. peltata* samples. The assessment was based on the relative abundance of metabolites detected in the LC-HRESI-MS analysis, rather than a fully quantitative determination of metabolite concentrations. Plant material was taxonomically classified by Prof. Orlando Ortiz and deposited at the Herbarium of the University of Panama (Table 1). To carry out this research project, a permit for the collection and export of specimens for scientific purposes was requested and received from the Ministry of the Environment (MiAmbiente, Republic of Panama).

Table 1. Collection points of *C. peltata* specimens.

No.	Collection site	Type of location	Collection date	Coordinates	Voucher specimen number
CP1	Santa Catalina	Mainland	8/12/2021	7°42'12"N, 81°15'11"W Alt: 32 m	4403
CP2	Santa Catalina	Mainland	8/12/2021	7°41'35"N, 81°13'26"W Alt: 14 m	4404
CP3	Santa Catalina	Mainland	8/12/2021	7°41'40"N, 81°13'50"W Alt: 20 m	4405
CP4	Santa Catalina	Mainland	8/12/2021	7°38'35"N, 81°12'38"W Alt: 21 m	4406
CP5	Arrimadero	Mainland	9/12/2021	7°41'55"N, 81°17'47"W Alt: 37 m	4415
CP6	Arrimadero	Mainland	9/12/2021	7°41'42"N, 81°19'05"W Alt: 28 m	4416
CP7	Santa Catalina	Mainland	7/12/2021	7°37'51"N, 81°15'09"W Alt: 22 m	4402
CP8	Santa Catalina	Mainland	8/12/2021	7°38'35"N, 81°12'38"W Alt: 21 m	4407
CP9	Coiba	Island	6/12/2021	7°37'36"N, 81°43'50"W	4401
CP10	Santa Catalina	Mainland	8/12/2021	7°37'58"N, 81°14'02"W Alt: 37 m	4408
CP11	Santa Catalina	Mainland	8/12/2021	7°37'58"N, 81°14'02"W Alt: 37 m	4409
CP12	Arrimadero	Mainland	9/12/2021	7°42'21"N, 81°15'29"W Alt: 22 m	4417
CP13	Ranchería	Island	6/12/2021	7°38'15"N, 81°42'10"W Alt: 103 m	4399
CP14	Arrimadero	Mainland	9/12/2021	7°39'47"N, 81°19'12"W Alt: 19 m	4418
CP15	Arrimadero	Mainland	9/12/2021	7°41'42"N, 81°19'05"W Alt: 28 m	4419
CP16	Santa Catalina	Mainland	8/12/2021	7°38'27"N, 81°14'58"W Alt: 63 m	4410
CP17	Santa Catalina	Mainland	8/12/2021	7°38'27"N, 81°14'58"W Alt: 64 m	4411
CP18	Santa Catalina	Mainland	8/12/2021	7°38'27"N, 81°14'58"W Alt: 64 m	4412
CP19	Ranchería	Island	6/12/2021	7°38'23"N, 81°42'05"W Alt: 103 m	4400
CP20	Arrimadero	Mainland	9/12/2021	7°41'37"N, 81°17'04"W Alt: 41 m	4420
CP21	Santa Catalina	Mainland	8/12/2021	7°38'27"N, 81°14'58"W Alt: 63 m	4413
CP22	Arrimadero	Mainland	19/12/2021	7°39'34"N, 81°18'36"W Alt: 14 m	4421
CP23	Santa Catalina	Mainland	8/12/2021	7°38'22"N, 81°14'53"W Alt: 55 m	4414

Preparation of extracts

To prepare the extracts, the leaves were dried in an oven at 40 °C for 3 days and then pulverized to obtain a fine powder (1.0 mm). The ground material was then stored in the herbarium under controlled conditions (20–25 °C) until further analysis. The plant material (1 g) was transferred to a 50 mL flask with a conical bottom, and 15 mL of 70% (v/v) MeOH was added to it. For exhausted extraction, the probe was placed in an ultrasonic bath (42 kHz, 100 W) (Model Branson 3510, Danbury, USA) at a temperature of 35 °C for 30 min. Once the extraction was achieved, the generated extract was centrifuged (Heraeus Labofuge, Germany) at 3000 g for 5 min. The combined MeOH extracts were evaporated and defatted three times with 50 mL of *n*-hexane each time. This extraction effectively removed chlorophyll and oils from the samples. The defatted extract was transferred into a 50 mL volumetric flask. Finally, the resulting extracts were diluted at a 1:2 ratio with 10% (v/v) MeOH. The samples were stored at -20 °C before being used in subsequent analysis (Rivera-Mondragón et al. 2019b).

Liquid chromatography-high resolution spectrometry (LC-HRESI-MS) analysis

LC-HRESI-MS analysis was carried out on the UHPLC system (Dionex Ultimate 3000 RSLC system, ThermoFisher Scientific, Bremen, Germany) coupled to a Q Exactive Plus Orbitrap Quadrupole Mass Spectrometer with heated electrospray ionization (HESI) ion source (ThermoFisher Scientific, Bremen, Germany). LC separations were carried out on a Kinetex RP-18 column (2.10 mm × 100 mm, 2.6 µm, Phenomenex Corporation, Torrence, CA, USA) at 40 °C. Elution was performed with a mobile phase consisting of H_2O + 0.1% (v/v) formic acid (A) and acetonitrile also with 0.1% (v/v) formic acid (B), which were pumped at a rate of 0.3 mL/min. A gradient program was set up as follows: 5% B (0–0.5 min), 85% B (0.5–20 min), 95% B (20–20.5 min), and full scan data were recorded in negative electrospray ionization (ESI-) mode from *m/z* 150 to 1500 with a resolution of 70,000 (at *m/z* 200). The operating conditions of the HR-ESI ionization source were at -2.5 or +3.5 kV and a capillary temperature of 320 °C, a sheath gas flow of 25 arbitrary units, and an auxiliary gas flow of 5 units (both N_2). All other detector parameters were adjusted such that the most intense $[M-H]^-$ signal was obtained. The MS scan was followed by a full dd-MS/MS scan of the five highest intensity ions above an absolute threshold of 3,000 counts with a resolution of 17,500 (at *m/z* 200). The diluted extract (mentioned in the previous section) was further diluted by adding 100 µL of the extract to 900 µL of H_2O/MeOH (60 : 40). The sample injection volume was set at 1 µL. All data were recorded and processed using Xcalibur software, version 2.0 (Thermo Fisher Scientific, Germering, Germany).

Data processing for untargeted metabolomic analysis

In the process, raw files were subjected to the data mining software MZmine 2.53. The workflow comprises raw data

import, mass detection, feature processing (chromatogram construction, chromatogram deconvolution, peak list deisotopation), data alignment, and gap filling (Pluskal et al. 2010; Olivon et al. 2017). MZmine parameters were set as follows: Feature extraction for MS was achieved with a signal threshold of 1.0×10^4 and 1.0×10^2 for MS/MS. A centroid algorithm was used. The chromatogram builder was run using the ADAP Module (Myers et al. 2017) with a minimum cluster size/number of scans of 5, a cluster intensity threshold of 5.0×10^4, a minimum highest intensity of 1.0×10^5, and an *m/z* tolerance of 0.0020 or 5 ppm. Chromatograms were deconvoluted with an *m/z* range tolerance of 5 ppm and a retention time tolerance (0.1 min). The detected peaks were aligned via the Join Aligner Module, considering a mass (5 ppm), 75% wt for *m/z*, and 25% for retention time. Normalized peak areas were converted to comma-separated values (.csv) and subsequently considered for chemometric analysis.

Chemometric analysis

The chemometric analysis was performed using MetaboAnalyst 5.0 software (Pang et al. 2022). In the initial stage, processed data was normalized by transforming variables to a logarithm base 10, and then autoscaling was applied (centered on the mean and divided by the standard deviation of each variable). Supervised discriminant analysis of orthogonal projections to latent structures (OPLS-DA) was conducted to identify differences in metabolite composition in the samples. Model quality was assessed using the goodness of fit parameter (R2) and the model's goodness of prediction (Q2) (Fig. 1). The variable importance in projection (VIP) approach was used to select those variables that had the highest discrimination potential (considering a VIP score > 1.5) in the OPLS-DA models. These variables were subsequently recognized as putative chemical markers.

Phytochemical characterization

During the phytochemical characterization, metabolites were identified using authentic standards or by comparison of MS and MS/MS data with those reported in scientific literature and common MS databases, such as the Human Metabolome Database (http://www.hmdb.ca/) and MassBank (https://massbank.eu). A precision error of 5 ppm was set in the MS search, and fragments were verified in the MS/MS search. The chemical composition of the methanolic extracts was defined according to the confirmation levels (CL) proposed by Schymanski et al. 2014: Level 1 (L1) - structure validated by reference standard; Level 2a (L2a) - probable structure by match with library spectrum or previously described in the literature; Level 3 (L3) - tentative candidates constructed on experimental MS and MS/MS data.

Results and discussion

Mass spectrometry (MS) analyses of methanolic extracts of *C. peltata* leaves revealed an exceptional variety of secondary metabolites, with a total of 444 peaks detected in the 23 plant samples used for the current study. For this investigation, the negative ionization mode was employed, which allowed for obtaining of more complex metabolite profiles for each extract.

To initiate chemometric analysis, a supervised OPLS-DA model was applied to identify the metabolites that possibly contribute to differentiating specimens collected on land from those collected on islands. The generated model demonstrated a robust performance (R2 = 0.69) and a significant predictive capacity (Q2 = 0.22). The OPLS-DA score plot (see Fig. 2A) revealed the presence of two distinct clusters, which allowed a clear differentiation between samples collected on land and those collected on islands. Specifically, extracts obtained from samples collected on

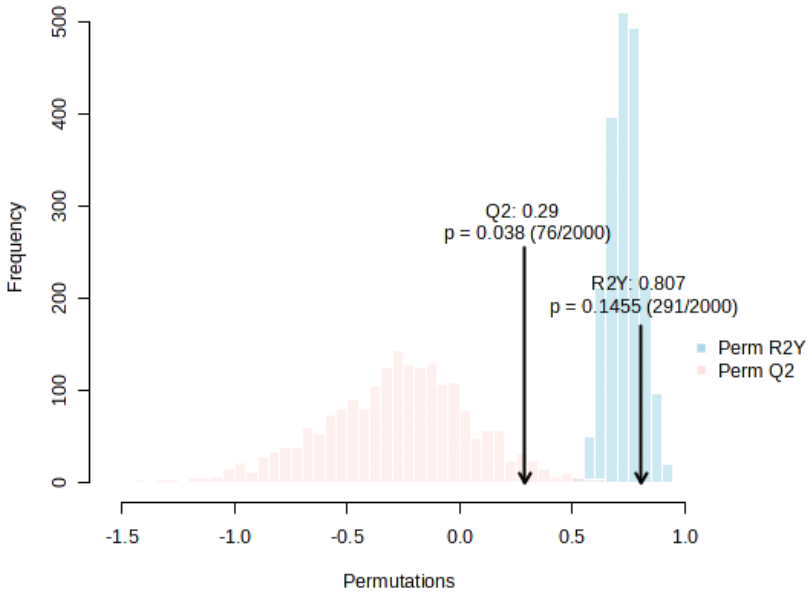

Figure 1. Permutation test for the OPLS-DA model showing R2 and Q2 values.

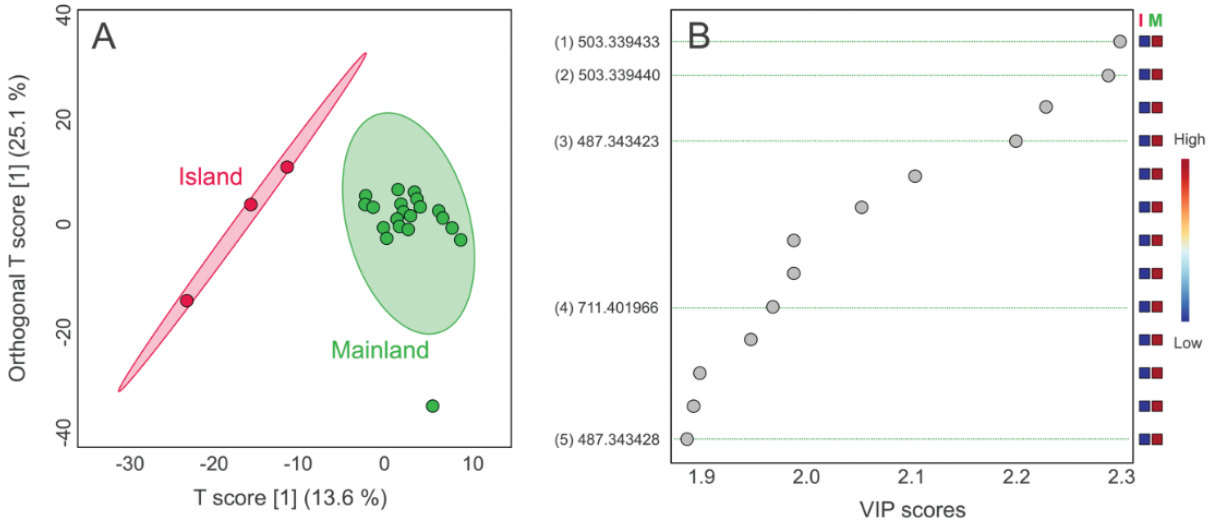

Figure 2. A. Score plot of the OPLS model; **B.** The most significant discriminant metabolites (identified by OPLS-DA) ranked by variable importance in projection (VIP). The relative abundance of every important metabolite is indicated by a color code, ranging from blue (low abundance) to red (high abundance). The higher the VIP score, the greater the potential of the metabolite to differentiate the two study groups. Only metabolites with a VIP score > 1.5 were considered.

land showed a separate and distinct cluster corresponding to samples collected on islands, indicating the presence of specific metabolites responsible for the differentiation between the two groups. Fig. 2B details the most relevant discriminating metabolites (identified by OPLS-DA), ranked by their variable importance in the projection (VIP). The relative abundance of each of these key metabolites is represented by a color code ranging from blue (low abundance) to red (high abundance). It is worth noting that the higher the VIP score is, the greater the potential of the metabolite to differentiate between the two groups analyzed. During this analysis, only metabolites with a VIP score greater than 1.5 were considered.

The identified metabolites were characterized by comparison of MS and MS/MS data with records available in scientific publications and common MS databases, such as the Human Metabolome Database (http://www.hmdb.ca) and MassBank (https://massbank.eu). For the MS search, a precision error margin of 5 ppm was established. It is important to note that this study employed a qualitative metabolomic approach. While the OPLS-DA model identified key metabolites with differential relative abundance, this does not represent a fully quantitative analysis, as absolute concentrations of metabolites were not determined.

Among the highest-scoring metabolites (VIP > 1.5) that were considered as potential chemical markers, five compounds were identified as the main metabolites strongly associated with the phytochemical difference between the two groups under study (see Table 2 and Fig. 3). These compounds, namely, buergericic acid (isomer 1), buergericic acid (isomer 2), euscaphic acid (isomer 1), niga-ichigoside F2, and euscaphic acid (isomer 2), are classified as triterpene saponins.

As shown in Fig. 3A–C, compounds from 1 to 5 exhibit a significantly higher relative abundance in the group of samples collected on land compared to those collected on islands. This observation underlines the potential of these metabolites identified as distinctive markers in the differentiation of *C. peltata* from different localities.

This study employed an untargeted metabolomic approach using UHPLC-Q-Orbitrap-HRMS to differentiate *C. peltata* samples collected from mainland and island environments in Panama. The findings revealed differences between the two geographic regions, highlighting the role of environmental factors in shaping the metabolite profiles of this species. The supervised OPLS-DA model provided robust differentiation between samples from mainland and island locations. This model identified five triterpene saponins, buergericic acid (isomers 1 and 2), euscaphic acid (isomers 1 and 2), and niga-ichigoside F2 as the most significant chemical markers. These compounds showed higher relative abundance in mainland samples. However, it is plausible that island plants produce lower quantities of certain defensive compounds as an adaptive response to the absence of specialized predators.

While the findings provide valuable insights, some limitations must be acknowledged. First, the relatively small sample size from island locations may reduce the applicability of the results. Future studies should aim to include a larger number of samples from both regions to strengthen the robustness of the conclusions. Second, environmental factors such as soil nutrients, light availability, and biotic interactions (e.g., herbivory or pathogen exposure) were not quantified in this study. Such factors are known to influence secondary metabolite production and should be incorporated into future investigations to provide a more holistic understanding of the observed variability (Salam et al. 2023).

Additionally, the predictive capacity of the OPLS-DA model (Q2 = 0.29) was moderate, suggesting that while the model effectively distinguishes the two groups, further validation is needed. Permutation testing conducted as part of this study demonstrated the robustness of the model but also highlighted the exploratory nature of the analysis. Expanding the dataset with temporal sampling

Table 2. Chemical markers with VIP values > 1.5.

N°	Chemical characterization	RT	Molecular formula	*m/z* / FS-MS	Delta ppm	CL
1	Buergericic acid (isomer 1)	10.63	$C_{30}H_{48}O_6$	503,3394 $[M-H]^-$	1.62	L3
2	Buergericic acid (isomer 2)	10.62	$C_{30}H_{48}O_6$	503,3394 $[M-H]^-$	1.62	L3
3	Euscaphic acid (isomer 1)	12.98	$C_{30}H_{48}O_5$	487,3434 $[M-H]^-$	0.53	L3
4	Niga-ichigoside F2	7.41	$C_{36}H_{58}O_{11}$	711,4020 $[M-H+HCOOH]^-$	0.68	L2
5	Euscaphic acid (isomer 2)	13.57	$C_{30}H_{48}O_5$	487,3434 $[M-H]^-$	0.53	L3

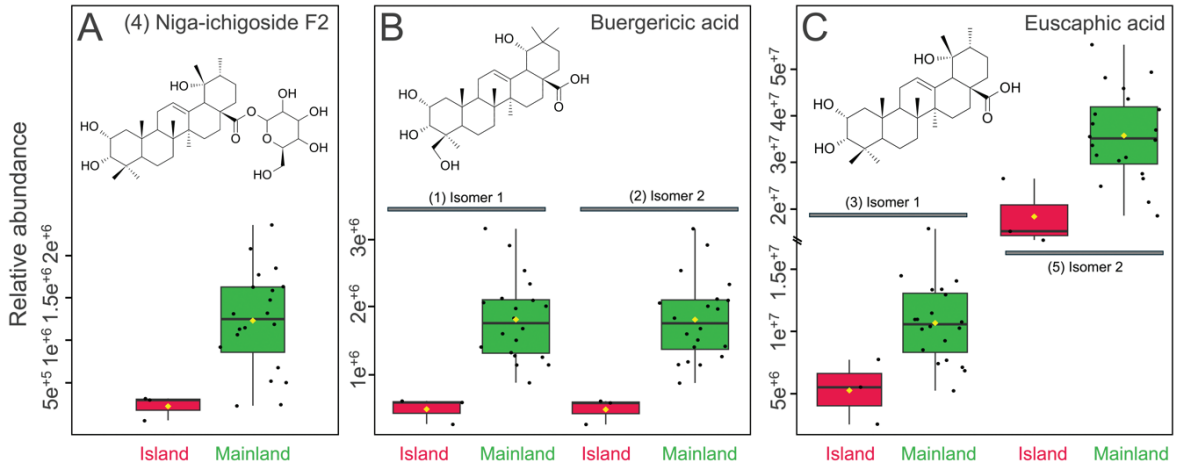

Figure 3. A–C. Relative abundance of the selected chemical markers: **A.** Niga-ichigoside F2; **B.** Buergericic acid (isomer 1 and isomer 2), Euscaphic acid (isomer 1 and isomer 2).

across different seasons or growth stages could enhance the reliability of these findings. The identification of triterpene saponins as key chemical markers is consistent with previous reports emphasizing their abundance in *Cecropia* species (Costa et al. 2011; Rivera-Mondragón et al. 2019a). These compounds have been associated with various pharmacological activities, including anti-inflammatory, antiviral, and hypoglycemic effects, underscoring their relevance to the medicinal potential of *C. peltata* (Costa et al. 2011; Rivera-Mondragón et al. 2021). By identifying these compounds as potential geographic markers, our study highlights the need to consider environmental factors in the standardization and quality control of herbal preparations derived from *C. peltata.*

Differences in metabolite abundance may influence the pharmacological efficacy of extracts derived from plants collected in different locations. For example, mainland samples, which exhibited higher levels of the identified triterpenes, may possess enhanced bioactivity compared to island samples.

Conclusion

The findings of this research offer proof that the phytochemical composition of *C. peltata* varies depending on the location from which the plants are collected. This information is important for researchers working on the extraction of compounds from this plant species, as it suggests that the biological activity of the plant may vary depending on its origin. Additionally, this study identifies five triterpene saponins as potential phytochemical markers to differentiate *C. peltata* collected on land from that collected on islands. This information can be used to develop quality control methods for the plant.

Acknowledgements

The authors thank the National Secretariat of Science, Technology, and Innovation (SENACYT) of the Republic of Panama for financially supporting Dr. Rivera-Mondragón through the National Research System (SNI) incentive program. We are grateful to the COIBA-AIP for funding the fieldwork.

Additional information

Conflict of interest

The authors have declared that no competing interests exist.

Ethical statements

The authors declared that no clinical trials were used in the present study.

The authors declared that no experiments on humans or human tissues were performed for the present study.

The authors declared that no informed consent was obtained from the humans, donors or donors' representatives participating in the study.

The authors declared that no experiments on animals were performed for the present study.

The authors declared that no commercially available immortalised human and animal cell lines were used in the present study.

Funding

This study is funded by the European Union-NextGenerationEU, through the National Recovery and Resilience Plan of the Republic of Bulgaria, project BG-RRP-2.004-0004-C01: "Strategic research and innovation program for development of Medical University – Sofia."

Author contributions

All authors have contributed equally.

Author ORCIDs

Yancho Zarev https://orcid.org/0000-0001-5830-4697
Anzhelika Dakovska https://orcid.org/0009-0003-6902-3008
Orlando O. Ortiz https://orcid.org/0000-0002-7805-0046
Yostin Añino https://orcid.org/0000-0002-8870-8155
Iliana Ionkova https://orcid.org/0000-0003-1411-7982
Andrés Rivera Mondragón https://orcid.org/0000-0001-7426-5405

Data availability

All of the data that support the findings of this study are available in the main text or Supplementary Information.

References

Berg CC (1978) *Cecropiaceae* a new family of the Urticales. TAXON 27: 39–44. https://doi.org/10.2307/1220477

Costa GM, Schenkel EP, Reginatto FH (2011) Chemical and pharmacological aspects of the Genus *Cecropia*. Natural Product Communications 6: 1934578X1100600637. https://doi.org/10.1177/1934578X1100600637

Fairbrothers DE, Mabry TJ, Scogin RL, Turner BL (1975) The Bases of angiosperm phylogeny: Chemotaxonomy. Annals of the Missouri Botanical Garden 62: 765. https://doi.org/10.2307/2395273

Myers OD, Sumner SJ, Li S, Barnes S, Du X (2017) One step forward for reducing false positive and false negative compound identifications from mass spectrometry metabolomics data: New algorithms for constructing extracted ion chromatograms and detecting chromatographic peaks. Analytical Chemistry 89: 8696–8703. https://doi.org/10.1021/acs.analchem.7b00947

Nicasio P, Aguilar- Santamaría L, Aranda E, Ortiz S, González M (2005) Hypoglycemic effect and chlorogenic acid content in two *Cecropia* species. Phytotherapy Research 19: 661–664. https://doi.org/10.1002/ptr.1722

Olivon F, Grelier G, Roussi F, Litaudon M, Touboul D (2017) MZmine 2 data-preprocessing to enhance molecular networking reliability. Analytical Chemistry 89: 7836–7840. https://doi.org/10.1021/acs.analchem.7b01563

Ortiz OO, Rivera-Mondragón A, Pieters L, Foubert K, Caballero-George C (2019) *Cecropia telenitida* Cuatrec. (Urticaceae: Cecropieae): Phytochemical diversity, chemophenetic implications and new records from Central America. Biochemical Systematics and Ecology 86: 103935. https://doi.org/10.1016/j.bse.2019.103935

Pang Z, Zhou G, Ewald J, Chang L, Hacariz O, Basu N, Xia J (2022) Using MetaboAnalyst 5.0 for LC–HRMS spectra processing, multi-omics integration and covariate adjustment of global metabolomics data. Nature Protocols 17: 1735–1761. https://doi.org/10.1038/s41596-022-00710-w

Pluskal T, Castillo S, Villar-Briones A, Orešič M (2010) MZmine 2: Modular framework for processing, visualizing, and analyzing mass spectrometry-based molecular profile data. BMC Bioinformatics 11: 395. https://doi.org/10.1186/1471-2105-11-395

Reynolds T (2007) The evolution of chemosystematics. Phytochemistry 68: 2887–2895. https://doi.org/10.1016/j.phytochem.2007.06.027

Rivera-Mondragón A, Ortíz OO, Gupta MP, Caballero-George C (2021) Pharmacognostic evaluation of ten species of medicinal importance of *Cecropia*: Current knowledge and therapeutic perspectives. Planta Medica 87: 764–779. https://doi.org/10.1055/a-1495-9785

Rivera-Mondragón A, Broeckx G, Bijttebier S, Fourbert K, Caballero-George C, Vander Heyden Y, Pieters L (2017) Optimization of extraction conditions for total flavonoids, chlorogenic acid and flavolignans contents from *Cecropia* sp. leaves using design-of-experiments methodology. Planta Medica International Open 4(S 01): S1–S202. https://doi.org/10.1055/s-0037-1608188

Rivera-Mondragón A, Bijttebier S, Tuenter E, Custers D, Ortíz OO, Pieters L, Caballero-George C, Apers S, Foubert K (2019a) Phytochemical characterization and comparative studies of four *Cecropia* species collected in Panama using multivariate data analysis. Scientific Reports 9: 1763. https://doi.org/10.1038/s41598-018-38334-4

Rivera-Mondragón A, Broeckx G, Bijttebier S, Naessens T, Fransen E, Kiekens F, Caballero-George C, Vander Heyden Y, Apers S, Pieters L, Foubert K (2019b) Ultrasound-assisted extraction optimization and validation of an HPLC-DAD method for the quantification of polyphenols in leaf extracts of *Cecropia* species. Scientific Reports 9: 2028. https://doi.org/10.1038/s41598-018-37607-2

Salam U, Ullah S, Tang Z-H, Elateeq AA, Khan Y, Khan J, Khan A, Ali S (2023) Plant metabolomics: An overview of the role of primary and secondary metabolites against different environmental stress factors. Life 13: 706. https://doi.org/10.3390/life13030706

Schymanski EL, Jeon J, Gulde R, Fenner K, Ruff M, Singer HP, Hollender J (2014) Identifying small molecules via high resolution mass spectrometry: Communicating confidence. Environmental Science & Technology 48: 2097–2098. https://doi.org/10.1021/es5002105

Silva IT, Costa GM, Stoco PH, Schenkel EP, Reginatto FH, Simões CMO (2010) In vitro antiherpes effects of a C-glycosylflavonoid-enriched fraction of *Cecropia glaziovii* Sneth*: Antiherpes effects of *Cecropia glaziovii*. Letters in Applied Microbiology. https://doi.org/10.1111/j.1472-765X.2010.02870.x

Zidorn C (2019) Plant chemophenetics – A new term for plant chemosystematics/plant chemotaxonomy in the macro-molecular era. Phytochemistry 163: 147–148. https://doi.org/10.1016/j.phytochem.2019.02.013

Supplementary material 1

MetaboAnalyst *Cecropia peltata* species

Authors: Yancho Zarev, Anzhelika Dakovska, Yuliana Christopher, Orlando O. Ortiz, Yostin Añino, Iliana Ionkova, Andrés Rivera Mondragón

Data type: csv

Explanation note: Text.

Link: https://doi.org/10.3897/pharmacia.72.e151142.suppl1