Published in final edited form as:

Biochem Syst Ecol. 2013 June 1; 48: 96–99. doi:10.1016/j.bse.2012.11.018.

Triterpenoids and flavonoids from *Cecropia schreberiana* Miq. (Urticaceae)

Jun Li^{a,b}, Christina M. Coleman^a, Hankui Wu^a, Charles L. Burandt Jr^c, Daneel Ferreira^a, and Jordan K. Zjawiony^{a,*}

^aDepartment of Pharmacognosy and Research Institute of Pharmaceutical Sciences, School of Pharmacy, University of Mississippi, University, Mississippi 38677-1848, USA

^bModern Research Center for Traditional Chinese Medicine, Beijing University of Chinese Medicine, Beijing 100029, P. R. China

^cNational Center for Natural Products Research, University of Mississippi, University, Mississippi 38677-1848, USA

Abstract

Phytochemical investigation of the leaves of *Cecropia schreberiana* Miq. (Urticaceae) led to the isolation of four triterpenoids (**1–4**), three flavone C-glycosides (**5–7**), two flavan-3-ols (**8, 9**), two flavanolignans (**10, 11**), and two proanthocyanidins (**12, 13**). All compounds were isolated from *C. schreberiana* for the first time. This is the first report demonstrating the presence of arjunolic acid (**4**), cinchonain Ia (**10**), and cinchonain Ib (**11**) in the Urticaceae family. The occurrence of flavanolignans within the family Urticaceae supports the likelihood that such compounds are more common within the class Magnoliopsida than previously thought.

Keywords

Urticaceae; *Cecropia schreberiana*; Triterpenoid; Flavonoid; Proanthocyanidin; Flavanolignan

1. Subjects and Source

The genus *Cecropia* (Rosales, Urticaceae) contains a number of ecologically significant tree species distributed across the tropical and subtropical regions of Central and South America, including Mexico, Brazil, Peru, Columbia, Argentina, and Paraguay (Parolin, 2002). The plants of this genus are well known for myrmecophytism (Dejean et al., 2012) and are ecologically significant as both primary colonizers of cleared tropical forest areas and as invasive species in non-native tropical regions due to their rapid growth rates (Parolin, 2002). Various species within this genus are also used interchangeably as traditional medicines to treat a wide array of diseases including respiratory, cardiovascular, inflammatory, cardiac, metabolic, and CNS diseases (Costa et al., 2011). Phytochemical investigations of this genus are warranted due to its widespread distribution, ecological significance, and common medicinal usage. Leaves of *C. schreberiana* were collected from

© 2012 Elsevier Ltd. All rights reserved.

*To whom correspondence should be addressed: Professor Jordan K. Zjawiony, Tel: +1 662 915 7290. Fax: +1 662 915 6975. jordan@olemiss.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Puerto Rico in April, 2010, and plant authentication was done by one of the authors (C. L. Burandt, Jr). A voucher specimen (JLI-CS-201004) was deposited at the Department of Pharmacognosy, School of Pharmacy, the University of Mississippi.

2. Previous Work

Various pharmacological properties have been reported for leaf extracts and preparations from a number of *Cecropia* species, including cardiovascular, hypoglycemic, central nervous system, antiviral, antioxidant, antimalarial, and cytotoxic activities (Costa et al., 2011). Phytochemical investigations of *Cecropia* species have also led to the identification of a variety of compounds as possible bioactive constituents, including triterpenoids, steroids, flavone-C-glycosides, proanthocyanidins, and other flavonoids (Costa et al., 2011). Phytochemical constituents of the species *C. schreberiana*, however, have yet to be characterized.

3. Present study

Dried powdered leaves of *C. schreberiana* (590 g) were extracted with acetone (3.4 L $\times$ 3) by percolation at room temperature. After filtration, combination and evaporation, the residue (33 g) was dissolved in 90% aqueous MeOH and partitioned with hexanes and EtOAc, successively. The dried EtOAc residue (4.6 g) was subjected to Sephadex LH-20 CC eluting with MeOH to give seven fractions (A–G). Fraction B (1.18 g) was repeatedly chromatographed on silica gel open columns to produce pomolic acid (**1**, 6.5 mg) (Saimaru et al., 2007), tormentic acid (**2**, 12 mg) (Saimaru et al., 2007), α -amyrin (**3**, 8.5 mg) (Mahato et al., 1994), and arjunolic acid (**4**, 2 mg) (Tripathi et al., 1992). Fraction D (75 mg) was subjected to silica gel CC, and further separated by semi-preparative RP-HPLC [MeOH-H₂O (35:65)] to afford vitexin (**5**, 8 mg) (Zhang and Xu, 2002). Fraction E (430 mg) was chromatographed via silica gel CC, and further separated by semi-preparative RP-HPLC [MeOH-H₂O (33:67)] to give orientin (**6**, 7 mg) and isoorientin (**7**, 15 mg) (Wen et al., 2007). Fraction F (1 g) was subjected to silica gel CC eluting with CH₂Cl₂-MeOH solvent system with increasing polarity to produce six subfractions (F1–F6). Subfraction F1 (100 mg) was further separated by semi-preparative RP-HPLC [gradient of MeOH-H₂O (0–30 min, 25:75 $\rightarrow$ 70:30)] to yield catechin (**8**, 1.4 mg), *epi*-catechin (**9**, 50 mg) (Ban et al., 2006), cinchonain Ia (**10**, 5 mg) and cinchonain Ib (**11**, 12 mg) (Nonaka and Nishioka, 1982). Subfraction F3 (100 mg) was further separated by semi-preparative RP-HPLC [gradient of MeOH-H₂O (0–30 min, 25:75 $\rightarrow$ 70:30)] to afford procyanidins B2 (**12**, 15 mg) and B5 (**13**, 7 mg) (Khan et al., 1997, Nonaka et al., 1982). The isolated compounds were identified by comparison of experimental with reported values for specific rotation, ESI-MS, ECD, and ¹H and ¹³C NMR spectra.

4. Chemotaxonomic significance

This report discusses the isolation and identification of a series of chemical constituents from *C. schreberiana*: four triterpenoids (**1–4**), three flavone C-glycosides (**5–7**), two flavan-3-ols (**8, 9**), two flavanolignans (**10, 11**), and two proanthocyanidins (**12, 13**). While the general chemotaxonomic pattern of *C. schreberiana* is similar to those of other *Cecropia* species in terms of chemical classes, this is the first report of compound **4** from the genus *Cecropia*, the first report of **10** and **11** from the family Urticaceae, and only the second report of compounds **10** and **11** from the order Rosales.

Several of the compounds isolated in this study have been previously isolated and identified from other *Cecropia* species. Pomolic acid (**1**) and α -amyrin (**3**) have been obtained from *C. pathystachya* (Hikawczuk et al., 1998, Schinella et al., 2008). Tormentic acid (**2**) has been

obtained from *C. pathystachya* (Uchoa et al., 2010), *C. catharinensis* (Machado et al., 2008) and *C. lyratiloba* (Rocha et al., 2007). Vitexin (**5**) has been identified from *C. adenopus* and *C. catharinensis* (Chanmahasathien et al., 2004, Machado 2008). Orientin (**6**) and isoorientin (**7**) from *C. adenopus*, *C. glaziovii*, *C. pathystachya*, *C. lyratiloba*, *C. hololeuca*, and *C. obtusifolia* (Chanmahasathien et al., 2004, Lacaille-Dubois et al., 2001, Aragão et al., 2010, Oliveira et al., 2003, Andrade-Cetto and Wiedenfeld, 2001). Catechin (**8**), epicatechin (**9**), and procyanidin B2 (**13**) were reported from *C. pachystachya*, *C. hololeuca* and *C. glaziovii* (Lacaille-Dubois et al., 2001), and procyanidin B5 from *C. glaziovii* (Tanae et al., 2007). The occurrence of these compounds in multiple *Cecropia* species indicates that they would be of limited usefulness as chemotaxonomic markers for individual species within the genus. Common occurrence of such bioactive compounds, however, supports the use of multiple *Cecropia* species for traditional medicine preparations.

The majority of previously isolated *Cecropia* triterpenoids are of the ursane type; oleanane type triterpenoids, such as arjunolic acid (**4**), have not been previously identified from *Cecropia* species. Identification of this class of triterpenoids indicates additional biosynthetic capabilities within the genus and adds an additional class of compounds to the list of those identified which may have medicinal properties, especially anti-inflammatory properties (Sporn et al., 2011).

Cinchonain Ia and cinchonain Ib are phenylpropanoid-substituted flavan-3-ols known commonly as flavanolignans. This class of compounds was first detected in the bark of *Cinchona succirubra* (Rubiaceae) (Nonaka and Nishioka, 1982) and later reported from plants of other families including *Eriobotrya japonica* (Rosales, Rosaceae) (Qa'dan et al., 2009), *Iryanthera megistophylla* (Magnoliales, Myristicaceae) (Ming et al., 2002), *Apocynum venetum* (Gentianales, Apocynaceae) (Xiong et al., 2000), *Camellia sinensis* (Ericales, Theaceae) (Zhou et al., 2005), *Anemopaegma arvense* (Lamiales, Bignoniaceae) (Tabanca et al., 2007), *Trichilia catigua* (Sapindales, Meliaceae) (Tang et al., 2007), and *Rhizophora stylosa* (Malpighiales, Rhizophoraceae) (Li et al., 2007). With the inclusion of this report, the above list of species represents eight genetically distinct phylogenetic orders, and nine families, all within the class Magnoliopsida (Angiosperms) (Kress et al., 2009). Thus, it appears that the capability to biosynthesize cinchonain type flavanolignans is widely present within this class of plants in spite of a relatively limited number of isolation reports for these compounds. The likelihood of widespread occurrence of cinchonans and biogenetically related compounds is encouraging as several have been reported to possess a variety of promising biological activities (Resende et al., 2011).

Acknowledgments

This project was financially supported by a grant from National Institutes of Health (R03DA023491). The authors are grateful to Ms. Bin Wang of the Department of Pharmacognosy, University of Mississippi, for running the ESIMS experiments.

References

- Andrade-Cetto A, Wiedenfeld H. J. Ethnopharmacol. 2001; 78:145. [PubMed: 11694359]
- Aragão DMO, Guarize L, Lanini J, Costa JC, Garcia RMG, Scio E. J. Ethnopharmacol. 2010; 128:629. [PubMed: 20064597]
- Ban JY, Jeon S, Bae K, Song K, Seong YH. Life Sci. 2006; 79:2251. [PubMed: 16978655]
- Costa GM, Schenkel EP, Reginatto FH. Nat. Prod. Commun. 2011; 6:913. [PubMed: 21815438]
- Chanmahasathien W, Li Y, Satake M, Oshima Y, Ohizumi Y. Nat. Med. 2004; 58:46.
- Dejean A, Petitclerc F, Roux O, Orivel J, Leroy C. C. R. Biol. 2012; 335:214. [PubMed: 22464429]
- Hikawczuk VJ, Saad JR, Guardia T, Juarez AO, Giordao OS. An. Asoc. Quim. Argent. 1998; 86:167.

- Khan ML, Halson E, Williamson MP. *Magn. Reson. Chem.* 1997; 35:854.
- Kress WJ, Erickson DL, Jones FA, Swenson NG, Perez R, Sanjur O, Bermingham E. *P. Natl. Acad. Sci. USA.* 2009; 106:18621.
- Lacaille-Dubois MA, Franck U, Wagner H. *Phytomedicine.* 2001; 8:47. [PubMed: 11292239]
- Li DL, Li XM, Peng ZY, Wang BG. *Molecules.* 2007; 12:1163. [PubMed: 17873850]
- Ming DS, López A, Hillhouse BJ, French CJ, Hudson JB, Towers GHN. *J. Nat. Prod.* 2002; 65:1412. [PubMed: 12398535]
- Mahato SB, Kundu AP. *Phytochemistry.* 1994; 37:1517.
- Machado EC, Yunes RA, Malheiros A, Gomes EC, Delle Monache F. *Nat. Prod. Res.* 2008; 22:1310. [PubMed: 19023787]
- Nonaka G, Kawahara O, Nishioka I. *Chem. Pharm. Bull.* 1982; 30:4277.
- Nonaka G, Nishioka I. *Chem. Pharm. Bull.* 1982; 30:4268.
- Oliveira RR, Moraes MCC, Castilho RO, Valente AP, Carauta JPP, Lopes D, Kaplan MAC. *Phytochem. Analysis.* 2003; 14:96.
- Parolin P. *Rev. Biol. Trop.* 2002; 50:531. [PubMed: 12298284]
- Qa'dan F, Verspohl EJ, Nahrstedt A, Petereit F, Matalka KZ. *J. Ethnopharmacol.* 2009; 124:224. [PubMed: 19397981]
- Resende FO, Rodrigues-Filho E, Luftmann H, Petereit F, Palazzo de Mello JC. *J. Braz. Chem. Soc.* 2011; 22:2087.
- Rocha GG, Simões M, Lúcio KA, Oliveira RR, Kaplan MAC, Gattass CR. *Bioorg. Med. Chem.* 2007; 15:7355. [PubMed: 17889544]
- Saimaru H, Orihara Y, Tansakul P, Kang YH, Shibuya M, Ebizuka Y. *Chem. Pharm. Bull.* 2007; 55:784. [PubMed: 17473469]
- Schinella G, Aquila S, Dade M, Giner R, Recio Mdel C, Spegazzini E, de Buschiazza P, Tournier H, Ríos JL. *Planta Med.* 2008; 74:215. [PubMed: 18260049]
- Sporn MB, Liby KT, Yore MM, Fu L, Lopchuk JM, Gribble GW. *J. Nat. Prod.* 74:537. [PubMed: 21309592]
- Tabanca N, Pawar RS, Ferreira D, Marais JP, Khan SI, Joshi V, Wedge DE, Khan IA. *Planta Med.* 2007; 73:1107. [PubMed: 17642036]
- Tanae MM, Lima-Landman MTR, De Lima TCM, Souccar C, Lapa AJ. *Phytomedicine.* 2007; 14:309. [PubMed: 17434301]
- Tang W, Hioki H, Harada K, Kubo M, Fukuyama Y. *J. Nat. Prod.* 2007; 70:2010. [PubMed: 18020420]
- Tripathi VK, Pandey VB, Udupa KN, Rücker G. *Phytochemistry.* 1992; 31:349.
- Uchoa VT, Paula RC, Krettli LG, Santana AEG, Krettli AU. *Drug Develop. Res.* 2010; 71:82.
- Wen P, Han H, Wang R, Wang N, Yao X. *Asian J. Tradit. Med.* 2007; 2:149.
- Xiong Q, Fan W, Tezuka Y, Adnyana IK, Stampoulis P, Hattori M, Namba T, Kadota S. *Planta Med.* 2000; 66:127. [PubMed: 10763585]
- Zhang PC, Xu SX. *Chin. Chem. Lett.* 2002; 13:337.
- Zhou ZH, Zahng YJ, Xu M, Yang CR. *J. Agr. Food Chem.* 2005; 53:8614–8617. [PubMed: 16248561]

Highlights

► Four triterpenoids, three flavone C-glycosides, two flavan-3-ols, two flavanolignans, and two proanthocyanidins were isolated from *Cecropia schreberiana* for the first time. ► One oleanane type triterpenoid and two flavanolignans are reported from the family Urticaceae for the first time. ► The occurrence of flavanolignans within the family Urticaceae supports the likelihood that such compounds are more common than previously thought within the class Magnoliopsida.

Figure 1.
Chemical structure of compounds 1–13 from *C. schreberiana*.