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Determination of the hydroxycinnamate profile of 12 members of the *Asteraceae* family

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ABSTRACT

The hydroxycinnamates of the leaves of 12 plants of the *Astreraceae* family, *Achillea millefolium*, *Arnica montana*, *Artemesia dracunculus*, *Cichorium intybus*, *Cnicus benedictus*, *Cynara scolymus*, *Echinops humilis*, *Inula helenium*, *Lactuca sativa*, *Petasites hybridus*, *Solidago virgaurea*, and *Tanacetum parthenium* were investigated qualitatively by LC–MS^n. Thirty-nine chlorogenic acids were detected and all characterized to regioisomeric level on the basis of their fragmentation pattern in the tandem MS spectra, most of them for the first time from these sources with two of them previously not reported in nature. Both chlorogenic acids based on *trans* and *cis*-cinnamic acid substituents were identified. Assignment to the level of individual regioisomers was possible for seven caffeoylquinic acids (**1–7**), 11 dicaffeoylquinic acids (**17–27**), six feruloylquinic acids (**9–14**), two *p*-coumaroylquinic acids (**15–16**), two caffeoyl–feruloylquinic acids (**28** and **29**), four caffeoyl-*p*-coumaroylquinic acids (**30–33**), three dicaffeoyl–succinoylquinic acids (**34–36**), two dicaffeoyl–methoxyoxaloylquinic acids (**37** and **38**), and one tricaffeoylquinic acid (**39**). Furthermore, one caffeoylshikimic acid (**40**), one caffeoyltartaric acid (**41**), three dicaffeoyltartaric acids (**42–44**), and three caffeoyl–feruloyltartaric acids (**45–47**) were detected and shown to possess characteristic tandem MS spectra and were tentatively assigned on the basis of their retention time and previously developed hierarchical keys.

1. Introduction

Hydroxycinnamates form a large class of low molecular weight, secondary plant metabolites, which are believed to be involved in UV protection, UV sensing and defense from herbivores, and pathogens in plants. Some compounds have also been reported to provide reproductive advantage as attractants of pollinators and seed dispersers.

Chlorogenic acids are hydroxycinnamic acid derivatives which are ubiquitous plant metabolites. Classically, chlorogenic acids (CGAs) are a family of esters formed between quinic acid and certain *trans*-cinnamic acids, most commonly caffeic, *p*-coumaric, and ferulic acid (Clifford, 1999, 2000; IUPAC, 1976); sinapic acid and dimethoxycinnamic acid are also present in certain plant species (Clifford et al., 2006a; Jaiswal et al., 2010a,b; Jaiswal and Kuhnert, 2010). Representative structures are shown in Fig. 1. The CGAs show a variety of biological activities like antioxidant, anti-inflammatory, anti-HIV, anti-HBV, radical scavenging, inhibit mutagenesis and carcinogenesis, and are considered to be beneficial to human health (Gorzalczany et al., 2008; Hemmerle et al., 1997; Kwon et al., 2000; Kweon et al., 2001; Wang et al., 2009).

Artemesia dracunculus is used in French cooking as one of the four fines herbs. *Petasites hybridus* is used for the treatment of migraine and asthma (Sutherland and Sweet, 2010; Sun-Edelstein and Mauskop, 2009). *Cynara scolymus* leaf extract reduces hepatic and oxidative stress (Kucukgergin et al., 2010) and it shows anti-HBV and anti-HCV activities (Lohr et al., 2009; Huber et al., 2009). *Solidago virgaurea* and *Tanacetum parthenium* show anticancer activity (Gross et al., 2002; Lesiak et al., 2010). *Cichorium intybus* is a source of caftaric acid and chicoric acid. For the remaining plants, phytochemical analysis and biological studies are not much explored.

These plants were previously investigated and chicoric acid, caftaric acid (Scarpati and Oriente, 1958), chlorogenic acids (Thiem et al., 2001; Wu et al., 2007), diterpenoids (Starks et al., 2010), sesquiterpenes (Han et al., 2009; Montsko et al., 2008), saponins (Bader et al., 1995), essential oils (Javidnia et al., 2010; Tkachev et al., 2006), and flavonoids (Tuberoso et al., 2009) were identified as their main secondary metabolites. Due to the presence of a large number of natural products and their biological effects, these plants are of great interest to the pharmaceutical industry and the scientific community. We have selected the above-mentioned 12 plants due to the following reasons. Firstly, it is well established that plants of the *Asteraceae* family are a particularly rich source of CGAs that considerably contribute to the dietary intake of CGAs (Clifford, 2000). The CGAs profile of herbal remedies is much less

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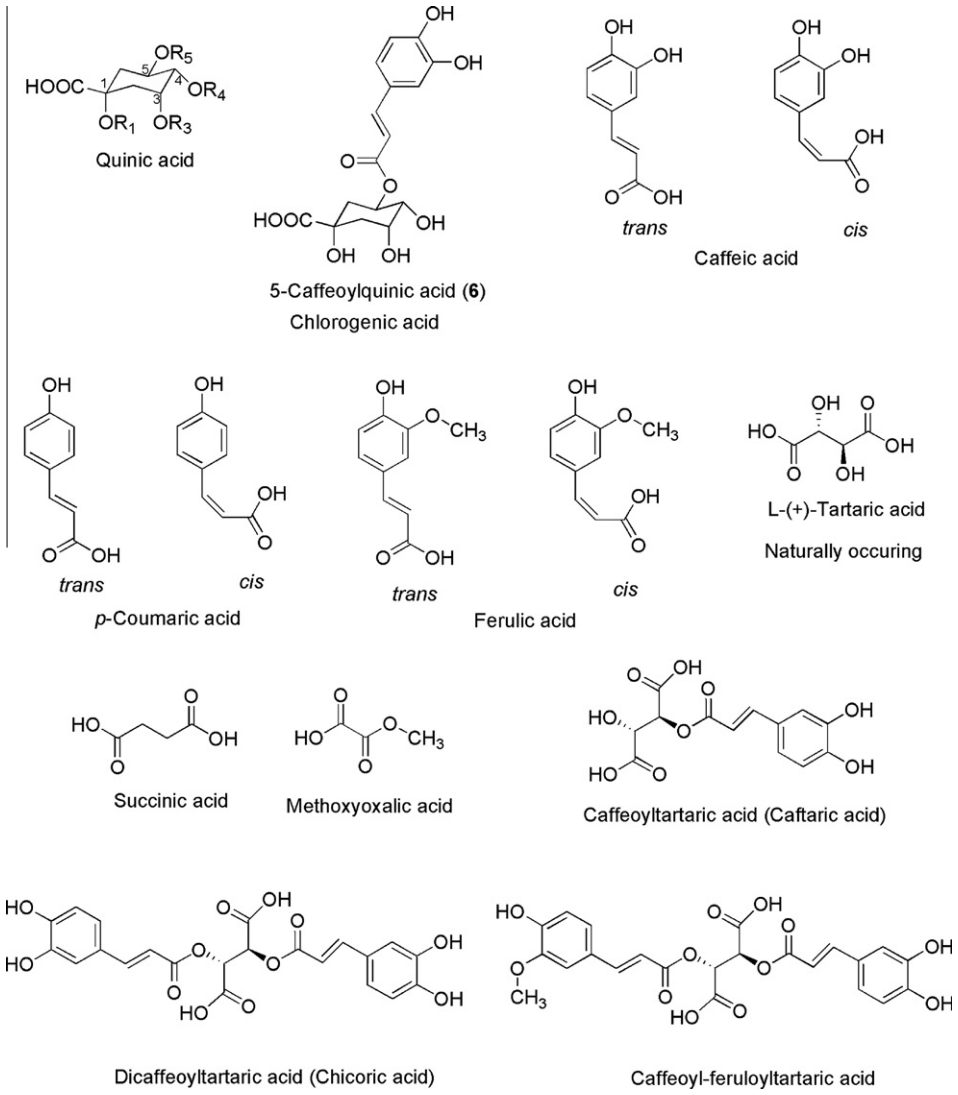

Fig. 1. Representative structures of hydroxycinnamates, where R_1, R_3–R_5 are H or a cinnamoyl residue.

explored and prompted in part this investigation. Secondly, all the 12 plants under investigation are traditionally used in the treatment of viral infections and therefore should contain compounds displaying certain anti-viral properties. Anti-viral properties, including anti-HIV, anti-hepatitis, and anti-influenza activities (Arakawa et al., 2009; Lohr et al., 2009; Slanina et al., 2001; Wang et al., 2009) were reported for a series of plants containing chlorogenic acids such as coffee (Freedman et al., 2009), yerba maté or artichoke. Cynarin and caffeoyldehydro quinic acids were even reported to be anti-HIV active (Ma et al., 2010). Therefore, by investigating the CGAs profile of anti-viral herbal remedies we aim at identifying selected chlorogenic acids commonly encountered in these plants, in order to establish suitable candidates for anti-viral screening. It should be noted that neuraminidase inhibitors recently introduced into the clinical practice, such as Tamiflu or Relenza, bear a remarkable structural similarity to CGAs, both carrying a shikimic acid core structure and being synthesized from shikimic acid.

In this study, all the hydroxycinnamates present in the leaves of *Achillea millefolium, Arnica montana, A. dracunculus, C. intybus, Cnicus benedictus, C. scolymus, Echinops humilis, Inula helenium, Lactuca sativa, P. hybridus, S. virgaurea*, and *T. parthenium* were identified qualitatively to their regioisomeric level without any purification or isolation, and assignment was based on their LC-MS^n behavior (Clifford et al., 2003, 2005, 2006ab,c; Jaiswal et al., 2010a,b; Jaiswal and Kuhnert, 2010).

2. Results and discussion

All the data for the hydroxycinnamates presented in this paper use the recommended IUPAC numbering system (IUPAC, 1976); specimen structures are presented in Fig. 1. When necessary, previously published data were amended to ensure consistency and avoid ambiguity.

When commercial standards were not available, peak identities were assigned on the basis of the structure-diagnostic hierarchical keys previously developed, supported by means of their parent ion, UV spectra, and sequence of elution/retention time relative to 5-caffeoylquinic acid (5-CQA) (**6**) using methods validated in our laboratory (Clifford et al., 2003, 2005, 2006a,b,c; Jaiswal et al., 2010a,b; Jaiswal and Kuhnert, 2010). For all compounds the high resolution mass data were in good agreement with the theoretical molecular formulas, all displaying a mass error of below 5 ppm, thus confirming their elemental composition.

In the following section we discuss in detail the identity of the hydroxycinnamates identified in the 12 plants under investigation.