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Review

Sesquiterpene lactones and their precursors as chemosystematic markers in the tribe Cichorieae of the Asteraceae

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ABSTRACT

This review summarizes all reports on sesquiterpene lactones and their immediate precursors from the Cichorieae (Lactuceae) tribe of the Asteraceae. A total of 360 compounds have been reported from this tribe. The reported substances belong to three classes of sesquiterpenoids: guaianolides (243 compounds), eudesmanolides (73 compounds), and germacranolides (44 compounds). Sources of these compounds encompass 139 taxa from 31 different genera. The distribution of these lactones within the tribe Cichorieae is discussed in a chemosystematic context. Moreover, some general ideas about the interpretation of chemosystematic data are discussed.

Contents

1. Introduction

The Cichorieae (synonym: Lactuceae) encompass approximately 100 genera and 1500 species (Bremer, 1994). Systematics of the tribe Cichorieae are still in a state of flux (Greuter, 2003; Samuel et al., 2006). Therefore, the system of Bremer, which is currently the most widely accepted, is generally followed here. Deviations from Bremer's monograph are summarized in Table 1 and are additionally mentioned in the accounts of the respective genera. The Cichorieae encompass a number of genera which are used as vegetables or for salads (e.g. *Cicerbita*, *Cichorium*, *Lactuca*, *Scorzonera*, *Taraxacum*, and *Tragopogon*) as well as a number of genera used in folk medicine (e.g. *Crepidiastrum*, *Ixeris*, *Lactuca*, *Pilosella*, *Taraxacum*, and *Youngia*). Knowledge about secondary metabolites from these commercially interesting genera is generally quite good. However, most of the other genera of the Cichorieae have not been studied phytochemically at all.

In contrast to other tribes of the Asteraceae (Zdero and Bohlmann, 1990), which contain numerous different types of basic carbon skeletons, the Cichorieae so far have yielded only eudesmanes, germacranes, and guaianes. A common feature of sesquiterpenoids from the Cichorieae tribe is the presence of sugar or carboxylic acid residues in the molecules.

Many sesquiterpenoids have pronounced bitter sensory qualities and are therefore believed to contribute to the plants' defence against herbivores (Rees and Harborne, 1985). In Cichorieae used as foods, the sesquiterpene lactones are the main ingredients

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Table 1
Deviations from Bremer's (1984) system and generic nomenclature of the Cichorieae

Genus according to Bremer	Generic concept used in this review	Reference
Calycocorsus	*Willemetia*	Kirschnerová and Kirschner (1996)
Leontodon s.l. (incl. *Scorzoneroides*)	two separate genera *Leontodon* and *Scorzoneroides* (=former subgenus Oporinia of the genus *Leontodon* s.l.)	Samuel et al. (2006)
Mulgedium	*Lactuca* s.l.	Greuter (2003) and Kilian et al. (2008)
Prenanthes s.l.	Members of *Prenanthes* s.l. were re-assigned to a number of genera, including *Prenanthes* s.str., which just contains *P. purpurea* L. *P. acerifolia* Maxim. is now member of the genus *Nabalus*	Kilian et al. (2008)
Pterocypsela	*Lactuca* s.l.	Kilian et al. (2008)

responsible for the characteristic bitter taste, e.g. in radicchio (*Cichorium intybus*) and lettuce (*Lactuca sativa*) (Sessa et al., 2000). As sesquiterpenoids exhibit a wide range of bioactivities which include toxicity for certain cancer cell lines and induction of detoxifying enzymes, the sesquiterpene content of salads and vegetables from the Cichorieae might contribute to the health promoting properties of these groceries (Zidorn et al., 1999c; Im et al., 2007).

2. Summary of literature data

The literature data on sesquiterpenoids from the Cichorieae tribe were retrieved with the help of the SciFinder database. Entries until the end of 2007 were considered. A total of 360 sesquiterpene lactones and related compounds from 139 taxa belonging to 31 different genera of the Cichorieae have been reported. Excluded from the reports considered here are reports solely based on compounds found in tissue culture or as artificially induced phytoalexins. Scheme 1 permits a fast and simple classification of the known sesquiterpenoids into 30 subgroups. Using this scheme assignments are made based on the basic carbon skeletons (eudesmane, germacrane, and guaiane) and further features such as double bonds within the ring system, symmetry of these double bonds, presence and absence and, if applicable, the position of the lactone ring. In Figs. 1–30 the chemical structures of the compounds belonging to the 30 subgroups of sesquiterpenoids are displayed. A list of trivial names of these compounds is available as Supplementary material (Table S1).

Guaianolides are the most diverse class of sesquiterpenoids within the Cichorieae. The guaianolides represent not only most of the compounds reported up to now but also contribute 13 of the 30 major compound classes as shown by the classification key (Scheme 1). Fig. 31 shows the structures of the substituents abbreviated in Figs. 1–30.

The three compound classes encompassing the largest number of compounds are also guaianolides: costus lactone type guaianolides with 92, lactucin type guaianolides with 75, and hieracin type guaianolides with 29 representatives.

As mentioned in Section 1, literature coverage of the various genera of the Cichorieae is quite different and presently there are no reports of sesquiterpene lactones from the following 65 genera of the Cichorieae (the numbers in brackets indicate the number of species assigned to these genera according to Bremer, 1994):

Acanthocephalus (2 species), *Actites* (1 species), *Aetheorrhiza* [1 species, recently transferred to the genus *Sonchus* (Greuter, 2003)], *Agoseris* (17 species), *Anisocoma* (1 species), *Aposeris* (1 species), *Arnoseris* (1 species), *Atrichoseris* (1 species), *Babcockia* (1 species), *Calycoseris* (2 species), *Catananche* (5 species), *Cephalorrhynchus* (15 species), *Chaetadelpha* (1 species), *Chaetoseris* (18 species), *Chorisis* (1 species), *Dianthoseris* (1 species), *Dubyaea* (10 species), *Embergeria* (1 species), *Epilasia* (3 species), *Garhadiolus* (4 species), *Geropogon* (1 species), *Glyptopleura* (2 species), *Heteracia* (2 species), *Heteroderis* (1 species), *Hispidiella* (1 species), *Holoeleion* (3 species), *Hymenonema* (2 species), *Hyoseris* (5 species), *Ixeridium* (ca. 15 species), *Kirkianella* (1 species), *Koelpinia* (5 species), *Krigia* (7 species), *Lactucella* (1 species), *Lactucosonchus* (1 species), *Lagedium* (1 species), *Lygodesmia* (1 species), *Malacothrix* (16 species), *Microseris* (15 species), *Munzothamnus* (1 species), *Nothocalais* (4 species), *Paraprenanthes* (11 species), *Phalacroseris* (1 species), *Picrosia* (2 species), *Pilosella* (depending on the species concept this genus encompasses around 20 or more than 200 species), *Pinaropappus* (10 species), *Prenanthella* (1 species), *Pterachaenia* (1 species), *Pyrrhopappus* (3 species), *Rafinesquia* (3 species), *Rhagadiolus* (2 species), *Rothmaleria* (1 species), *Scariola* (10 species), *Scolymus* (3 species), *Shinnersoseris* (1 species), *Spiroseris* (1 species), *Stebbinsoseris* (2 species), *Stephanomeria* (17 species), *Steptorrhampus* (7 species), *Sventenia* (1 species), *Syncalathium* (4 species), *Thamnoseris* (1 species), *Tolpis* (20 species), *Tourneuxia* (1 species), *Tragopogon* (110 species), and *Uropappus* (1 species).

Two genera, *Gundelia* and *Warionia*, which until now have never been included in the Cichorieae tribe, have very recently been transferred to the Cichorieae by Kilian et al. (2008) based on molecular data. The genus *Gundelia*, which encompasses two species and was placed into the Arctoteae tribe by Bremer (1994), has so far yielded no sesquiterpene lactones. The monotypic genus *Warionia* was included in the Cichorioideae subfamily of Asteraceae by Bremer but was not assigned to any of its tribes. This genus yielded sesquiterpene lactones and is therefore included in this review. In the following paragraphs the sesquiterpene lactones reported so far for each genus are summarized. As the classification of genera into subtribal groups is currently under revision (Kilian et al., 2008), genera are treated in alphabetic rather than in systematic order. Immediately after the name of the species the following details – if available – are summarized in abbreviated form and printed in square brackets: (1) country of origin of the plant material (if plants were cultivated, this is stated and the country of origin of the seeds is additionally indicated if this information is available); (2) plant parts used for the phytochemical investigation; and (3) the solvent(s) used for the extraction of the plant material. Whether the study was just aimed at major compounds or was comprehensive is indirectly deducible from the number of sesquiterpenoids reported. The employed methodology of the studies is usually correlated with the publication year of the studies. In the exceptional cases where the employed methodology seems to be problematic, e.g. because the temperatures acting upon the investigated extracts were too high, this fact is also stated. In cases where later more appropriately performed studies confirmed all the initial findings from methodologically problematic studies, these hints are omitted. Problematic techniques like extraction with hot organic solvents or (worse) hot water, which might induce artifact formation, are not always discussed as being problematic in detail but are marked by an exclamation mark in brackets (!).

Andryala (20 species) – *Andryala integrifolia* L. [Spain/whole plants/hot (!) EtOH] yielded costus lactone type guaianolides