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Chemistry and biological activities of *Calceolaria* spp. (Calceolariaceae: scrophulariaceae)

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Abstract *Calceolaria* spp. is regarded both as a notorious weed and a popular ornamental garden plant and have medicinal application. Some taxa of the America distributed *Calceolaria* genus are toxic to insects and its effect has been associated with the presence of diterpenes, triterpenes and naphthoquinones. However, *Calceolaria* spp. also produces a number of flavonoids and phenylpropanoids that have been shown to possess interesting biological activities. All these aspects are considered in this review to allow an evaluation of the potential for utilization of the large biodiversity of *Calceolaria* available. The phytochemistry of many members of the *Calceolaria* genus is included.

Keywords Calceolariaceae · Diterpenes · Pimaradiene · Abietatriene · Biological activity

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Introduction

The increasing interest in the possible application of plant secondary metabolites for pest management highlights the importance of the search for new sources of biologically active natural products with biodegradability, low mammalian toxicity and environmentally-friendly qualities (González and Estevez-Braun 1998). The impact of synthetic pesticides on the environment has been largely negative, producing resistant strains. For a friendlier and more efficient alternative to pest control we propose organic molecules from botanical origin (Muñoz et al. 2013a).

There is a widespread effort to find new biopesticides and in several cases diterpenes are a good source due to their potent effects on insect pests and low toxicity (Xie et al. 1993; Ortego et al. 1995; Isman 2006; Koul and Walia 2009; Coll and Tandron 2007; Isman and Akthar 2007; Simmonds et al. 1996). Cespedes' group have undertaken studies on biopesticides from shrubs belonging to the genus *Calceolaria* that was included due to its strong resistance to insect attack observed in nature, making these plants an excellent source of new biopesticides for the control of insect pests (Cespedes et al. 2013).

Calceolaria L. is perhaps one of the widest genera in the Andean region, distributed from Patagonia to central Mexico. The last revision recognized more than 180 species in *Calceolaria* almost all restricted to America, being divided into three subgenera (Molau 1988, 2003): *Calceolaria* (19 sections), *Cheiloncos*

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(two sections), and *Rosula* (three sections) (Anderson 2006). Ehrhart (2000, 2005) revised the Chilean representatives of the genus and recognized 50 species, between them *C. integrifolia* s.l. complex with nine species: *C. andina*, *C. angustifolia*, *C. auriculata*, *C. georgiana*, *C. integrifolia* s.str., *C. rubiginosa*, *C. talcana*, *C. verbascifolia*, *and C. viscisissima* (Calceolariaceae: formerly Scrophulariaceae) (Ehrhart 2005). Many of these species are commonly known as "zapatito de doncella" or "capachito de hoja larga", generally are strong erect shrubs which grow from 50 to 150 cm, although depending on locality, it might reach a shorter height with fragile ascending branches.

Biological activities

Plants belonging to this family have very interesting properties to study: aerial parts of these plants have medicinal activities that are used for digestive, diuretic and antimicrobial treatments (Harborne and Baxter 2001; Woldemichael et al. 2003). Few studies of many *Calceolaria* species from around the world show that this genus is characterized by the presence of substances with important agrochemical and pharmacological potential such as insecticide (Khambay et al. 1999) and antimicrobial properties (Falcao et al. 2006; Woldemichael et al. 2003).

Although endogenous functions of diterpenes have not yet been fully elucidated, these play important roles within the plant, especially in cell energy, and these types of substances have been shown to have important biological function in defensive activity. They can function as both constitutive and inducible defense mechanisms, also in dormancy and growth inhibition of plants (Cespedes et al. 2006; Feeny 1976), in pest-resistance and antimicrobial activities, and as storage in trichomes (Kakuta et al. 1992; Mercado et al. 2010).

Several studies have investigated the sites and mechanisms of action of allelochemicals, and insecticidal or insect growth inhibitory (IGR) activity shows that different diterpenes are enzymatic and metabolic inhibitors (Calderón et al. 2001; Cespedes et al. 2006; Feeny 1976) and have insecticidal, IGR and antifeedant effects on phytophagous insects (Rhoades and Cates 1976; Simmonds et al. 1996; Xie et al. 1993; Ortego et al. 1995; Mullin et al. 1997). We have previously demonstrated that diverse secondary metabolites have different sites of action and different molecular targets when they interact with enzymes and metamorphosis processes (Cespedes et al. 2006).

To date, no studies have been performed investigating the phytochemical qualities or biological activities of many *Calceolaria* sp.pl. Because previously gathered information about this genus and our own field observations indicated that these plant species appear to possess a strong resistance to pathogen attack, Cespedes' group undertook examination of Chilean members of this genus specifically the *C. integrifolia* s. l. complex. (Muñoz et al. 2013a, b, c) whose long-term goal is to learn about the role of the phytochemical composition with the inhibitory behavior on growth and development of a model system of pest insect such as *Drosophila melanogaster* (Diptera: Drosophilidae) and *Spodoptera frugiperda* (J.E. Smith, Lepidoptera: Noctuidae). In short, they are in search of botanicals for potential use as biopesticides. Those data are important for studies of insect control.

Despite the few studies of biological activities of the secondary metabolites isolated from *Calceolaria* species, these have been shown to be antifeedant, tyrosinase inhibition, antibacterial, antioxidant, and trypanocidal (Bravo et al. 2005; Cespedes et al. 2013; Falcao et al. 2006; Khambay et al. 1999; Morello et al. 1995; Muñoz et al. 2013a, b, c; Woldemichael et al. 2003).

Chemistry of *Calceolaria*

Despite the abundance of species placed in the genus, although there are few studies on the chemistry of them. The reported chemistry of the Genus was reviewed previously by Garbarino and collaborators covering up to 2001 (Garbarino et al. 2000, 2001). Only 15 % of existing species of *Calceolaria* in Chile have been studied chemically indicating the presence of flavonoids, glucophenylpropanoids, and mainly diterpenes (Di Fabio et al. 1995; Garbarino et al. 2000).

The systematic study of the chemical constituents of *Calceolaria* led to the discovery of new molecules. A total of 117 have been reported to date, i.e. **1–117**, secondary metabolites isolated from Chilean *Calceolaria* that includes diterpenes, flavonoids and naphthoquinones founded in nonpolar extracts, while in the polar extracts were isolated phenylpropanoids as verbascoside and others (Di Fabio et al. 1995). Triterpenes, sterols and other polyphenols described in the literature are reviewed here. The structures, names and corresponding source of *Calceolaria* species are showed in Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 and 11, and Figs. 1, 2, 3, 4, 5, 6, 7 and 8.

Diterpenes

The structural diversity of diterpenes is represented in the chemistry of Chilean *Calceolaria* with five different skeletons types: abietane, pimarane, stemarane, labdane and scopadulane. These diterpenes are arranged according to its biosynthetic pathway and structural characteristics (Hanson 2009). In many of the structures of diterpenes described in numerous articles published by Garbarino's group were used different nomenclature; here we have described all published structures under a uniform nomenclature.

Abietane diterpenes

Abietane type skeleton was found in 11 diterpenes, **1–11**, isolated from several species of *Calceolaria*. In many of them a common feature is the aromatization of ring C and oxygenation patterns at carbons 19 and 2, in the latter with the alpha configuration. From *C. purpurea* were isolated two abietanes with two epoxide functionality on the ring C (Chamy et al. 1992, 1993a). The unique compounds having substitution on the carbon in position 3 with alpha configuration are 3β-acetoxy-abietatrien and abietatrien-3β-ol, both isolated from *C. thyrsiflora* (Chamy et al. 1991a). For details see Table 1 and Fig. 1.

Pimarane diterpenes

The chemistry of pimarane diterpenes from *Calceolaria* is very complex, due to the great diversity of changes in stereochemistry at the pimarane skeleton. The first compound isolated during the chemical study of *Calceolaria glandulosa* (Piovano et al. 1988) was **12**, in which a methine carbon appears at an unusually upfield position (δ 38 ppm); this fact made that a normal isopimaradiene structure was discarded and 18-malonyloxy-9-*epi*-*ent*-isopimara-7,15-diene was assigned for **12** which structure was further confirmed by X-ray analysis.

Since then, it has been reported in the literature, the isolation of 10 different diterpenes with 9-*epi*-*ent*-7, 15-isopimaradiene skeleton, **12–21**, seven with 9-*epi*-*ent*-7,15-pimara-diene skeleton, **22–28**, five with the *ent*-isopimara-9 (11),15-diene skeleton, in which the double bond has migrated to the position 9 (11), **29–33**, four compounds with the *ent*-isopimara-8 (9), 15-diene skeleton, in which the double bond migrated

Table 1 Abietanes diterpenes (**1–11**) from *Calceolaria*

No.	Compound	Part	Plant	References
1	Dehydroabietinol	Aerial parts	*C. ascenden*,	Chamy et al. (1987)
			C. pinifolia	Woldemichael et al. (2003)
2	4-*Epi*-dehydroabietic acid	Aerial parts	*C. polifolia*	Chamy et al. (1991b)
3	19-Malonyloxy-dehydroabietinol	Aerial parts	*C. ascendens*	Chamy et al. (1987)
			C. pinifolia	Woldemichael et al. (2003)
4	3β-Acetoxy-abietatrien	Aerial parts	*C. thyrsiflora*	Chamy et al. (1991a)
5	Abietatrien-3β-ol	Aerial parts	*C. thyrsiflora*	Chamy et al. (1991a)
6	2α-Acetoxy-abietatriene	Aerial parts	*C. purpurea*	Chamy et al. (1992)
7	2α-Hydroxy-abietatriene	Aerial parts		
8	2α-Malonyloxy-abietatriene	Aerial parts		
9	2α-Malonyloxy-abieta-11(12)ene-9α,13α-endoperoxide	Aerial parts	*C. purpurea*	Chamy et al. (1993a)
10	2α-Malonyloxy-abieta-11(12)ene-9β,13β-endoperoxide	Aerial parts	*C. purpurea*	Chamy et al. (1993a)
11	2α, 19-Dihydroxy-dehydroabietane	Aerial parts	*C. hypericina*	Chamy et al. (1995b)

Table 2 Pimarane diterpenes (**12**–**45**) from *Calceolaria*

No.	Compound	Part	Plant	References
12	18-Malonyloxy-9-*epi*-*ent*-isopimara-7,15-diene	Aerial parts	*C. glandulosa*	Piovano et al. (1988)
			C. pseudoglandulosa	Chamy et al. (1995a)
			C. recta	Chamy et al. (1998a, b)
			C. paposana	
13	17-Acetoxy-9-*epi*-*ent*-isopimara-7,15-diene	Aerial parts	*C. foliosa*	Chamy et al. (1989)
			C. glandulifera	Chamy et al. (1998a, b)
14	17-Hydroxy-9-*epi*-*ent*-isopimara7, 15-diene	Aerial parts	*C. foliosa*	Chamy et al. (1989)
			C. glandulifera	Chamy et al. (1998a, b)
			C. dentata	Chamy et al. (1995c)
15	9-*Epi*-*ent*-isopimara-7,15-diene-17-oic acid	Aerial parts	*C. foliosa*	Chamy et al. (1989)
16	17-Malonyloxy-9-*epi*-*ent*-isopimara-7,15-diene	Aerial parts	*C. foliosa*	Chamy et al. (1989)
17	19-Malonyloxy-9-*epi*-*ent*-isopimara-7,15-diene	Aerial parts	*C. glandulifera*	Chamy et al. (1998a, b)
18	19-Hydroxy-9-*epi*-*ent*-isopimara-7,15-diene	Aerial parts	*C. glandulifera*	Chamy et al. (1998a, b)
19	18-Hydroxy-9-*epi*-*ent*-isopimara-7,15-diene	Aerial parts	*C. glandulifera*	Chamy et al. (1998a, b)
			C. pseudoglandulosa, C. glandulosa	Chamy et al. (1998a, b) Piovano et al. (1989)
20	3α,18-Dihydroxy-9-*epi*-*ent*-isopimara-7,15-diene	Aerial parts	*C. pseudoglandulosa*	Chamy et al. (1998a, b)
21	18-Formyloxy-9-*epi*-*ent*-isopimara-7,15-diene	Aerial parts	*C. glandulosa*	Piovano et al. (1989)
22	2α-Hydroxy-19-isovaleroyl-9-*epi*-*ent*-pimara-7,15-diene	Aerial parts	*C. hypericina*	Chamy et al. (1995b)
23	2α,19-Dihydroxy-9-*epi*-*ent*-pimara-7,15-diene	Aerial parts		
24	2α,19-Diacetoxy-9-*epi*-*ent*-pimara-7,15-diene	Aerial parts		
25	2α-Malonyloxy-9-*epi*-*ent*-pimara-7,15-diene		*C. purpurea*	Chamy et al. (1992)
26	18-Malonyloxy-9-*epi*-*ent*-pimara-7,15-diene	Aerial parts	*C. petioalaris*	Silva et al. (1993)
			C. sessilis	Chamy et al. (1993b)
			C. recta and	Chamy et al. (1995a)
			C. paposana	
27	18-Hydroxy-9-*epi*-*ent*-pimara-7,15-diene	Aerial parts	*C. petioalaris*	Silva et al. (1993)
28	18-Acetoxy-9-*epi*-*ent*-pimara-7,15-diene	Aerial parts	*C. petioalaris*	Silva et al. (1993)
29	19-Hydroxy-*ent*-isopimara-9(11),15-diene	Aerial parts	*C. lepida*	Chamy et al. (1990)
			C. polifolia	Chamy et al. (1991b)
			C. sessilis	Chamy et al. (1993b)
			C. pinifolia	Chamy et al. (2006)
30	19-Acetoxy-*ent*-isopimara-9(11), 15-diene	Aerial parts	*C. polifolia*	Chamy et al. (1991b)
			C. sessilis	Chamy et al. (1993b)
			C. paralia	Chamy et al. (2006)
31	*Ent*-isopimara-9(11),15-diene-19-oic acid	Aerial parts	*C. polifolia*	Chamy et al. (1991b)
			C. hypericina	Garbarino et al. (1993)
			C. sessilis	Chamy et al. (1993b)
			C. pinifolia	Woldemichael et al. (2003)
			C. paralia	Chamy et al. (2006)
32	19-Malonyloxy-*ent*-isopimara-9(11),15-diene	Aerial parts	*C. polifolia*	Chamy et al. (1991b)
			C. sessilis	Chamy et al. (1993b), Woldemichael et al. (2003)
			C. pinifolia	

Table 2 continued

No.	Compound	Part	Plant	References
33	Ethyl-19-malonyl-oxy-*ent*-isopimara-9(11), 15-diene	Aerial parts	*C. polifolia*	Chamy et al. (1991b)
34	18-Hydroxy-*ent*-isopimara-8(9), 15-diene	Aerial parts	*C. latifolia*	Garbarino and Molinari (1990a)
35	19-Hydroxy-*ent*-isopimara-8(9), 15-diene	Aerial parts	*C. latifolia*, *C. pinifolia*	Garbarino and Molinari (1990)
				Woldemichael et al. (2003)
36	19-Methyl-malonyloxy-*ent*-isopimara-8(9), 15-diene	Aerial parts	*C. pinifolia*, *C. polifolia*	Woldemichael et al. (2003)
				Garbarino et al. (2007)
37	19-Malonyloxy-*ent*-isopimara-8(9), 15-diene	Aerial parts	*C. pinifolia*	Woldemichael et al. (2003)
38	19-Pentyloxy-9α-hydroxy-*ent*-pimar-15-ene	Aerial parts	*C. lepida*	Chamy et al. (1990)
39	9α-19-Dihydroxy-*ent*-pimar-15-ene	Aerial parts		
40	9α-Hydroxy-19-malonyloxy-*ent*-pimar-15-ene	Aerial parts		
41	19-Butyloxy-9α-hydroxy-*ent*-isopimar-15-ene	Aerial parts	*C. paralia*	Chamy et al. (2006)
42	9α,19-Dihydroxy-*ent*-isopimar-15-ene	Aerial parts		
43	7α-Malonyloxy-18-isovaleroyl-*ent*-isopimara-9(11), 15-diene	Aerial parts	*C. alba*	Chamy et al. (2007)
44	3β-Hydroxy-18-isovaleroyl-7α-malonyloxy-*ent*-isopimara-9(11), 15-diene	Aerial parts		
45	3β-Isovaleroyl-18-hydroxy-7α-malonyloxy-*ent*-isopimara-9(11), 15-diene	Aerial parts		

Table 3 Dimeric diterpenes (**46–51**) from *Calceolaria*

No.	Compound	Part	Plant	References
46	Foliosate	Aerial parts	*C. foliosa*	Chamy et al. (1989)
47	Glandulosate	Aerial parts	*C. glandulosa*	Piovano et al. (1989)
			C. pseudoglandulosa	Chamy et al. (1998a, b)
			C. recta	Chamy et al. (1995a)
			C. paposana	
48	Lepidato	Aerial parts	*C. lepida*	Chamy et al. (1990)
49	Polifosate	Aerial parts	*C. polifolia*	Chamy et al. (1991b)
			C. paralia	Chamy et al. (2006)
			C. sessilis	Chamy et al. (1993b)
50	Petiolate	Aerial parts	*C. petioalaris*	Silva et al. (1993)
51	Bis-[*ent*-9-*epi*-labda-8(17),(12Z), 14-trien-19-yl] malonate	Aerial parts	*C. densifolia*	Garbarino and Molinari (1992)

to position 8(9), **34–37**, three-9α-hydroxy-*ent*-pimar-15-ene, in which the double bond is gone and there is an hydroxyl group at C9, **38–40**, two diterpenes having the skeleton isopimarane with an hydroxyl group at C9, **41–42**, and finally three isopimaranes, **43–45**, isolated from *C. alba* (Chamy et al. 2007), whose structures were reported with discrepancies between the skeleton type and the proposed name. Other feature of pimarane diterpenes from *Calceolaria* is the oxidation patterns of carbons 2, 3, 17, 18, or 19 which are oxidized in most cases to form alcohols, or esterified with malonyloxy, **12**, **14**, **17**, **25**, **26**, **32**,

Table 4 Stemarane diterpenes (**52**–**62**) from *Calceolaria*

No.	Compound	Part	Plant	References
52	19-Hydroxy-*ent*-stemara-13(14)-ene	Aerial parts	*C. latifolia*	Garbarino and Molinari (1990a)
			C. lepida	Chamy et al. (1990)
			C. polifolia	Chamy et al. (1991b)
53	18-Hydroxy-*ent*-stemara-13(14)-ene	Aerial parts	*C. latifolia*	Garbarino and Molinari (1990a)
54	17-Acetoxy-18-hydroxy-*ent*-stemara-13(14)-ene	Aerial parts	*C. kingii*	Garbarino and Molinari (1990b)
55	*Ent*-stemara-13(14)-ene-19-oic acid	Aerial parts	*C. lepida*	Chamy et al. (1990)
			C. paralia	Chamy et al. (2006)
56	19-Malonyloxy-*ent*-stemar-13(14)-ene	Aerial parts	*C. polifolia*	Chamy et al. (1991b)
57	17-Acetoxy-19-malonyloxy-*ent*-stemar-13(14)-ene			
58	19-Acetoxy-*ent*-stemar-13(14)-ene	Aerial parts	*C. polifolia*	Chamy et al. (1991b), Garbarino et al. (2007)
59	7α-Malonyloxy-13-methylene-stemarane	Aerial parts	*C. dentata*	Chamy et al. (1995c)
60	2β-Acetoxy-13-methylene-stemarane	Aerial parts		
61	7α-Acetoxy-13-methylene-stemarane	Aerial parts	*C. glabrata*	Chamy et al. (2001)
62	19-Hydroxy-13,14-epoxy-*ent*-stemarane	Aerial parts	*C. polifolia*	Garbarino et al. (2007)

Table 5 Scopadulane diterpenes (**63**–**75**) from *Calceolaria*

No.	Compound	Part	Plant	References
63	Thyrsiflorin A	Aerial parts	*C. thyrsiflora*	Chamy et al. (1991a)
			C. recta	Chamy et al. (1995a)
			C. paposana	Chamy et al. (1991b)
			C. polifolia	Garbarino et al. (2007)
64	Thyrsiflorin B	Aerial parts	*C. thyrsiflora*	Chamy et al. (1991a)
65	Thyrsiflorin C	Aerial parts	*C. thyrsiflora*	Chamy et al. (1991a)
66	Thyrsiflorin B acetoxy	Aerial parts	*C. dentata*	Chamy et al. (1995c)
67	7-Acetoxy-13-isovaleroyl-thyrsiflorane	Aerial parts	*C. dentata*	Chamy et al. (1995c)
68	13-Isovaleroyl-7-malonyloxy-thyrsiflorane		*C. glabrata*	Chamy et al. (2001)
69	13,18-Dihydroxy-thyrsiflorare	Aerial parts	*C. filicaulis ssp Luxurians*	Garbarino et al. (2006)
70	13-Isovaleroyl-18-hydroxy-thyrsiflorane			
71	13-Hydroxy-thyrsiflorin	Aerial parts	*C. recta*	Chamy et al. (1995a)
72	13-Acetoxy-thyrsiflorin		*C. paposana*	Garbarino et al. (2007)
			C. polifolia	
73	19-Malonyloxy-9-*epi*-scapadul-15-ene	Aerial parts	*C. polifola*	Garbarino et al. (2007)
74	9-*Epi*-scopadul-15-ene-19-oic acid			
75	19-Hydroxy-9-*epi*-scopadul-15 ene			

36, **37**, **40**, **43**, **44**, **45**, isovaleroyl, **22**, **43**–**45**, acetoxy, **13**, **24**, **28**, **30**, formyloxy, **21**, pentyloxy, **38**, butyloxy, **41**, groups, or completely oxidized to form the respective carboxylic acids, **15** and **31**. For full details of the literature consulted and the structures see Table 2 and Fig. 2. Finally, Fraga and coworkers drew the correct structure of **23**, making the mention that it was drawn incorrectly in the original paper (Fraga et al. 1998; Chamy et al. 1995b).

Dimeric diterpenes

From several species have been isolated some dimeric compounds conformed of two isopimaryl type units,

Table 6 Labdane diterpenes (76–81) from *Calceolaria*

No.	Compound	Part	Plant	References
76	19-Hydroxy-9-*epi*-*ent*-labda-8(17), 12 Z, 14-triene	Aerial parts	*C. densifolia*	Garbarino and Molinari (1992)
77	19-Malonyloxy-9-*epi*-*ent*-labda- 8(17), 12 Z, 14-triene	Aerial parts	*C. corymbosa*	Garbarino and Molinari (1993)
78	2β-Hydroxy-9-*epi*-*ent*-labda-8(17), 13 (E)-dien-15-oic acid	Aerial parts	*C. inamoena*	Garbarino et al. (2004)
79	2β-Hydroxy-9-*epi*-*ent*-labda-8(17), 13 (E)-dien-15-al	Aerial parts		
80	2β-Hydroxy-9-*epi*-*ent*-labda-8(17), 13 (Z)-dien-15-oic acid	Aerial parts		
81	2β-Hydroxy-9-*epi*-*ent*-labda-8(17), 13 (Z)-dien-15-al	Aerial parts		

Table 7 Sterols and triterpenes (**82–85**) from *Calceolaria*

No.	Compound	Part	Plant	References
82	β-Sitosterol	Aerial parts	*C. hypericina*	Chamy et al. (1995b)
			C. recta	Chamy et al. (1995a)
			C. paposana	Garbarino et al. (2006)
			C. filicaulis	
83	3α-Ursolic acid	Aerial parts	*C. pinifolia*	Woldemichael et al. (2003)
84	3α-Oleanolic acid			
85	Oleanolic acid	Aerial parts	*C. recta*	Chamy et al. (1995a)
			C. paposana	

Table 8 Phenylpropanoid glycosides (**86–93**) from *Calceolaria*

No.	Compound	Part	Plant	References
86	Calceolarioside A	Aerial parts	*C. hypericina*, *C. corymbosa*, *C. crassifolia*	Nicoletti et al. (1986)
			C. paposana, *C. glandulosa*, *C. purpurea*	Nicoletti et al. (1988a)
			C. recta, *C. thyrsiflora*, *C. integrifolia*	Di Fabio et al. (1995)
			C. andina, *C. densifolia*, *C. dentata*	
87	Verbascoside	Aerial parts	*C. hypericina*, *C. adscendens*, *C. talcana*	Nicoletti et al. (1988a)
			C. biflora, *C. corymbosa*, *C. crassifolia*	Nicoletti et al. (1988b)
			C. foliosa, *C. polifolia*, *C. glandulosa*	Di Fabio et al. (1995)
			C. purpúrea, *C. recta*, *C. kingii*	Muñoz et al. (2013a, b, c)
			C. thyrsiflora, *C. integrifolia*, *C. andina*	
88	Calceolarioside C	Aerial parts	*C. hypericina*, *C. crassifolia*, *C. purpurea*	Di Fabio et al. (1995)
			C. recta, *C. thyrsiflora*, *C. integrifolia*	Nicoletti et al. (1988a)
			C. andina	
89	Calceolarioside E	Aerial parts	*C. adscendens*, *C. foliosa*, *C. polifolia*	Nicoletti et al. (1988b)
				Di Fabio et al. (1995)
90	Forsythoside A	Aerial parts	*C. biflora*, *C. foliosa*, *C. adscendens*	Di Fabio et al. (1995)
			C. kingii, *C. densifolia*, *C. dentata*	
91	Calceolarioside B	Aerial parts	*C. hypericina*, *C. biflora*, *C. crassifólia*	Nicoletti et al. (1986)
			C. glandulosa, *C. purpurea*, *C. recta*	Di Fabio et al. (1995)
			C. thyrsiflora, *C. integrifolia*, *C. andina*	
92	Isoarenarioside	Aerial parts	*C. foliosa*	Di Fabio et al. (1995)
93	Calceolarioside D	Aerial parts	*C. hypericina*, *C. crassifolia*, *C. recta*	Nicoletti et al. (1988a)
			C. thyrsiflora, *C. integrifolia*, *C. andina*	Di Fabio et al. (1995)

Table 9 Quinones (**94–96**) from *Calceolaria*

No.	Compound	Part	Plant	References
94	2-Hydroxy-3-(1,1-dimethylallyl)-1,4-naphthoquinone	Aerial parts	*C. andina*	Khambay et al. (1999)
			C. sessilis	Morello et al. (1995)
95	2-Acetoxy-3-(1,1.dimethylallyl)-1,4-napthoquinone	Aerial parts	*C. andina*	Khambay et al. (1999)
			C recta	Chamy et al. (1995a)
			C. paposana	Morello et al. (1995)
			C. sessilis	
96	(-)-2,3,3-Trimethyl-2-3-dihydronaphtho[2,3-b]furan-4,9-quinone	Aerial parts	*C. sessilis*	Ruedi and Eugster (1977)
			C. integrifolia	Morello et al. (1995)

Table 10 Aromatic compounds (**97–101**) from *Calceolaria*

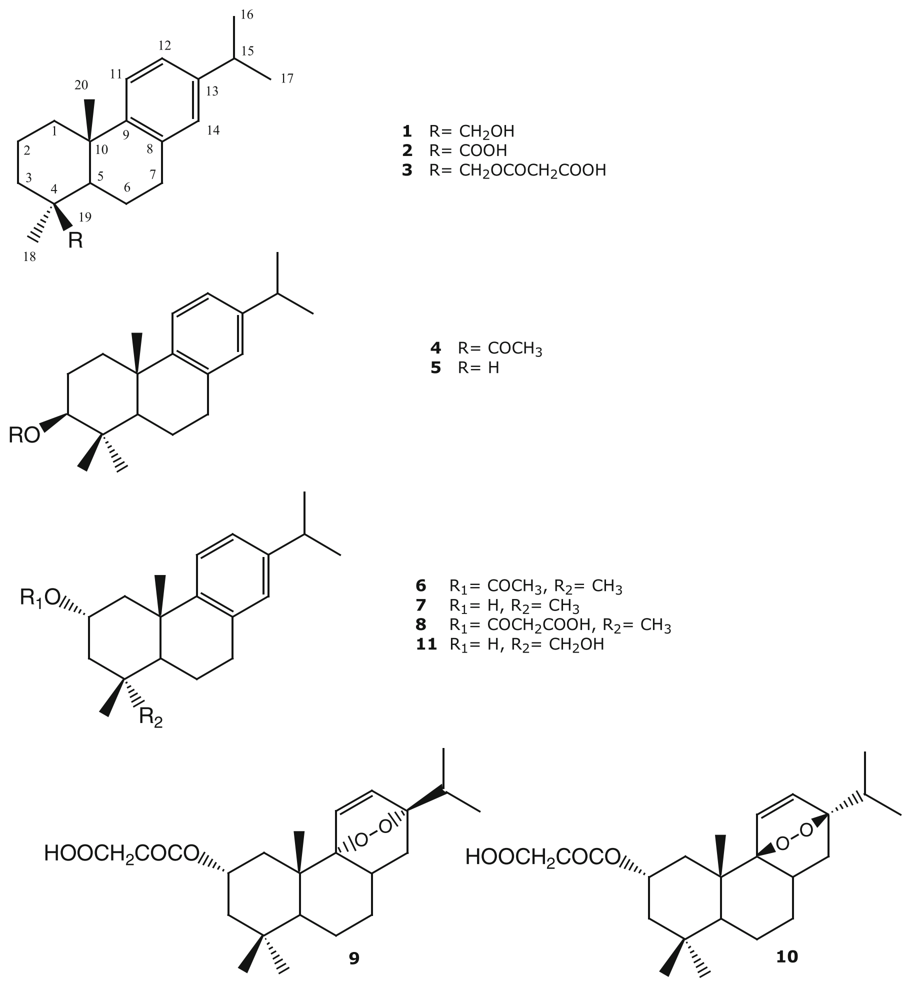
No.	Compound	Part	Plant	References
97	GA	Leaf, flowers	*C. thyrsifolia*	Bravo et al. (2005)
98	DIBOA	Leaf, flowers		
99	HBOA	Leaf, flowers		
100	7-OH-HBOA	Leaf, flowers		
101	BOA	Leaf, flowers		

46–48, two pimaryl units, **49**, **50**, or two labdane units, **51**. All the bis compounds are linked through carbons 17, 18, or 19 by a malonic acid unit. Only from eleven species of *Calceolaria*, have been isolated this dimeric diterpenes: *C. foliosa*, *C. glandulifera*, *C. pseudoglandulosa*, *C. recta*, *C. paposana*, *C. lepida*, *C. polifolia*, *C. paralia*, *C. sessilis*, *C. petiolaris*, and *C. densifolia*.(Chamy et al. 1989, 1990, 1991b, 1993, 1995a; 1998a, b; 2006; Silva et al. 1993; Garbarino and Molinari 1992; Piovano et al. 1989). For details see Table 3 and Fig. 3.

Table 11 Cyclohexanone (**102**) and Flavonoids (**103–117**) from *Calceolaria*

No.	Compound	Part	Plant	References
102	Halleridone	Aerial parts	*C. hypericina*	Nicoletti et al. (1986)
103	Taxifolin	Aerial parts	*C. hypericina*	Nicoletti et al. (1986)
104	Naringenin 4′-Me ether	Aerial parts		
105	5-Hydroxy-7,8,4′-trimethoxyflavone	Leaf glands	*C. irazuensis*	Wollenweber et al. (1989)
106	3,5-Dihydroxy-7,8,4′-trimethoxyflavone	Leaf glands		
107	Isoscutellarein 8,4′-dimethyl ether	Leaf glands		
108	Herbacetin 8,4′-dimethyl ether	Leaf glands		
109	Gossypetin-7,8,3′-trimethyl ether	Leaf glands		
110	Kaempferol-7-methyl ether	Leaf glands		
111	Kaempferol-4′-methyl ether	Leaf glands		
112	Kaempferol-7,4′-dimethyl ether	Leaf glands		
113	Apigenin 4′-methyl ether	Leaf glands		
114	Gossypetin 3,8,3′-trimethyl ether	Leaf glands	*C. scabiosifolia*	Wollenweber et al. (1989)
			C. chelidonioides	
115	Quercetin 3-methyl ether	Leaf glands	*C. scabiosifolia*	
			C. chelidonioides	
116	Quercetin 3,3′-dimethyl ether	Leaf glands	*C. scabiosifolia*	
			C. chelidonioides	
117	Kaempferol 3-methyl ether	Leaf glands	*C. scabiosifolia*	

Fig. 1 Abietanes diterpenes (**1–12**) from *Calceolaria*



Stemarane diterpenes

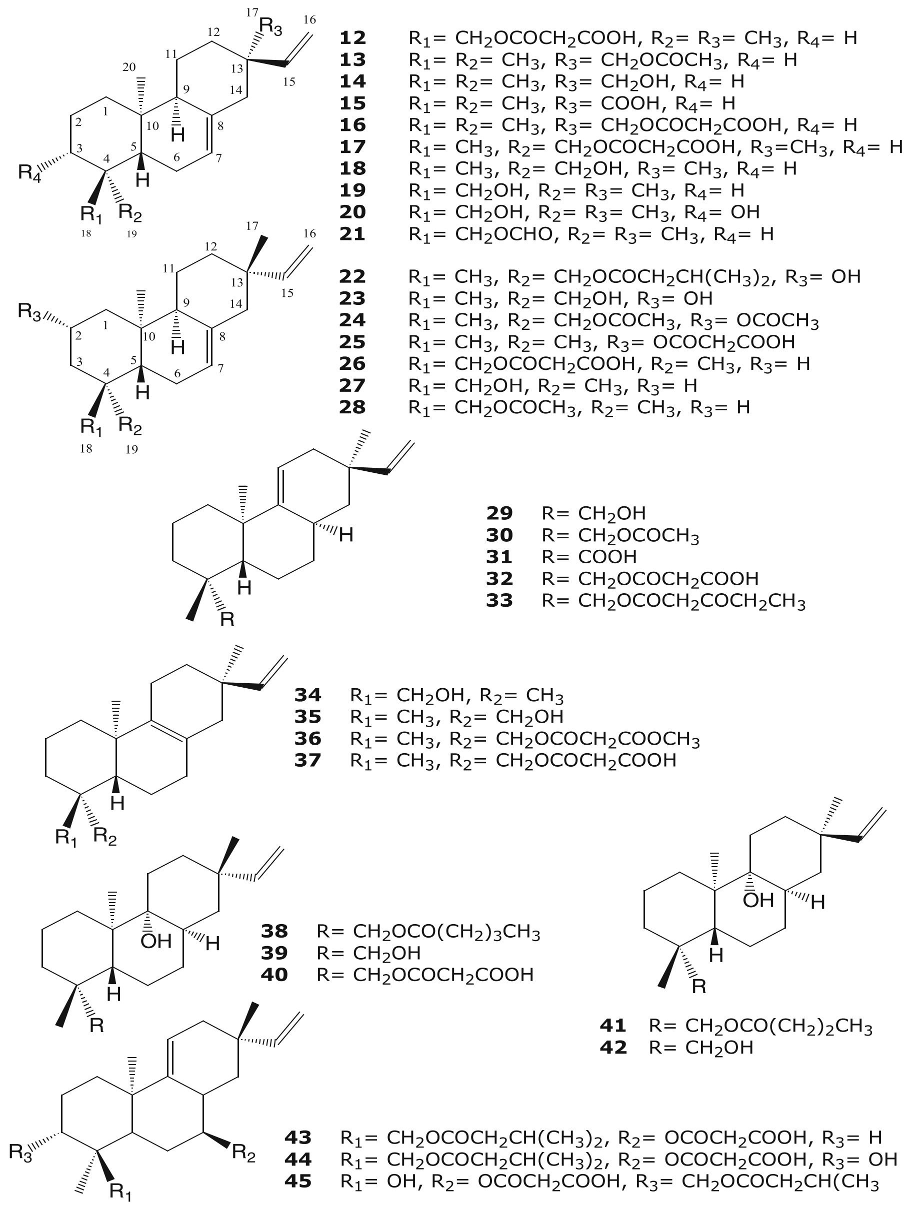
The stemaranes isolated from *Calceolaria* presents three main characteristics: the presence of a double bond at position 13(14), **52–58**; the isomerization of the double bond to the exocyclic position at carbon 13, **59–61**; and the epoxidation at carbons 13 and 14, **62**. The pattern of oxidation includes carbons 2, 7, 17, 18 and 19, in which are presents free alcohols, or esterified with malonyloxy, or acetoxy groups, or completely oxidized to the respective carboxylic acid. For details see Table 4 and Fig. 4.

Recently, Leonelli and coworkers conducted the regio-and diastereoselective synthesis of 19-hydroxy-*ent*-stemara-13(14)-ene, **52**, finding differences between the structure proposed by Garbarino and that one synthetically prepared (Leonelli et al. 2012; Garbarino and Molinari 1990b). The later results suggest that the chemistry and the proposed structures of *Calceolaria* diterpenes could be reviewed in order to avoid incorrect structures.

Scopadulane diterpenes

There is reported in literature the isolation of thirteen scopadulanes from *Calceolaria* species, **63–75**. Because the first compound was isolated from *C. thyrsiflora*, it was assigned the trivial name thyrsiflorine A, B and C, **63–65** respectively (Chamy et al. 1991a, b, 1995a; Garbarino et al. 2007). Some other derivatives from thyrsiflorine, 13-hydroxy-thyrsiflorine, **71**, and its acetoxy derivative, **72**, have been isolated from *C. recta*, *C. paposana* and *C. polifolia* (Chamy et al. 1995a), while 7-acetoxy-13-isovaleroyl-thyrsiflorane, **67**, 13-isovaleroyl-7-malonyloxy-thyrsiflorane, **68**, 13,18-dihydroxy-thyrsiflorare, **69**, and

Fig. 2 Pimarane diterpenes (**13–45**) from *Calceolaria*



13-isovaleroyl-18-hydroxy-thyrsiflorane, **70**, where isolated from other species (Chamy et al. 1995c, 2001; Garbarino et al. 2006). For details see Table 5 and Fig. 4.

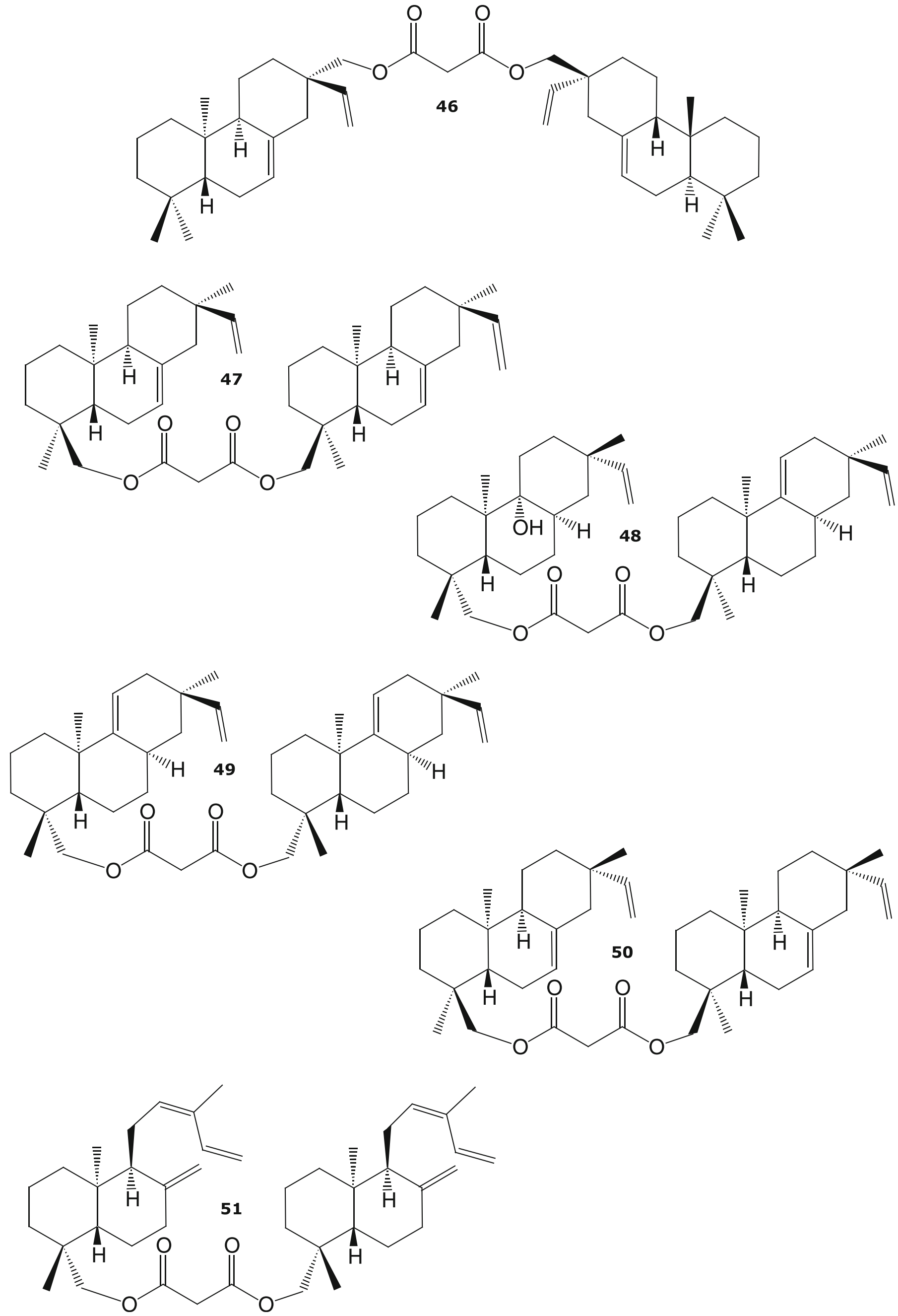
Labdane diterpenes

The labdane skeleton is represented in *Calceolaria* metabolites with 6 compounds isolated from *C. densifolia*, **76**, *C. corymbosa*, **77**, and *C. inamoena*, **78–81** (Garbarino and Molinari 1992, 1993a; Garbarino et al. 2004). The common feature of the labdane series of metabolites isolated from *Calceolaria* is 9-*epi*-*ent*-labda-8(17)-en core, present in all structures. For details see Table 6 and Fig. 5.

Sterols and triterpenes

Although the sterols and triterpenes are widely distributed in plants, there are only five reports about the isolation and structural elucidation of this class of compounds. From *C. hypericina*, *C. recta*, *C. paposana*, and *C. filicaulis*, was isolated β-sitosterol, **82**

Fig. 3 Dimeric diterpenes (**46**–**51**) from *Calceolaria*



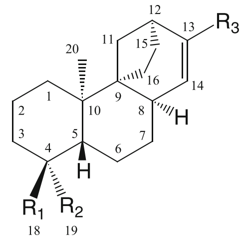
(Garbarino et al. 2006; Chamy et al. 1995a, b). From *C. pinifolia* were isolated 3-*epi*-ursolic acid, **83**, and 3-*epi*-oleanolic acid, **84** (Woldemichael et al. 2003). Finally, from *C. recta*, *C. paposana*, was isolated oleanolic acid, **85**, (Chamy et al. 1995a). For details see Table 7 and Fig. 5.

Aromatics

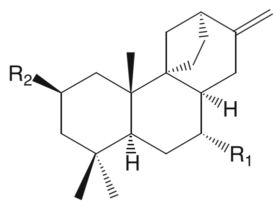
Phenylpropanoid glycosides

The first phenylpropanoid glycosides isolated from *Calceolaria* were calceolariosides A and B, **86** and **91**

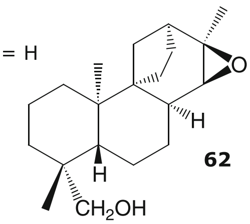
Fig. 4 Stemarane (**52**–**62**) and Scopadulane diterpenes (**63**–**75**) from *Calceolaria*



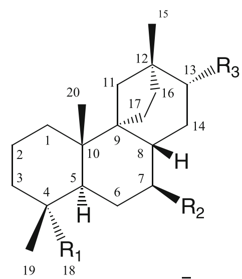
52 R_1= CH_3, R_2=CH_2OH, R_3= CH_3
53 R_1= CH_2OH, R_2= R_3= CH_3
54 R_1= CH_2OH, R_2= CH_3, R_3= CH_2OCOCH_3
55 R_1= CH_3, R_2= COOH, R_3= CH_3
56 R_1= CH_3, R_2= CH_2OCOCH_3COOH, R_3= CH_3
57 R_1= CH_3, R_2= CH_2OCOCH_2COOH, R_3= CH_2OCOCH_3
58 R_1= CH_3, R_2= CH_2OCOCH_3, R_3= CH_3



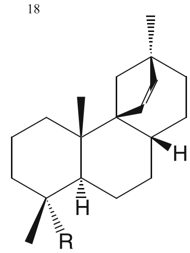
59 R_1= $OCOCH_2COOH$, R_2= H
60 R_1= H, R_2= $OCOCH_3$
61 R_1= $OCOCH_3$, R_2= H



62



63 R_1= CH_3, R_2= H, R_3= $OCOCH_2COOH$
64 R_1= CH_3, R_2= OH, R_3= $OCOCH_2COOH$
65 R_1= CH_3, R_2= R_3= OH
66 R_1= CH_3, R_2= $OCOCH_3$, R_3= $OCOCH_2COOH$
67 R_1= CH_3, R_2= $OCOCH_3$, R_3= $OCOCH_2CH(CH_3)_2$
68 R_1= CH_3, R_2= $OCOCH_2COOH$, R_3= $OCOCH_2CH(CH_3)_2$
69 R_1= CH_2OH, R_2= H, R_3= OH
70 R_1= CH_2OH, R_2= H, R_3= $OCOCH_2CH(CH_3)_2$
71 R_1= CH_3, R_2= H, R_3= OH
72 R_1= CH_3, R_2= H, R_3= $OCOCH_3$



73 R= CH_2OCOCH_2COOH
74 R= COOH
75 R= CH_2OH

respectively, from *C. hypericina* (Nicoletti et al. 1986). Later, from the same plant were isolated, verbascoside, **87**, calceolariosides C and D, **88** and **93** respectively (Nicoletti et al. 1988a). The most abundant is **87**, which is present in *C. adscendens*, *C. talcana*, *C. biflora*, *C. corymbosa*, *C. crassifolia*, *C. foliosa*, *C. polifolia*, *C. glandulosa*, *C. purpurea*, *C. recta*, *C. kingii*, *C. thyrsiflora*, *C. integrifolia*, *C. andina*, together with the species mentioned above (Di Fabio et al. 1995; Garbarino and Molinari 1993; Garbarino et al. 1993; Muñoz et al. 2013a, 2013b, 2013c; Nicoletti et al. 1988a, b). For details see Table 8 and Fig. 6.

Naphthoquinones

2-hydroxy-3-(1,1-dimethylallyl)-1,4-naphthoquinone, **94**, was isolated from *C. andina*, *C. talcana* and *C. sessilis* (Khambay et al. 1999; Morello et al. 1995; Muñoz et al. 2013b), while 2-acetoxy-3-(1,1.dimethylallyl)-1,4-napthoquinone, **95**, was isolated from *C. andina*, *C. recta*, *C. paposana*, and *C. sessilis* (Chamy et al. 1995a; Morello et al. 1995). Also the compound dunnione, **96**, was isolated from *C. integrifolia*, *C. sessilis* and *C. talcana* (Ruedi and Eugster 1977; Morello et al. 1995; Muñoz et al. 2013b). For details see Table 9 and Fig. 7.

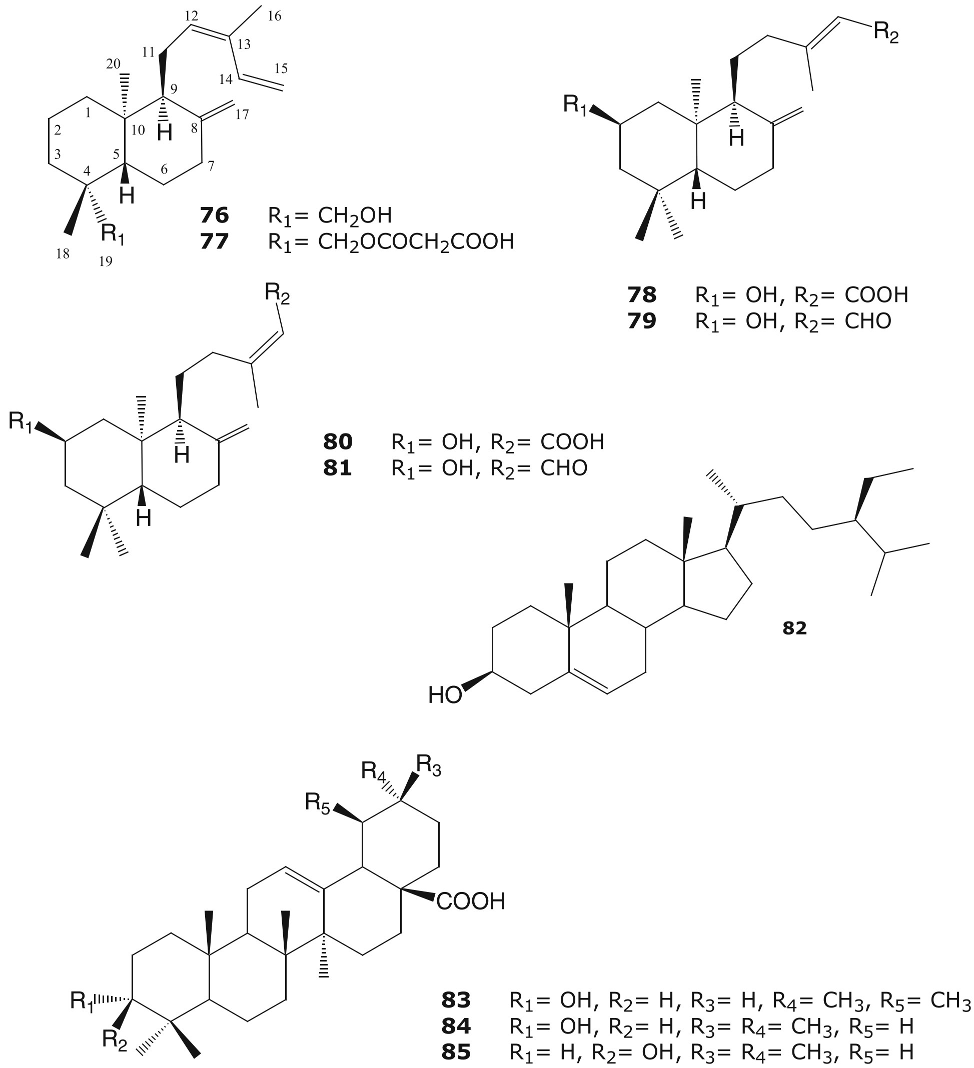


Fig. 5 Labdane diterpenes (**76–81**), sterols and triterpenes (**82–85**) from *Calceolaria*

Phenylpropanoids

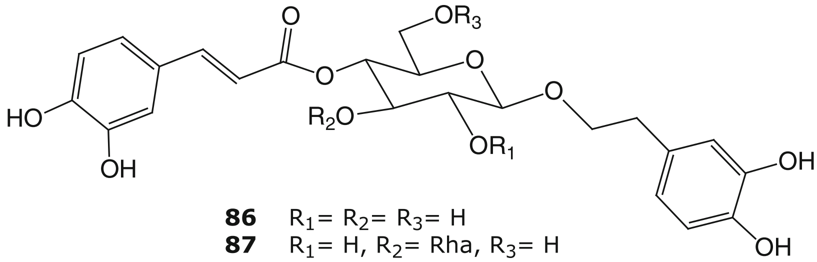
A total of five aromatic compounds have been isolated from *C. thyrsiflora*. Gallic acid, **97**, three 1-4-benzoxazin-3-ones, **98–100**, and one benzoxazolinone, **101** (Bravo et al. 2005). For details see Table 10 and Fig. 7.

Miscellaneous compounds

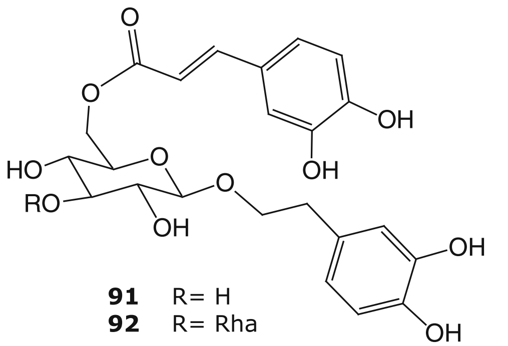
From *C. hypericina* was isolated halleridone, **102** (Nicoletti et al. 1986), a benzofurane derived ciclohexanone isolated previously from *Halleria lucida* (Messana et al. 1984) plant belonging to the Scrophulariaceae Family like the genus *Calceolaria*. As far as we know, any other molecule like this has been isolated from *Calceolaria*. For details see Table 11 and Fig. 7.

Flavonoids

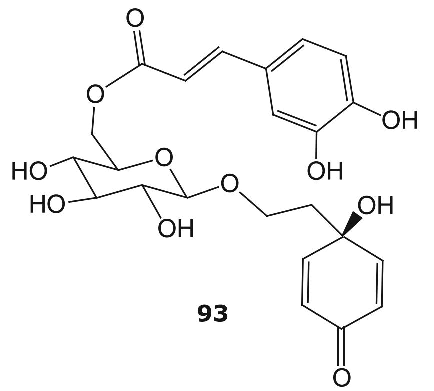
A total of fifteen flavonoids have been isolated from *Calceolaria*. Only a flavanol have been isolated from *C. hypericina*, **103** (Garbarino et al. 1993; Nicoletti et al. 1986), the rest of the flavonoids belongs to the flavone group, **105**, **107**, **113**, or the flavonol group, **104**, **106**, **108–112**, and presents O-methylation at



86 $R_1 = R_2 = R_3 = H$
87 $R_1 = H$, $R_2 = Rha$, $R_3 = H$
88 $R_1 = R_2 = H$, $R_3 = Xyl$
89 $R_1 = H$, $R_2 = Api$, $R_3 = H$
90 $R_1 = R_2 = H$, $R_3 = Rha$

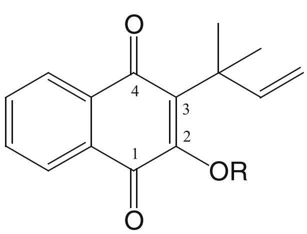


91 R= H
92 R= Rha

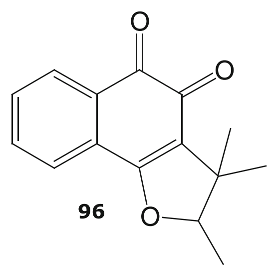


93

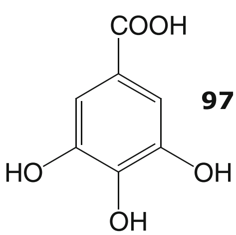
Fig. 6 Phenylpropanoid glycosides (**86**–**93**) from *Calceolaria*



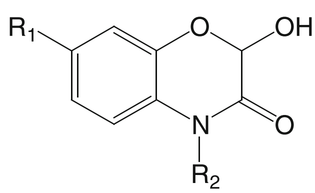
94 R= H
95 R= $COCH_3$



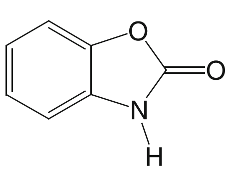
96



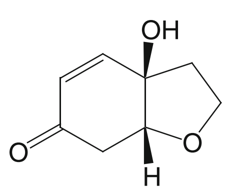
97



98 $R_1 = H$, $R_2 = OH$
99 $R_1 = R_2 = H$
100 $R_1 = OH$, $R_2 = H$

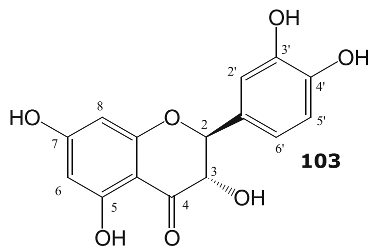


101

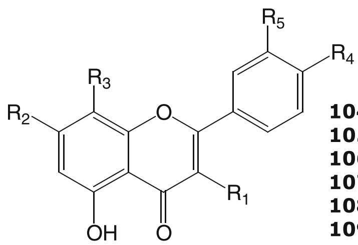


102

Fig. 7 Quinones (**94**–**96**) and Aromatic compounds (**97**–**101**) and halleridone (**102**) from *Calceolaria*



103



104 $R_1 = R_2 = OH, R_3 = H, R_4 = OCH_3, R_5 = H$
105 $R_1 = H, R_2 = R_3 = R_4 = OCH_3, R_5 = H$
106 $R_1 = OH, R_2 = R_3 = R_4 = OCH_3, R_5 = H$
107 $R_1 = H, R_2 = OH, R_3 = R_4 = OCH_3, R_5 = H$
108 $R_1 = R_2 = OH, R_3 = R_4 = OCH_3, R_5 = H$
109 $R_1 = OH, R_2 = R_3 = OCH_3, R_4 = OH, R_5 = OCH_3$
110 $R_1 = OH, R_2 = OCH_3, R_3 = H, R_4 = OH, R_5 = H$
111 $R_1 = R_2 = OH, R_3 = H, R_4 = OCH_3, R_5 = H$
112 $R_1 = OH, R_2 = OCH_3, R_3 = H, R_4 = OCH_3, R_5 = H$
113 $R_1 = H, R_2 = OH, R_3 = H, R_4 = OCH_3, R_5 = H$
114 $R_1 = OCH_3, R_2 = OH, R_3 = OCH_3, R_4 = OH, R_5 = OCH_3$
115 $R_1 = OCH_3, R_2 = OH, R_3 = H, R_4 = R_5 = OH$
116 $R_1 = OCH_3, R_2 = OH, R_3 = H, R_4 = OH, R_5 = OCH_3$
117 $R_1 = OCH_3, R_2 = OH, R_3 = H, R_4 = OH, R_5 = H$

Fig. 8 Flavonoids (**103–117**) from *Calceolaria*

position 3, **114–117**. The flavonoids isolated from *Calceolaria* are primary excreted by glandular organs (Wollenweber et al. 1989). For details see Table 11 and Fig. 8.

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References

Anderson S (2006) On the phylogeny of the genus *Calceolaria* (Calceolariaceae) as inferred from ITS and plastid *matK* sequences. Taxon 55(1):125–137

Bravo HR, Copaja SV, Figueroa-Duarte S, Lamborot M, San Martin J (2005) 1,4-Benzoxazin-3-one, 2-benzoxazolinone and Gallic acid from *Calceolaria thyrsiflora* Graham and their antibacterial activity. Z Naturforsch C 60(5/6): 389–393

Calderón JS, Cespedes CL, Rosas R, Gomez-Garibay F, Salazar JR, Lina L, Aranda E, Kubo I (2001) Acetylcholinesterase and insect growth inhibitory activities of *Gutierrezia microcephala* on fall armyworm *Spodoptera frugiperda* J. E. Smith. Z. Naturforschung 56c: 382–394

Cespedes CL, Avila JG, Marin JC, Dominguez M, Torres P, Aranda E (2006) Natural compounds as antioxidant and molting inhibitors can play a role as a model for search of new botanical pesticides. In: Rai M, Carpinella MC (eds) Naturally occurring bioactive compounds. Advances in Phytomedicine Series, vol 3. Elsevier, The Netherlands, pp 1–27

Cespedes CL, Muñoz E, Lamilla L, Molina SF, Alarcon J (2013) Insect growth regulatory, molting disruption and insecticidal activity of *Calceolaria talcana* (Calceolariaceae: Scrophulariaceae) and *Condalia microphylla* Cav. (Rhamnaceae). Chapter 15, In: Cespedes CL, Sampietro DA, Seigler DS, Rai MK. Natural antioxidants and biocides from wild medicinal plants. Cabi Publishing, Wallingford, UK

Chamy MC, Piovano M, Gambaro V, Garbarino JA, Nicoletti M (1987) Dehydroabietane diterpenoids from *Calceolaria ascendens*. Phytochemistry 26(6):1763–1765

Chamy MC, Piovano M, Garbarino JA, Gambaro V, Miranda C (1989) Diterpenoids from *Calceolaria* species. Part 3. Foliosate, a bis-diterpene and 9-*epi*-*ent*-7,15-isopimaradiene-derivatives from *Calceolaria foliosa*. Phytochemistry 28(2):571–574

Chamy MC, Piovano M, Garbarino JA, Miranda C, Gambaro V (1990) Diterpenoids from *Calceolaria* species. Part 5. Diterpenes from *Calceolaria lepida*. Phytochemistry 29(9):2943–2946

Chamy MC, Piovano M, Garbarino JA, Miranda C, Gambaro V, Rodriguez ML, Ruiz-Perez C, Brito I (1991a) Diterpenoids from *Calceolaria* species. Part 8. Diterpenoids from *Calceolaria thyrsiflora*. Phytochemistry 30(2):589–592

Chamy MC, Piovano M, Garbarino JA, Gambaro V (1991b) Diterpenoids from *Caleolaria* species. Part 10. Diterpenes from *Calceolaria polifolia*. Phytochemistry 30(10): 3365–3368

Chamy MC, Piovano M, Garbarino JA (1992) Diterpenoids from *Calceolaria* species. Part 11. Diterpenoids from *Calceolaria purpurea*. Phytochemistry 31(12):4233–4235

Chamy MC, Piovano M, Garbarino JA, Pascard C, Cesario M (1993a) Endoperoxide diterpenes from *Calceolaria purpurea*. Phytochemistry 34(4):1103–1106

Chamy MC, Jimenez I, Piovano M, Garbarino JA, Didyk B (1993b) Diterpenoids of *Calceolaria* species. Secondary metabolites from *Calceolaria sessilis*. Bol Soc Chil Quim 38(3):187–190

Chamy MC, Piovano M, Espana MI, Vargas L, Garbarino JA (1995a) Secondary metabolites from two species of *Calceolaria*: *Calceolaria recta* and *C. paposana*. Bol Soc Chil Quim 40(3):237–239

Chamy MC, Piovano M, Garbarino JA, Chaparro A (1995b) Diterpenoids from *Calceolaria hypericina*. Phytochemistry 40(4):1209–1212

Chamy MC, Piovano M, Garbarino JA, Vargas C (1995c) Diterpenoids from *Calceolaria dentata*. Phytochemistry 40(6):1751–1754

Chamy MC, Piovano M, Garbarino JA, Amestica MP (1998a) Diterpenoids from *Calceolaria glandulifera*. Phytochemistry 49(8):2595–2597

Chamy MC, Garbarino JA, Piovano M, Hernandez C (1998b) Diterpenoids from *Calceolaria* species: part 18 Diterpenoids from *Calceolaria pseudoglandulosa*. Bol Soc Chi Quim 43(2):241–245

Chamy MC, Piovano M, Garbarino JA, Mendoza J (2001) Diterpenoids from *Calceolaria glabrata*. Bol Soc Chil Quim 46(2):223–225

Chamy MC, Piovano M, Garbarino JA, Espinoza L (2006) Diterpenoids from *Calceolaria paralia*. J Chil Chem Soc 51(1):779–780

Chamy MC, Piovano M, Garbarino JA (2007) Diterpenoids from *Calceolaria alba*. Nat Prod Res 21(2):141–148

Coll J, Tandron YA (2007) *neo*-Clerodane diterpenoids from *Ajuga*: structural elucidation and biological activity. Phytochem Rev 7:25–49

Di Fabio A, Bruni A, Poli F, Garbarino JA, Chamy MC, Piovano M, Nicoletti M (1995) The distribution of phenylpropanoid glycosides in Chilean *Calceolaria* spp. Biochem Syst Ecol 23(2):179–182

Ehrhart Ch (2000) Die gattung *Calceolaria* (Scrophulariaceae) in Chile. Bibliotheca Botanica H. 153:1–283

Ehrhart Ch (2005) The Chilean *Calceolaria integrifolia* s.l. species complex (Scrophulariaceae). Syst Bot 30:383–411

Falcao DQ, Costa ER, Alviano DS, Alviano CS, Kuster RM, Menezes FS (2006) Atividade antioxidante e antimicrobiana de *Calceolaria chelidonioides* Humb. Bonpl Kunth Br J Pharmacog 16(1):73–76

Feeny PP (1976) Plant apparency and chemical defense. In: Wallace JW, Mansell RL (eds) Biochemical interactions between plants and insects. Plenum Press, New York, pp 1–40

Fraga BM, Gonzalez P, Hernandez MG, Chamy MC, Garbarino JA (1998) The microbiological transformation of a 9-*epi-ent*-pimaradiene diterpene by *Gibberella fujikuroi*. Phytochemistry 47(2):212–215

Garbarino JA, Molinari A (1990a) Diterpenoids from *Calceolaria* species. Part 6. Diterpenes from *Calceolaria latifolia*. Phytochemistry 29(9):3037–3039

Garbarino JA, Molinari A (1990b) Diterpenoids from *Calceolaria* species. Part 7. A stemarane diterpene from *Calceolaria kingii*. Phytochemistry 29(9):3040–3041

Garbarino JA, Molinari A (1992) Diterpenoids from *Calceolaria* species. 9. Labdane diterpenes from *Calceolaria densifolia*. J Nat Prod 55(6):744–747

Garbarino JA, Molinari A (1993) A labdane diterpene from *Calceolaria corymbosa*. J Nat Prod 56(4):624–626

Garbarino JA, Chamy MC, Guiorguiadez ME (1993) Diterpene and flavanones from *Calceolaria hypericina*. Fitoterapia 64(1):94

Garbarino JA, Chamy MC, Piovano M (2000) Chemistry of the *Calceolaria* genus. Structural and biological aspects. Molecules 5(3):302–303

Garbarino JA, Fraga BM, Hernandez MG, Chamy MC, Piovano M (2001) Chemistry and biotransformations in the *Scrophulariaceae* family. Pure Appl Chem 73(3):579–582

Garbarino JA, Chamy MC, Piovano M, Espinoza L, Belmonte E (2004) Diterpenoids from *Calceolaria inamoena*. Phytochemistry 65(7):903–908

Garbarino JA, Chamy MC, Piovano M, Espinoza L (2006) Diterpenoids from *Calceolaria filicaulis ssp luxurians*. J Chil Chem Soc 51(4):1057–1058

Garbarino JA, Piovano M, Chamy MC, Espinoza L (2007) Diterpenoids from *Calceolaria* species. New diterpenoids from *Calceolaria polifolia*. Nat Prod Res 21(2):135–140

González JA, Estevez-Braun A (1998) Effect of *E*-chalcone on potato-cyst nematodes (*Globodera pallida* and *G. rostochiensis*). J Agric Food Chem 46:1163–1165

Hanson JR (2009) Diterpenoids. Nat Prod Rep 26:1156–1171

Harborne J, Baxter H (2001) Chemical dictionary of economic plants. Wiley, Chichester 236 pp

Isman MB (2006) Botanical insecticides, deterrents, and repellents in modern agriculture and an increasingly regulated world. Annu Rev Entomol 51:45–66

Isman MB, Akthar Y (2007) Plant natural products as a source for developing environmentally acceptable insecticides. In: Ishaaya I, Nauen R, Horowitz AR (eds) Insecticides design using advanced technologies. Springer, Berlin, pp 235–248

Kakuta H, Seki T, Hashidoko Y, Mizutani J (1992) Ent-kaurenic acid and its related compounds from glandular trichome exudate and leaf extracts of *Polymnia sonchifolia*. Biosci Biotechnol Biochem 56:1562–1564

Khambay BPS, Batty D, Cahill M, Denholm I, Mead-Briggs M, Vinall S, Niemeyer HM, Simmonds MSJ (1999) Isolation, characterization, and biological activity of naphthoquinones from *Calceolaria andina* L. J Agric Food Chem 47(2):770–775

Koul O, Walia S (2009) Comparing impacts of plant extracts and pure allelochemicals and implications for pest control. CAB Reviews: *perspectives in Agriculture*, *Veterinary Science*, *Nutrition and Natural Resources*. CAB Intern 4(049)30

Leonelli F, Latini V, Trombetta A, Bartoli G, Ceccacci F, La Bella A, Sferrazza A, Lamba D, Migneco LM, Bettolo RM (2012) Regio- and diastereoselective synthesis and X-ray structure determination of (+)-2-deoxyoryzalexin S from (+)-podocarpic acid. Structural nonidentity with its nominal natural isolated enantiomer. J Nat Prod 75(11): 1944–1950

Mercado MI, Coll MV, Grau A, Catalan CAN (2010) New acyclic diterpenic acids from Yacon (*Smallanthus sonchifolius*) leaves. Nat Prod Commun 5:1721–1726

Messana I, Sperandei M, Multari G, Galeffi C, Bettolo GBM (1984) A cyclohexadienone and a cyclohexenone from *Halleria lucida*. Phytochemistry 23(11):2617–2619

Molau U (1988) Scrophulariaceae—Part I. Calceolarieae. Flora Neotropica 47:1–326

Molau U (2003) Two new species of *Calceolaria* (Scrophulariaceae) from the tropical Andes. Novon 13:101–103

Morello A, Pavani M, Garbarino JA, Chamy MC, Frey C, Mancilla J, Guerrero A, Repetto Y, Ferreira J (1995) Effects and mode of action of 1,4-naphthoquinones isolated from *Calceolaria sessilis* on tumoral cells and *Trypanosoma* parasites. Comp Biochem Physiol C: Pharmacol Toxicol Endocrinol 112C(2):119–128

Mullin ChA, Gonzalez-Coloma A, Gutierrez C, Reina M, Eichenseer H, Hollister B, Chyb S (1997) Antifeedant effects of some novel terpenoids on chrysomelidae Beetles: comparisons with alkaloids on an alkaloid-adapted and nonadapted species. J Chem Ecol 23:1851–1866

Muñoz E, Lamilla C, Marin JC, Alarcon J, Cespedes CL (2013a) Antifeedant, insect growth regulatory and insecticidal effects of *Calceolaria talcana* (*Calceolariaceae*) on *Drosophila melanogaster* and *Spodoptera frugiperda*. Ind Crop Prod 42:137–144

Muñoz E, Escalona D, Salazar JR, Alarcon J, Cespedes CL (2013b) Insect growth regulatory effects by diterpenes from *Calceolaria talcana* Grau & Ehrhart (Calceolariaceae: Scrophulariaceae) against *Spodoptera frugiperda* and *Drosophila melanogaster*. Ind Crop Prod 45:283–292

Muñoz E, Avila JG, Alarcon J, Kubo I, Cespedes CL (2013c) Tyrosinase inhibitors from *Calceolaria integrifolia* s.l.: *Calceolaria talcana* aerial parts. J Agric Food Chem (in press)

Nicoletti M, Galeffi C, Messana I, Garbarino JA, Gambaro V, Nyandat E, Marini-Bettolo GB (1986) New phenylpropanoid glucosides from *Calceolaria hypericina*. Gazz Chim Ital 116(8):431–433

Nicoletti M, Galeffi C, Messana I, Marini-Bettolo GB, Garbarino JA, Gambaro V (1988a) Studies in *Calceolaria* genus. Part 2. Phenylpropanoid glycosides from *Calceolaria hypericina*. Phytochemistry 27(2):639–641

Nicoletti M, Galeffi C, Multari G, Garbarino JA, Gambaro V (1988b) Studies on the genus *Calceolaria*. Part 3. Polar constituents of *Calceolaria ascendens*. Planta Med 54(4):347–348

Ortego F, Rodriguez B, Castañera P (1995) Effects of *neo*-clerodane diterpenes from *Teucrium* on feeding behavior of Colorado potato beetle larvae. J Chem Ecol 21:1375–1386

Piovano M, Gambaro V, Chamy MC, Garbarino JA, Nicoletti M, Guilhem J, Pascard C (1988) Diterpenoids from *Calceolaria* species. Part 2. 18-Malonyloxy-9-*epi*-*ent*-isopimarol, a diterpene from *Calceolaria glandulosa*. Phytochemistry 27(4):1145–1149

Piovano M, Chamy MC, Garbarino JA, Gambaro V (1989) Diterpenoids from *Calceolaria* species. Part 4. 9-*epi*-*ent*-7,15-Isopimaradiene derivatives from *Calceolaria glandulosa*. Phytochemistry 28(10):2844–2845

Rhoades DF, Cates RG (1976) Toward a general theory of plant antiherbivore chemistry. Recent Adv Phytochemistry 10:168–213

Ruedi P, Eugster CH (1977) Isolation of (-)-dunnione from *Calceolaria integrifolia* Murr. (*Scrophulariaceae*). Helv Chim Acta 60(3):945–947

Silva P, Chamy MC, Piovano M, Garbarino JA (1993) Diterpenoids from *Calceolaria* species. 14. Diterpenoids from *Calceolaria petioalaris*. Phytochemistry 34(2):449–451

Simmonds MSJ, Blaney WM, Esquivel B, Rodriguez-Hahn L (1996) Effect of clerodane-type diterpenoids isolated from *Salvia* spp. on the feeding behaviour of *Spodoptera littoralis*. Pestic Sci 47:17–23

Woldemichael GM, Waechter G, Singh MP, Maiese WM, Timmermann BN (2003) Antibacterial diterpenes from *Calceolaria pinifolia*. J Nat Prod 66(2):242–246

Wollenweber E, Mann K, Roitman JN (1989) Flavonoid aglycons excreted by three *Calceolaria* species. Phytochemistry 28(8):2213–2214

Xie Y, Isman MB, Feng Y, Wong A (1993) Diterpene resin acids: major active principles in tall oil against variegated cutworm, *Peridroma saucia* (Lepidoptera: Noctuidae). J Chem Ecol 19:1075–1084