

Progress in the Chemistry of Organic Natural Products

A. Douglas Kinghorn · Heinz Falk
Simon Gibbons · Jun'ichi Kobayashi
Yoshinori Asakawa · Ji-Kai Liu *Editors*

113

Progress in the Chemistry of Organic Natural Products

 Springer

Progress in the Chemistry of Organic Natural Products

Volume 113

Series Editors

A. Douglas Kinghorn , College of Pharmacy, The Ohio State University, Columbus, OH, USA

Heinz Falk , Institute of Organic Chemistry, Johannes Kepler University, Linz, Austria

Simon Gibbons , School of Pharmacy, University of East Anglia, Norwich, UK
Jun'ichi Kobayashi, Graduate School of Pharmaceutical Sciences, Hokkaido University, Sapporo, Japan

Yoshinori Asakawa , Faculty of Pharmaceutical Sciences, Tokushima Bunri University, Tokushima, Japan

Ji-Kai Liu , School of Pharmaceutical Sciences, South-Central University for Nationalities, Wuhan, China

Advisory Editors

Giovanni Appendino , Department of Pharmaceutical Sciences, University of Eastern Piedmont, Novara, Italy

Roberto G. S. Berlinck , Instituto de Química de São Carlos, Universidade de São Paulo, São Carlos, Brazil

Verena M. Dirsch , Department of Pharmacognosy, University of Vienna, Vienna, Austria

Agnieszka Ludwiczuk , Department of Pharmacognosy, Medical University of Lublin, Lublin, Poland

Rachel Mata , Facultad de Química, Universidad Nacional Autónoma de México, Mexico City, Mexico

Nicholas H. Oberlies , Department of Chemistry and Biochemistry, University of North Carolina at Greensboro, Greensboro, NC, USA

Deniz Tasdemir , Marine Natural Products Chemistry, GEOMAR Helmholtz Centre for Ocean Research Kiel, Kiel, Germany

Dirk Trauner , Department of Chemistry, New York University, New York, NY, USA

Alvaro Viljoen , Department of Pharmaceutical Sciences, Tshwane University of Technology, Pretoria, South Africa

Yang Ye , State Key Laboratory of Drug Research and Natural Products Chemistry Department, Shanghai Institute of Materia Medica, Shanghai, China

The volumes of this classic series, now referred to simply as “Zechmeister” after its founder, Laszlo Zechmeister, have appeared under the Springer Imprint ever since the series’ inauguration in 1938. It is therefore not really surprising to find out that the list of contributing authors, who were awarded a Nobel Prize, is quite long: Kurt Alder, Derek H.R. Barton, George Wells Beadle, Dorothy Crowfoot-Hodgkin, Otto Diels, Hans von Euler-Chelpin, Paul Karrer, Luis Federico Leloir, Linus Pauling, Vladimir Prelog, with Walter Norman Haworth and Adolf F.J. Butenandt serving as members of the editorial board.

The volumes contain contributions on various topics related to the origin, distribution, chemistry, synthesis, biochemistry, function or use of various classes of naturally occurring substances ranging from small molecules to biopolymers.

Each contribution is written by a recognized authority in the field and provides a comprehensive and up-to-date review of the topic in question. Addressed to biologists, technologists, and chemists alike, the series can be used by the expert as a source of information and literature citations and by the non-expert as a means of orientation in a rapidly developing discipline.

All contributions are listed in PubMed.

More information about this series at <http://www.springer.com/series/10169>

A. Douglas Kinghorn • Heinz Falk
Simon Gibbons • Jun'ichi Kobayashi
Yoshinori Asakawa • Ji-Kai Liu
Editors

Progress in the Chemistry of Organic Natural Products 113

 Springer

Editors

A. Douglas Kinghorn 
College of Pharmacy
Ohio State University
Columbus, OH, USA

Simon Gibbons 
School of Pharmacy
University of East Anglia
Norwich, UK

Yoshinori Asakawa 
Faculty of Pharmaceutical Sciences
Tokushima Bunri University
Tokushima, Japan

Heinz Falk 
Institute of Organic Chemistry
Johannes Kepler University
Linz, Oberösterreich, Austria

Jun'ichi Kobayashi
Graduate School of Pharmaceutical Science
Hokkaido University
Fukuoka, Japan

Ji-Kai Liu 
School of Pharmaceutical Sciences
South Central University for Nationality
Wuhan, China

ISSN 2191-7043

ISSN 2192-4309 (electronic)

Progress in the Chemistry of Organic Natural Products

ISBN 978-3-030-53027-3

ISBN 978-3-030-53028-0 (eBook)

<https://doi.org/10.1007/978-3-030-53028-0>

© The Editor(s) (if applicable) and The Author(s), under exclusive license to Springer Nature Switzerland AG 2020

This work is subject to copyright. All rights are solely and exclusively licensed by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.

The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

The publisher, the authors, and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, expressed or implied, with respect to the material contained herein or for any errors or omissions that may have been made. The publisher remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Contents

Chemical Constituents of <i>Ligularia</i> Species (Asteraceae) and Their Diversity in East Asia	1
Motoo Tori and Chiaki Kuroda	

Chemical Constituents of *Ligularia* Species (Asteraceae) and Their Diversity in East Asia



Motoo Tori and Chiaki Kuroda

Contents

1	Introduction.....	3
2	Compounds.....	7
3	<i>Ligularia</i> Species.....	59
3.1	<i>Ligularia virgaurea</i> (Maximowicz) Mattfeld ex Rehder & Kobuski.....	59
3.2	<i>Ligularia dentata</i> (A. Gray) H. Hara.....	79
3.3	<i>Ligularia japonica</i> (Thunberg) Lessing.....	82
3.4	<i>Ligularia hookeri</i> (C. B. Clarke) Handel-Mazzetti.....	83
3.5	<i>Ligularia atroviolacea</i> (Franchet) Handel-Mazzetti.....	84
3.6	<i>Ligularia kanaitzensis</i> (Franchet) Handel-Mazzetti.....	86
3.7	<i>Ligularia intermedia</i> Nakai.....	92
3.8	<i>Ligularia vellerea</i> (Franchet) Handel-Mazzetti.....	96
3.9	<i>Ligularia wilsoniana</i> (Hemsley) Greenman.....	99
3.10	<i>Ligularia melanothyrsa</i> Handel-Mazzetti.....	101
3.11	<i>Ligularia lapathifolia</i> (Franchet) Handel-Mazzetti.....	107
3.12	<i>Ligularia macrophylla</i> (Ledebour) de Candolle.....	109
3.13	<i>Ligularia knorringiana</i> Pojarkova (= <i>L. thyrsoides</i>) and <i>Ligularia narynensis</i> (C. Winkler) O. Fedtschenko & B. Fedtschenko.....	119
3.14	<i>Ligularia rumicifolia</i> S. W. Liu.....	126
3.15	<i>Ligularia songarica</i> (Fischer) Y. Ling.....	130
3.16	<i>Ligularia stenocephala</i> (Maximowicz) Matsumura & Koidzumi.....	135
3.17	<i>Ligularia alticola</i> Voroschilov.....	137
3.18	<i>Ligularia brassicoides</i> Handel-Mazzetti.....	140

M. Tori (✉)

Faculty of Pharmaceutical Sciences, Tokushima Bunri University,
Yamashiro-cho, Tokushima, Japan

e-mail: tori@ph.bunri-u.ac.jp

C. Kuroda

Department of Chemistry, Rikkyo University, Tokyo, Japan

e-mail: chkkuroda@rikkyo.ac.jp

© The Editor(s) (if applicable) and The Author(s), under exclusive license to
Springer Nature Switzerland AG 2020

A. D. Kinghorn, H. Falk, S. Gibbons, J. Kobayashi, Y. Asakawa, J.-K. Liu (eds.),
Progress in the Chemistry of Organic Natural Products 113, Progress
in the Chemistry of Organic Natural Products 113,

https://doi.org/10.1007/978-3-030-53028-0_1

3.19	<i>Ligularia caloxantha</i> (Diels) Handel-Mazzetti.....	143
3.20	<i>Ligularia przewalskii</i> (Maximowicz) Diels.....	145
3.21	<i>Ligularia sagitta</i> (Maximowicz) Mattfeld ex Rehder & Kobuski.....	150
3.22	<i>Ligularia pleurocaulis</i> (Franchet) Handel-Mazzetti.....	156
3.23	<i>Ligularia fischeri</i> (Ledebour) Turczaninow, <i>Ligularia anoleuca</i> Handel-Mazzetti, and <i>Ligularia veitchiana</i> (Hemsley) Greenman.....	158
3.24	<i>Ligularia cyathiceps</i> Handel-Mazzetti.....	165
3.25	<i>Ligularia cymbulifera</i> (W. W. Smith) Handel-Mazzetti.....	167
3.26	<i>Ligularia dictyoneura</i> (Franchet) Handel-Mazzetti.....	169
3.27	<i>Ligularia duciformis</i> (C. Winkler) Handel-Mazzetti, <i>Ligularia konkalingensis</i> Handel-Mazzetti, <i>Ligularia nelumbifolia</i> (Bureau & Franchet) Handel-Mazzetti, and <i>Ligularia limprichtii</i> (Diels) Handel-Mazzetti.....	172
3.28	<i>Ligularia hodgsonii</i> J. D. Hooker.....	176
3.29	<i>Ligularia lamarum</i> (Diels) C. C. Chang and <i>Ligularia subspicata</i> (Bureau & Franchet) Handel-Mazzetti.....	179
3.30	<i>Ligularia lankongensis</i> (Franchet) Handel-Mazzetti.....	185
3.31	<i>Ligularia latihastata</i> (W. W. Smith) Handel-Mazzetti and <i>Ligularia villosa</i> (Handel-Mazzetti) S. W. Liu.....	186
3.32	<i>Ligularia villosa</i> Handel-Mazzetti.....	187
3.33	<i>Ligularia oligonema</i> Handel-Mazzetti.....	189
3.34	<i>Ligularia tongolensis</i> (Franchet) Handel-Mazzetti.....	190
3.35	<i>Ligularia tsangchanensis</i> (Franchet) Handel-Mazzetti.....	191
3.36	<i>Ligularia yunnanensis</i> (Franchet) C. C. Chang.....	193
3.37	Hybrid <i>Ligularia</i> Species.....	194
3.38	Further <i>Ligularia</i> Species I: <i>altaica</i> de Candolle, <i>L. dolichobotrys</i> Diels, <i>L. franchetiana</i> (H. Léveillé) Handel-Mazzetti, <i>L. persica</i> Boissier, <i>L. speciosa</i> Fischer et Meyer, and <i>L. thyrsoidea</i> (Ledebour) de Candolle.....	197
3.39	Further <i>Ligularia</i> Species II: <i>L. achyrotricha</i> (Diels) Y. Ling, <i>L. nanchuanica</i> S. W. Liu, <i>L. purdomii</i> (Turrill) Chittenden, <i>L. odontomanes</i> Handel-Mazzetti, <i>L. sibirica</i> (Linnaeus) Cassini, and <i>L. thomsonii</i> (C. B. Clarke) Pojarkova.....	199
3.40	Further <i>Ligularia</i> Species III: <i>L. angusta</i> (Nakai) Kitamura, <i>L. calthifolia</i> Maximowicz, <i>L. fauriei</i> (Franchet) Koidzumi, <i>L. hiberniflorum</i> (Makino) Kitamura, <i>L. kangtingensis</i> S. W. Liu, <i>L. lingiana</i> S. W. Liu, <i>L. myriocephala</i> Y. Ling ex S. W. Liu, <i>L. platyglossa</i> (Franchet) Handel-Mazzetti, and <i>L. schmidtii</i> (Maximowicz) Makino.....	201
3.41	Further <i>Ligularia</i> Species IV: <i>L. brachyphylla</i> Handel-Mazzetti (= <i>L. latihastata</i>), <i>L. calthifolia</i> (Maximowicz) Diels, <i>L. clivorum</i> Maximowicz (= <i>L. dentata</i>), <i>L. sachalinensis</i> Nakai, <i>L. tangutica</i> (Maximowicz) Bergmans, <i>L. trichocephala</i> (Maximowicz) Matsumura et Koidzumi, and <i>L. vorobierii</i> Worosh.....	204
4	Genetic Analyses.....	206
5	Synthesis Aspects.....	209
5.1	Synthesis of Ligularol (= Petasalbin), Ligularone, and Related Compounds.....	210
5.2	Synthesis of Tetrahydroligularenolide Using Biogenetic Type Rearrangement.....	211
5.3	Synthesis of Furanoeremophilan-15,6-olide.....	212
5.4	Synthesis of Isopetasol.....	213
5.5	Synthesis of Eremophila-9,11-dien-8-one, Dehydrofukinone, and Furanoeremophilanes.....	213
5.6	Synthesis of Eremoligenol and Eremophilone.....	214
5.7	Synthesis of Eremophiladienes.....	214
5.8	Synthesis of Fukinone and Related Compounds.....	215
5.9	Synthesis of Eremophiladiene.....	215

5.10	Synthesis of 6-Hydroxyeurypsins.....	216
5.11	Synthesis of 3 β -Angeloyloxyfuraneremophilane.....	217
5.12	Synthesis of Ligularone and Isoligularone.....	218
5.13	Synthesis of (-)-(<i>R</i>)-Ligularenone and (-)-(<i>R</i>)-PF1092C.....	219
5.14	Synthesis of Nootkatone.....	220
5.15	Synthesis of Cacalol.....	220
5.16	Synthesis of Noreremophilanes.....	221
5.17	Synthesis of Bakkane-type Sesquiterpenoids.....	223
5.18	Synthesis of Bisabolane-type Sesquiterpenoids.....	226
5.19	Synthesis of Nelumol A.....	228
6	Biological Activities.....	229
	References.....	230

1 Introduction

To understand diversification of secondary metabolites in plants is a major theme in natural product chemistry. The genus *Ligularia* Cass., belonging to the family Asteraceae tribe Senecioneae, is highly diversified in the Hengduan Mountains area of China. More than a hundred species are recorded in the “Flora of China” [1, 2] and the evolution and diversification is considered to be still ongoing [3]. *Ligularia* species in this area occupy a great variety of habitats from streams to alpine meadows, ranging from 1000 to 5000 m in elevation [2]. Thus, *Ligularia* species in this domain provide natural products scientists with very interesting materials for the study of the diversity of their secondary metabolite profiles [4, 5].

Ligularia species have been studied with respect to secondary metabolites for a long time, and many sesquiterpenoids have been isolated from them [6, 7]. It is well known that *Ligularia* is a major source of eremophilane sesquiterpenoids, which have also been isolated from other genera in the family Senecioneae, including *Parasenecio* (*Cacalia*), *Senecio*, and *Petasites* [8–10]. Certain derivatives, such as rearranged- or *seco*-compounds as well as dimers, have been recorded. Among various eremophilane sesquiterpenoids, furanoeremophilanes and eremophilan-12,8-olides constitute the major class. During the 1960s and the 1970s, many furanoeremophilanes were isolated from roots of Japanese *Ligularia* species by the groups of Minato and Takahashi [11, 12]. The structure of ligularol (= petasalbin) (**161**), the most commonly isolated furanoeremophilane, was determined by Minato’s group. During this same period, Bohlmann’s group also obtained a large number of eremophilanes and related compounds from European *Ligularia* species [13]. Many eremophilanes and other types of sesquiterpenoids have been isolated and characterized from a number of other species in the family Senecioneae as well. Following these pioneering reports, especially from around 2000 and over the last two decades, an abundance of related compounds has been obtained from Chinese *Ligularia* species [14].

Over the last 20 years, the individual groups of the current authors have studied the diversity of compounds present in the roots of *Ligularia* species growing in the in northwestern Yunnan Province, western Sichuan Province, and, in part, in southern Qinghai and Gansu Provinces of (Hengduan Mountains area) (Plates 1 and 2). In



Plate 1 A typical collection site in Aba, Sichuan Province, China



Plate 2 A typical collection site in Shangri-La, Yunnan Province, China

our studies on the diversity of *Ligularia* species, root phytochemicals and evolutionary neutral DNA sequences were chosen as indices, in addition to morphological identification and ecological observation in the field. As neutral DNA samples, internal transcribed spacer (ITS1-5.8S-ITS2) sequences were analyzed in the ribosomal RNA gene, and, for chemical investigations, EtOH or AcOEt extracts of dried roots were selected. The root phytochemical profiles and the ITS sequences were examined as independent parameters to one another. To date, many sesquiterpenoids, euparin-type benzofurans, and phenylpropanoids have been isolated. Eremophilanes, particularly furanoeremophilanes and eremophilan-12,8-olides,

were the major class found among the sesquiterpenoids, although bisabolanes, bakkanes, and other types of compounds were also obtained.

In this contribution are described phytochemical studies carried out by our groups mainly from 2000 onward, inclusive of our results on the diversity in secondary metabolites of *Ligularia* growing in the Hengduan Mountains area, focusing on eremophilane sesquiterpenoids and other metabolites. The present contribution deals with 1049 compounds, not only those that were new when first characterized but also known analogs, as isolated from *Ligularia* species. Genetic analyses, synthesis aspects, and biological activities will also be discussed.

In our own work, plants were collected from selected locations in Yunnan, Sichuan, Qinghai, and Gansu Provinces, and Chongqing City, China. They were identified by Dr. Xun Gong, Kunming Institute of Botany, China. The DNA (ITS1-5.8S-ITS2) sequences were also investigated, as carried out by Prof. Ryo Hanai, Rikkyo University, Tokyo Japan (see Sect. 4). Plant collection expeditions have been conducted since the summer of 2000.

In this contribution, the plant names and their constituents will be tabulated for each species, with the year of collection included if mentioned in the literature. In the case of our own work, the first four digits provide the year of collection and the latter two or three digits are specimen numbers for that year. Collection locations and their elevation (m) are indicated, if known. For our own work, the county and city/province are given (C = Chongqing, G = Gansu, Q = Qinghai, S = Sichuan, Y = Yunnan; other provinces are spelled out in full). Chemical constituents were grouped roughly into eight categories: (1) bicyclic eremophilanes (without ring C and *nor*-eremophilanes); (2) 10*H* tricyclic eremophilanes (furans and lactones (12,8-olides) with a hydrogen at C-10); (3) 10-OH tricyclic eremophilanes (furans and lactones with a hydroxy group at C-10); (4) tricyclic eremophilanes with 1(10)-ene, 9-ene, and 1,10-epoxide; (5) the cacalol group; (6) bakkanes and other sesquiterpenoids; (7) aromatics; and (8) others. Mono-, di-, and triterpenes are grouped within the “others” category. The groups have been slightly changed for each table depending on the species. The major constituents are underlined, if they were described. In this work, alkaloids and sterols are not acquired.

Furanoeremophilanes can be detected by TLC using Ehrlich’s reagent. Thus, their trisubstituted furan ring reacts with *p*-dimethylaminobenzaldehyde in the presence of HCl to show a yellow, pink, purple, or blue color, depending on the nature of the substituent [15]. Examples are included in Plate 3. Preliminary TLC experiments may be conducted in a facile manner, so that diversity in chemical composition can be indicated without the isolation of each compound (Sect. 3.1). However, because a TLC experiment does not yield any structural detail, conventional phytochemical analysis investigations, involving isolation and structure determination, were also carried out.

Total ion chromatograms (TIC) of extracts were measured in LCMS analysis to compare chemical constituents. Typical TICs are shown in Plate 4. For example, these represent five chemotypes found in *L. virgaurea*. Although the V, C, N, and H types are more or less continuous, typical samples show characteristic peaks corresponding to their representative compounds. By obtaining their LC-MS profiles, it

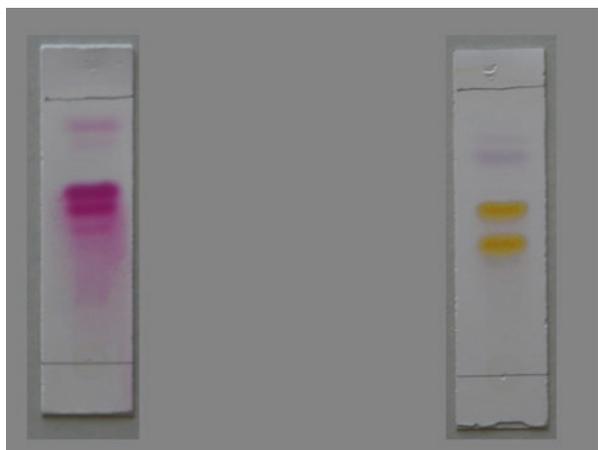


Plate 3 Typical TLC patterns visualized by spraying Ehrlich's reagent. Left: the L type of *L. virgaurea*; the largest pink spot is ligularol (**160**). Right: the V type of *L. virgaurea*; the two yellow spots are virgaurenones A (**273**) and B (**272**)

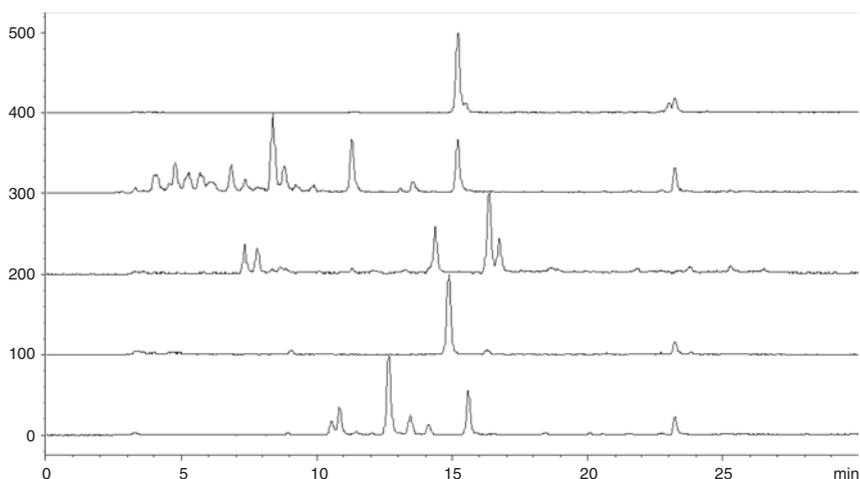


Plate 4 Typical TIC profiles of *L. virgaurea*; from top to bottom: the L, V, C, H, and N types

is relatively facile to compare chemical constituents of each sample and to see if intraspecific similarities are present or not.

The following conditions for LC-MS measurement were used: HPLC 1100 system with a DAD detector and an automatic sample injector (column, 5C18-MS-II (COSMOSIL) 4.6 × 150 mm; solvent, MeOH-H₂O gradient; flow rate, 0.5 cm³/min). An Agilent 1100 series LC/MSD mass spectrometer was employed with an atmospheric pressure chemical ionization interface (APCI) (capillary voltage, 3.5 kV; corona current, 4 μA; capillary exit voltage (fragmentor), 90 V; drying temperature, 330°C; drying flow, 9 dm³/min; nebulizer pressure, 50 psig; positive ion mode; scan range, *m/z* 100–1000 amu).

2 Compounds

Most compounds reported from *Ligularia* spp. are sesquiterpenoids belonging to the eremophilane, bakkane, oplopane, bisabolane, and eudesmane types. Only minor amounts of germacrane, guaiane, aromadendrane, caryophyllane, valencane, and cadinane types are produced. Cacalol and its derivatives have been categorized within a separate cacalol group, in which the C-14 eremophilane methyl group is shifted to the C-6 position. There has been some confusion in compound numbering in the literature, particularly for the C-14 and C-15 methyl groups, and the numbering herein is that proposed by Connolly and Hill [16]. Plate 5 shows the major skeletons and their numbering as used in this contribution. The structures drawn show relative configurations, and absolute configurations are presented where they have been determined. When X-ray structural analysis has been used, this is also mentioned. Questionable structures that have been proposed are pointed out, as necessary. A total of 1049 compounds isolated from *Ligularia* spp. are listed in Table 1. The plant sourcing for each compound is also listed in this table along with appropriate references. Structures of compounds isolated from *Ligularia* spp. are shown in Figs. 1–72.

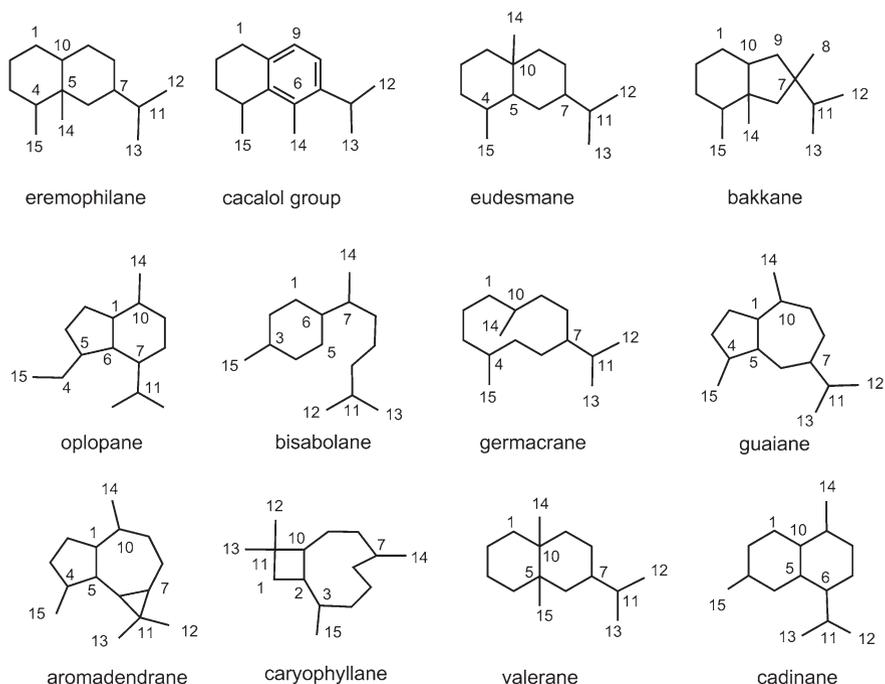


Plate 5 Skeletons of sesquiterpenoids isolated from *Ligularia* plants and their numbering

Table 1 Compounds isolated from *Ligularia*

Structure number	Name of compound	Plant source	Ref.	Comments
1		<i>L. cyathiceps</i>	[17]	
		<i>L. duciformis/L. cyathiceps</i>	[18]	
		<i>L. franchetiana</i>	[19]	
		<i>L. intermedia</i>	[20]	
		<i>L. kanaitzensis</i>	[21, 22]	
		<i>L. lamarum</i>	[23]	
		<i>L. subspicata</i>	[23, 24]	
		<i>L. tsangchanensis</i>	[25]	
		<i>L. vellerea</i>	[26]	
2		<i>L. virgaurea</i>	[27, 28]	
		<i>L. dictyoneura</i>	[29]	
		<i>L. fischeri</i>	[30]	
		<i>L. kanaitzensis</i>	[21, 22, 31]	
		<i>L. lamarum</i>	[23]	
		<i>L. longihastata</i>	[32]	
		<i>L. nelumbifolia/C. stenoglossum</i>	[33]	
3		<i>L. subspicata</i>	[23, 24, 34]	
		<i>L. tsangchanensis</i>	[35]	
		<i>L. dictyoneura</i>	[29]	
		<i>L. kanaitzensis</i>	[22]	
		<i>L. longihastata</i>	[32]	
4	Fukinone	<i>L. subspicata</i>	[23, 24]	
		<i>L. tsangchanensis</i>	[35]	
		<i>L. duciformis</i>	[36]	
		<i>L. fischeri</i>	[37]	
<i>L. kanaitzensis</i>		[21, 22, 31]		
<i>L. lamarum</i>		[23]		
<i>L. lamarum/L. subspicata</i>		[38]		
<i>L. melanothyrsa</i>		[21]		
<i>L. persica</i>		[39]		
<i>L. subspicata</i>		[23, 34]		
<i>L. subspicata/L. cyathiceps</i>	[38, 40]			
<i>L. vellerea</i>	[26]			
<i>L. virgaurea</i>	[27]			

(continued)

Table 1 (continued)

Structure number	Name of compound	Plant source	Ref.	Comments
5	Dehydrofukinone	<i>L. alticola</i>	[41]	
		<i>L. dictyoneura</i>	[29, 42]	
		<i>L. duciformis</i>	[36]	
		<i>L. fischeri</i>	[30]	
		<i>L. intermedia</i>	[20]	
		<i>L. kanaitzensis</i>	[22]	
		<i>L. longihastata</i>	[32]	
		<i>L. subspicata</i>	[23, 34]	
6		<i>L. intermedia</i>	[20]	
7	Isofukinone	<i>L. speciosa</i>	[43]	
8		<i>L. subspicata</i>	[23]	
9		<i>L. melanothyrsa</i>	[44]	
10		<i>L. virgaurea</i>	[28]	
11		<i>L. intermedia</i>	[20]	
12		<i>L. intermedia</i>	[20]	
		<i>L. virgaurea</i>	[45]	
13		<i>L. cyathiceps</i>	[17]	
14	Eremoligenol	<i>L. brassicoides</i>	[46, 47]	
		<i>L. cymbulifera</i>	[48, 49]	
		<i>L. fischeri</i>	[50]	
		<i>L. nelumbifolia</i>	[51]	
		<i>L. subspicata</i>	[34]	
		<i>L. virgaurea</i>	[45]	
15		<i>L. veitchiana</i>	[52]	
16		<i>L. pleurocaulis</i>	[53]	
		<i>L. veitchiana</i>	[52]	
17		<i>L. fischeri</i>	[54]	
18	Ligudicin C	<i>L. dictyoneura</i>	[55]	
19	Ligudicin D	<i>L. dictyoneura</i>	[55]	
20		<i>L. alticola</i>	[41]	
		<i>L. duciformis</i>	[36]	
		<i>L. kanaitzensis</i>	[31]	
		<i>L. lamarum</i>	[23]	
		<i>L. subspicata</i>	[23]	
21		<i>L. kanaitzensis</i>	[56, 57]	
22	Ligudicin A	<i>L. dictyoneura</i>	[55]	
23		<i>L. alticola</i>	[41]	
24		<i>L. lamarum</i>	[23]	
25		<i>L. lamarum</i>	[23]	X-ray
		<i>L. subspicata</i>	[23]	

(continued)

Table 1 (continued)

Structure number	Name of compound	Plant source	Ref.	Comments
26		<i>L. cymbulifera</i>	[49]	
		<i>L. fischeri</i>	[58]	
27		<i>L. fischeri</i>	[54]	
28	Kanaitzensol	<i>L. kanaitzensis</i>	[22]	
		<i>L. subspicata</i>	[34]	
29		<i>L. sagitta</i>	[59]	
30		<i>L. macrophylla</i>	[60]	
		<i>L. sagitta</i>	[61]	
31		<i>L. sagitta</i>	[62]	
32		<i>L. sagitta</i>	[62]	
33		<i>L. kanaitzensis</i>	[22]	
		<i>L. lamarum</i>	[23]	
		<i>L. melanothyrsa</i>	[44]	
		<i>L. subspicata</i>	[23, 34]	
		<i>L. virgaurea</i>	[27, 28, 63]	Both C-11(S) and (R) determined
34		<i>L. przewalskii</i>	[64]	
35		<i>L. virgaurea</i>	[65]	
36		<i>L. veitchiana</i>	[66]	
37		<i>L. macrophylla</i>	[67]	
38		<i>L. sagitta</i>	[68]	
39		<i>L. melanothyrsa</i>	[44]	
		<i>L. virgaurea</i>	[27]	
40		<i>L. brassicoides</i>	[46, 47]	
		<i>L. virgaurea</i>	[27]	
41		<i>L. atroviolacea</i>	[69]	
42		<i>L. atroviolacea</i>	[69]	
43		<i>L. przewalskii</i>	[70]	
44		<i>L. sagitta</i>	[68, 71]	
45		<i>L. myriocephala</i>	[72]	
46		<i>L. macrophylla</i>	[73]	
47		<i>L. veitchiana</i>	[74]	
48	Petasol	<i>L. fischeri</i>	[30]	
		<i>L. rumicifolia</i>	[75]	
		<i>L. speciosa</i>	[43]	
49	Neopetasol	<i>L. speciosa</i>	[43]	
50	Isopetasol	<i>L. fischeri</i>	[30]	
		<i>L. virgaurea</i>	[76]	
51		<i>L. longihastata</i>	[32]	
52		<i>L. longihastata</i>	[32]	
53	Rumicifoline K	<i>L. rumicifolia</i>	[75]	

(continued)

Table 1 (continued)

Structure number	Name of compound	Plant source	Ref.	Comments
54	Petasin	<i>L. dictyoneura</i>	[29]	
		<i>L. fischeri</i>	[30]	X-ray structure
		<i>L. intermedia</i>	[77]	
		<i>L. lamarum</i>	[23]	
		<i>L. lingiana</i>	[78]	
		<i>L. longihastata</i>	[32]	
		<i>L. nelumbifolia/C. stenoglossum</i>	[33]	
		<i>L. rumicifolia</i>	[75]	
		<i>L. sagitta</i>	[62]	
		<i>L. subspicata</i>	[23, 24]	
			<i>L. tsangchanensis</i>	[35]
55		<i>L. dictyoneura</i>	[29]	
		<i>L. tangutica</i>	[13]	
56	Isopetasin	<i>L. dictyoneura</i>	[55]	
		<i>L. fischeri</i>	[30]	
		<i>L. intermedia</i>	[77]	
		<i>L. sagitta</i>	[62]	
		<i>L. subspicata</i>	[23]	
57	Rumicifoline J	<i>L. rumicifolia</i>	[75]	
58	1- <i>epi</i> -Rumicifoline J	<i>L. rumicifolia</i>	[75]	
59		<i>L. dentata</i>	[13]	
60		<i>L. fischeri</i>	[30]	
		<i>L. kanaitzensis</i>	[22]	
		<i>L. lamarum</i>	[23]	
		<i>L. longihastata</i>	[32]	
		<i>L. rumicifolia</i>	[75]	
		<i>L. subspicata</i>	[23, 24]	
61		<i>L. longihastata</i>	[32]	
62		<i>L. longihastata</i>	[32]	
		<i>L. subspicata</i>	[23]	
63		<i>L. kanaitzensis</i>	[22]	
		<i>L. lamarum</i>	[23]	
		<i>L. longihastata</i>	[32]	
		<i>L. rumicifolia</i>	[75]	
		<i>L. subspicata</i>	[23, 24]	
64		<i>L. subspicata</i>	[23]	
65	Rumicifoline L	<i>L. rumicifolia</i>	[75]	
66		<i>L. pleurocaulis</i>	[79]	
67		<i>L. przewalskii</i>	[64]	
68		<i>L. hodgsonii</i>	[80]	

(continued)

Table 1 (continued)

Structure number	Name of compound	Plant source	Ref.	Comments
69		<i>L. przewalskii</i>	[64]	
70		<i>L. przewalskii</i>	[64]	
71		<i>L. kanaitzensis</i>	[22]	
		<i>L. longihastata</i>	[32]	
72		<i>L. virgaurea</i>	[27]	
73		<i>L. rumicifolia</i>	[75]	
74		<i>L. rumicifolia</i>	[75]	
75		<i>L. lingiana</i>	[78]	
76		<i>L. lingiana</i>	[78]	
77		<i>L. lingiana</i>	[78]	
78		<i>L. lingiana</i>	[78]	
79		<i>L. lapathifolia</i>	[81]	
80	Ligumacrophyllatin	<i>L. macrophylla</i>	[67]	
81	Alticoloside A	<i>L. alticola</i>	[82]	
		<i>L. calthifolia</i>	[83]	
82	Alticoloside B	<i>L. alticola</i>	[82]	
		<i>L. calthifolia</i>	[83]	
83	Alticoloside C	<i>L. alticola</i>	[82]	
84	Alticoloside D	<i>L. alticola</i>	[82]	
		<i>L. calthifolia</i>	[83]	
85	Alticoloside E	<i>L. alticola</i>	[82]	
86	Alticoloside F	<i>L. alticola</i>	[82]	
87	Alticoloside G	<i>L. alticola</i>	[82]	
88	Alticoloside H	<i>L. alticola</i>	[84]	
89	Alticoloside I	<i>L. alticola</i>	[84]	
90	2'- <i>O</i> -Acetylalticoloside A	<i>L. calthifolia</i>	[83]	
91	6'- <i>O</i> -Acetylalticoloside A	<i>L. calthifolia</i>	[83]	
92	2'- <i>O</i> -Acetylalticoloside D	<i>L. calthifolia</i>	[83]	
93		<i>L. virgaurea</i>	[65]	
94		<i>L. fischeri</i>	[85]	
95		<i>L. sagitta</i>	[59, 61]	
96		<i>L. sagitta</i>	[59]	
97		<i>L. tsangchanensis</i>	[86]	
98		<i>L. kanaitzensis</i>	[22]	
		<i>L. lamarum</i>	[23]	
		<i>L. subspicata</i>	[34]	
		<i>L. tsangchanensis</i>	[86]	
		<i>L. virgaurea</i>	[27, 28, 63, 87]	
99	Knorringianalarin B	<i>L. knorringiana</i>	[88]	
100		<i>L. virgaurea</i>	[27]	

(continued)

Table 1 (continued)

Structure number	Name of compound	Plant source	Ref.	Comments
101		<i>L. knorringiana</i>	[88]	
		<i>L. sagitta</i>	[61, 62]	
		<i>L. veitchiana</i>	[62]	
102		<i>L. sagitta</i>	[62]	
103		<i>L. virgaurea</i>	[87]	
104		<i>L. virgaurea</i>	[89]	
105		<i>L. sagitta</i>	[59]	
106	Sagittacin E	<i>L. sagitta</i>	[61]	
107		<i>L. sagitta</i>	[62]	
		<i>L. veitchiana</i>	[62]	
108		<i>L. sagitta</i>	[61]	
		<i>L. veitchiana</i>	[66]	
109		<i>L. sagitta</i>	[59]	
110		<i>L. przewalskii</i>	[64]	
111		<i>L. japonica</i>	[90]	
112		<i>L. hodgsonii</i>	[91]	
113		<i>L. hodgsonii</i>	[80]	
		<i>L. japonica</i>	[90]	
114		<i>L. virgaurea</i>	[87]	
115		<i>L. japonica</i>	[90]	
116		<i>L. lapathifolia</i>	[92]	
117		<i>L. hodgsonii</i>	[93]	
118	Ligudentatol	<i>L. dentata</i>	[94, 95]	
		<i>L. intermedia</i>	[77]	
		<i>L. rumicifolia</i>	[75]	
119	Platyphyllide	<i>L. fischeri</i>	[85, 96]	
		<i>L. intermedia</i>	[20]	
		<i>L. przewalskii</i>	[70]	
		<i>L. veitchiana</i>	[66]	
120		<i>L. fischeri</i>	[58, 96]	
121	2-Hydroxyplatyphyllide	<i>L. dentata</i>	[94, 95, 97]	
		<i>L. fischeri</i>	[85]	
		<i>L. hodgsonii</i>	[91]	
		<i>L. intermedia</i>	[20]	
		<i>L. knorringiana</i>	[88]	
		<i>L. macrophylla</i>	[67, 98]	
		<i>L. przewalskii</i>	[70]	
		<i>L. songarica</i>	[99]	
<i>L. speciosa</i>	[43]			
		<i>L. veitchiana</i>	[66]	

(continued)

Table 1 (continued)

Structure number	Name of compound	Plant source	Ref.	Comments
122		<i>L. fischeri</i>	[96]	
123	Ligujapone	<i>L. dentata</i>	[94, 95, 97]	
		<i>L. hodgsonii</i>	[93]	
		<i>L. intermedia</i>	[77]	
		<i>L. japonica</i>	[13]	
		<i>L. odontomanes</i>	[100]	
124		<i>L. przewalskii</i>	[64]	
125	Liguhodgsonal	<i>L. brachyphylla</i>	[13]	
		<i>L. clivorum</i>	[13]	
		<i>L. dentata</i>	[13, 94, 95, 97]	
		<i>L. dolichobotrys</i>	[101]	
		<i>L. hodgsonii</i>	[13]	
		<i>L. intermedia</i>	[20, 77, 102]	
		<i>L. japonica</i>	[13]	
		<i>L. kangtingensis</i>	[103]	
		<i>L. lamarum</i>	[23]	
		<i>L. nanchuanica</i>	[104]	
		<i>L. odontomanes</i>	[100]	
		<i>L. sagitta</i>	[105, 106]	
		<i>L. speciosa</i>	[43]	
		<i>L. veitchiana</i>	[107, 108]	
126	Ligudentatin A	<i>L. dentata</i>	[94]	
		<i>L. kangtingensis</i>	[103]	
		<i>L. nanchuanica</i>	[104]	
127	Ligudentatin B	<i>L. dentata</i>	[94]	
128	Ligukangtinol	<i>L. kangtingensis</i>	[109]	
129	Rumicifoline A	<i>L. rumicifolia</i>	[75]	
130	Norsubspicatin A	<i>L. subspicata/L. cyathiceps</i>	[40]	
131	Normelanothyrsin A	<i>L. melanothyrsa</i>	[44]	
132		<i>L. lamarum</i>	[23]	
		<i>L. melanothyrsa</i>	[44]	
		<i>L. vellerea</i>	[26]	
		<i>L. virgaurea</i>	[27, 28, 63]	
133		<i>L. virgaurea</i>	[28]	

(continued)

Table 1 (continued)

Structure number	Name of compound	Plant source	Ref.	Comments
134		<i>L. lapathifolia</i>	[81]	
		<i>L. macrophylla</i>	[73]	
		<i>L. przewalskii</i>	[70]	
135		<i>L. fischeri</i>	[96]	
136		<i>L. melanothrsa</i>	[44]	
		<i>L. virgaurea</i>	[27, 28]	
137		<i>L. fischeri</i>	[96]	
138		<i>L. fischeri</i>	[96]	
139	Ligupleurol	<i>L. pleurocaulis</i>	[53]	
139a	Eremopetasinorol	<i>L. tsangchanensis</i>	[86]	
140		<i>L. fischeri</i>	[110]	
		<i>L. hodgsonii</i>	[80]	
141		<i>L. intermedia</i>	[111]	
142		<i>L. virgaurea</i>	[27]	
143		<i>L. virgaurea</i>	[27]	
144		<i>L. lapathifolia</i>	[92]	X-ray structure
145		<i>L. virgaurea</i>	[112]	
146		<i>L. cymbulifera</i>	[49]	
		<i>L. dictyoneura</i>	[113]	
147	Secovirgaurenol A	<i>L. virgaurea</i>	[45]	
148	Secovirgaurenol B	<i>L. virgaurea</i>	[76]	
149	Secovirgaurenol C	<i>L. virgaurea</i>	[45, 76, 114]	
150	Secovirgaural	<i>L. virgaurea</i>	[45]	
151	Secobakkane A	<i>L. lamarum</i>	[23]	
		<i>L. melanothyrsa</i>	[44]	
152	Secobakkane B	<i>L. virgaurea</i>	[76]	
153		<i>L. lamarum</i>	[115]	
154		<i>L. hodgsonii</i>	[116]	
155		<i>L. brassicoides</i>	[117]	
156		<i>L. virgaurea</i>	[118]	
157	Ligulolide C	<i>L. virgaurea</i>	[118]	
158	Ligumacrophyllal	<i>L. macrophylla</i>	[67, 119]	
159		<i>L. virgaurea</i>	[27, 28]	

(continued)

Table 1 (continued)

Structure number	Name of compound	Plant source	Ref.	Comments
160		<i>L. brassicoides</i>	[46, 47]	
		<i>L. dictyoneura</i>	[29, 120, 121]	
		<i>L. fischeri</i>	[37, 50, 122]	
		<i>L. hodgsonii</i>	[123–125]	
		<i>L. schmidtii</i>	[20]	
		<i>L. subspicata/L. cyathiceps</i>	[40]	
		<i>L. vellerea</i>	[21]	
161	Ligularol = petasalbin	<i>L. dictyoneura</i>	[29, 120]	
		<i>L. duciformis</i>	[126]	
		<i>L. fischeri</i>	[11, 37, 50]	
		<i>L. kanaitzensis</i>	[22, 31]	
		<i>L. lamarum</i>	[23]	
		<i>L. lamarum/L. subspicata</i>	[38]	
		<i>L. nelumbifolia</i>	[51]	
		<i>L. nelumbifolia/L. subspicata</i>	[127]	
		<i>L. schmidtii</i>	[20]	
		<i>L. subspicata</i>	[24, 38, 127]	
		<i>L. subspicata/L. cyathiceps</i>	[38, 40]	
		<i>L. tongolensis/L. cymbulifera</i>	[128]	
		<i>L. vellerea</i>	[21, 26]	
		<i>L. virgaurea</i>	[27, 63]	
162		<i>L. kanaitzensis</i>	[22]	
		<i>L. lamarum</i>	[23]	
		<i>L. subspicata</i>	[24]	
		<i>L. vellerea</i>	[26]	
		<i>L. virgaurea</i>	[63]	

(continued)

Table 1 (continued)

Structure number	Name of compound	Plant source	Ref.	Comments
163		<i>L. brassicoides</i>	[46, 47]	
		<i>L. dictyoneura</i>	[120]	
		<i>L. fischeri</i>	[37]	
		<i>L. lamarum</i>	[23, 115]	
		<i>L. lamarum/L. subspicata</i>	[38]	
		<i>L. subspicata</i>	[24, 38]	
		<i>L. subspicata/L. cyathiceps</i>	[38, 40]	
		<i>L. tsangchanensis/L. vellerea</i>	[25]	
		<i>L. vellerea</i>	[21, 26]	
164		<i>L. virgaurea</i>	[63]	
		<i>L. kanaitzensis</i>	[22]	
		<i>L. lamarum</i>	[23]	
165		<i>L. tsangchanensis/L. vellerea</i>	[25]	
		<i>L. lamarum</i>	[23]	
166		<i>L. subspicata/L. cyathiceps</i>	[40]	
167		<i>L. lamarum</i>	[23]	
168	Ligularone	<i>L. lamarum</i>	[23]	
		<i>L. subspicata/L. cyathiceps</i>	[40]	
		<i>L. dictyoneura</i>	[29, 120]	
		<i>L. fischeri</i>	[11, 37, 50, 110, 122]	
169		<i>L. lamarum</i>	[115]	
		<i>L. macrophylla</i>	[129]	
170	Subspicatol A	<i>L. lamarum</i>	[115]	
		<i>L. subspicata/L. cyathiceps</i>	[40]	

(continued)

Table 1 (continued)

Structure number	Name of compound	Plant source	Ref.	Comments
171	Subspicatin A	<i>L. lamarum</i>	[23]	
		<i>L. lamarum/L. subspicata</i>	[38]	
		<i>L. nelumbifolia/L. subspicata</i>	[127]	
		<i>L. subspicata</i>	[23, 24, 38, 127]	
		<i>L. subspicata/L. cyathiceps</i>	[38, 40]	
172	Subspicatin B	<i>L. lamarum</i>	[23]	
		<i>L. lamarum/L. subspicata</i>	[38]	
		<i>L. subspicata</i>	[24, 38]	
		<i>L. subspicata/L. cyathiceps</i>	[38, 40]	
173	Subspicatin C	<i>L. lamarum/L. subspicata</i>	[38]	
		<i>L. subspicata</i>	[24]	
174	Subspicatin G	<i>L. lamarum</i>	[23]	
175	Subspicatin O1	<i>L. subspicata/L. cyathiceps</i>	[40]	
176	Subspicatin O2	<i>L. subspicata/L. cyathiceps</i>	[40]	
177		<i>L. lamarum/L. subspicata</i>	[38]	
178		<i>L. vellerea</i>	[21, 26]	
179		<i>L. vellerea</i>	[21]	
180		<i>L. tsangchanensis/L. vellerea</i>	[25]	
181		<i>L. lamarum/L. subspicata</i>	[38]	
		<i>L. subspicata/L. cyathiceps</i>	[38, 40]	
182		<i>L. lamarum/L. subspicata</i>	[38]	
		<i>L. subspicata/L. cyathiceps</i>	[38, 40]	
183		<i>L. cyathiceps</i>	[17, 38]	
184		<i>L. brassicoides</i>	[117]	
185		<i>L. subspicata/L. cyathiceps</i>	[40]	
186		<i>L. macrophylla</i>	[60]	
187		<i>L. oligonema</i>	[130]	

(continued)

Table 1 (continued)

Structure number	Name of compound	Plant source	Ref.	Comments
188		<i>L. oligonema</i>	[130]	
189		<i>L. dictyoneura</i>	[29]	
190		<i>L. virgaurea</i>	[27]	
191		<i>L. cymbulifera</i>	[128]	
		<i>L. tongolensis/L. cymbulifera</i>	[128]	
192		<i>L. dictyoneura</i>	[29]	
		<i>L. virgaurea</i>	[27]	
193	Franchetianone B	<i>L. franchetiana</i>	[19]	
194		<i>L. oligonema</i>	[130]	
195		<i>L. thyrsoidea</i>	[131]	
196		<i>L. intermedia</i>	[132, 133]	
197		<i>L. macrophylla</i>	[134]	
198		<i>L. melanothyrsa</i>	[21]	
199		<i>L. alticola</i>	[135]	
		<i>L. dictyoneura</i>	[120]	
		<i>L. hodgsonii</i>	[136]	
		<i>L. melanothyrsa</i>	[21]	
		<i>L. vellerea</i>	[21, 26]	
200		<i>L. dictyoneura</i>	[120]	
		<i>L. macrophylla</i>	[129]	
		<i>L. melanothyrsa</i>	[21]	
		<i>L. vellerea</i>	[21, 26]	
201		<i>L. cymbulifera</i>	[128]	
202		<i>L. schmidtii</i>	[20]	
203		<i>L. cymbulifera</i>	[128]	
		<i>L. tongolensis/L. cymbulifera</i>	[128]	
204		<i>L. atroviolacea</i>	[48]	
		<i>L. cymbulifera</i>	[128]	
		<i>L. schmidtii</i>	[20]	
		<i>L. tongolensis</i>	[128, 137]	
		<i>L. tongolensis/L. cymbulifera</i>	[128]	
205		<i>L. atroviolacea</i>	[48]	
206		<i>L. tongolensis</i>	[48, 137]	
207		<i>L. tongolensis</i>	[137]	

(continued)

Table 1 (continued)

Structure number	Name of compound	Plant source	Ref.	Comments
208		<i>L. tongolensis</i>	[128, 137]	
		<i>L. tongolensis/L. cymbulifera</i>	[128]	
209		<i>L. hookeri</i>	[138]	
210		<i>L. tongolensis</i>	[48, 137]	
211		<i>L. melanothyrsa</i>	[21]	
		<i>L. persica</i>	[39]	
		<i>L. thyrsoidea</i>	[131]	
		<i>L. vellerea</i>	[21, 26]	
212		<i>L. alticola</i>	[135]	
		<i>L. angusta</i>	[139]	
		<i>L. atroviolacea</i>	[69]	
		<i>L. calthifolia</i>	[13]	
		<i>L. dictyoneura</i>	[29, 120]	
		<i>L. fauriei</i>	[139]	
		<i>L. hodgsonii</i>	[123–125, 136]	
		<i>L. intermedia</i>	[132, 133, 140, 141]	
		<i>L. knorringiana</i>	[88]	
		<i>L. lapathifolia</i>	[142]	
		<i>L. macrophylla</i>	[129, 143]	
		<i>L. melanothyrsa</i>	[21]	
		<i>L. persica</i>	[39]	
		<i>L. przewalskii</i>	[13, 144, 145]	
	<i>L. thyrsoidea</i>	[131]		
	<i>L. vellerea</i>	[21, 26]		
213		<i>L. hookeri</i>	[138]	
214		<i>L. hookeri</i>	[138]	

(continued)