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Review

Metabolites of *Serratula* L. and *Klasea* Cass. (Asteraceae): Diversity, Separation Methods, and Bioactivity

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Abstract: *Serratula* L. and *Klasea* Cass. are two systematically related genera of the family Asteraceae, which are distributed in most of the Eurasia area and are used as food and colorants and in traditional medicines as a drug. Since 1967, 261 metabolites have been isolated and identified from five *Serratula* species and 21 *Klasea* species. This review provides information on the chemodiversity of the terpenes, penolics, lipids, and other compounds found in both genera and their occurrence in individual species. Among the studied species, the most studied are *S. coronata* subsp. *coronata*, *K. centauroides*, and *K. centauroides* subsp. *centauroides*. This review also provides information on the methods of extraction, isolation, and analysis of ecdysteroids and flavonoids as the most valuable metabolites. For the first time, we provide general information about the biological activity of these extracts and individual compounds. The data presented in this review demonstrate the prospects of *Serratula* and *Klasea* species as sources of bioactive metabolites.

Keywords: *Serratula*; *Klasea*; ecdysteroids; flavonoids; chemodiversity; isolation; chromatography; bioactivity

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1. Introduction

The genus *Serratula* L. of the Asteraceae family, which is distributed in a wide range of temperature zones from Western Europe to the Far East, Japan, and Korea, currently includes four species and some subspecies [1]. The distribution area of the systematically closely related genus *Klasea* Cass. differs in a more southern location with centers of species diversity in the mountains of Central Asia, Western Iran, and the Iberian Peninsula, and it includes more than 50 species [2]. The systematic position of *Serratula* and *Klasea* has changed several times over the past two centuries. In 1825, A.H.G. Cassini proposed a theory about the presence of phylogenetic differences between the genera *Serratula* and *Klasea*, which was disproved by a number of authors [3]. To date, the existence of *Serratula* and *Klasea* as two separate genera has been confirmed based on morphological [3] and molecular data [4]. However, despite their differences, plants included in *Serratula* and *Klasea* have similar appearances and ethnopharmacological uses; thus, both genera are regarded in this paper together. Botanically, serratulas and klaseas are perennial herbs with erect stems and are usually branched in the upper half (Figure 1) [5]. The leaves are generally pinnate and rarely undivided and have a margin dentate or serrate. Capitulas are hetero- or homogamous, one or many in the panicle, paniculate, or corymbose, solitary at the end of stems and branches, and have an ovoid, hemispheric, or bowl-shaped involucre. Phyllaries are usually darker toward the apex, imbricate, and apex acute; the inner phyllaries are the longest, and the corolla is purple to pink or rarely almost white or yellow.

Figure 1. *Serratula* L. (S.) and *Klasea* Cass. (K.) species in their natural habitat: (**a**) S. coronata; (**b**) S. coronata subsp. coronata; (**c**) S. tinctoria; (**d**) K. cardunculus; (**e**) K. erucifolia; (**f**) K. centauroides; (**g**) K. latifolia; (**h**) K. lycopifolia; (**i**) K. lyratifola; (**j**) K. procumbens; (**k**) K. quinquefolia; (**l**) K. radiata; (**m**) K. gmelinii; (**n**) K. sogdiana.

The wide distribution of *Serratula* and *Klasea* in Europe and Asia meadows, steppes, and forests determines its medical, food, and economic importance. Probably the best-known use of the herb of plumeless sawwort (*S. coronata*) has been reported to be medicinal uses among the indigenous peoples of the Far East for curing epilepsy, neurosis, and fatigue, as well as having anti-tumor and wound healing effects [6].

In Tibetan medicine, the herbs *K. centauroides* and *K. cardunculus* have been used as hemostatic and wound-healing remedies [7], and the fermented leaves of *K. centauroides* in Siberia are applied as a tea surrogate [8]. In Mongolia, a decoction of *K. cardunculus* flowers can be added to bath water to treat scrofulous and dropsy [9]. The herb powder of *K. sogdiana* has been known as an insecticide against spider mites and cotton aphids in Middle Asia [10]. In Europe, the roots and herb of *S. tinctoria* or sawwort were a source of wood, cotton, and flax textile dyes until the 19th century [11].

While studying the biological activity of *Serratula* and *Klasea*, it was shown that their preparations have adaptogenic, anti-stress, and anabolic activity due to the presence of ecdysteroids and flavonoids [12]. These substances are characterized by high biological

activity due to their tonic and stimulating effect on the human body [13]. Taking into account the unquenchable scientific interest in the study of plant adaptogens, as well as the prospects and practical significance of *Serratula* and *Klasea* species as sources of valuable compounds, we have analytically studied the scientific literature data related to chemodiversity, methods for isolating and analyzing metabolites, as well as the bioactivity of both genera.

2. Review Strategy

The resources of international databases (e.g., Scopus, Web of Science, PubMed, and Google Scholar) were used, and only original papers written in English and published in journals prior to November 2022 were considered. The search keywords used included plant names (e.g., "*Serratula*", "*Klasea*", etc.) and metabolite names. Metabolites with a tentative structure (e.g., "luteolin-*O*-hexoside", etc.) were excluded from the study. The structures of well-known metabolites (e.g., monoterpenes, sesquiterpenes, fatty acids, amino acids, etc.) are not discussed in this paper. The list of compounds includes secondary metabolites mostly correlated to ethnopharmacological uses and bioactivities of plants, and for a more complete picture, information about primary metabolites is also mentioned in this manuscript.

3. Chemodiversity of *Serratula* L. and *Klasea* Cass. Genera

The study of the chemical composition of the still unified genus *Serratula* began in the late 1960s after the discovery of polyacetylenes in *S. coronata* [14], which was continued later for other species of this genus. In the early stages of the scientific history of the genus arbutin [15], some flavonoids [16] were described in plants, and only after the discovery of 20-hydroxyecdysone in *K. sogdiana* (syn. *S. sogdiana*) in the early 70s [17] did plants of this genus began to become interesting for scientists as promising sources of ecdysteroids. As a result, more than 50 years of study of both genera resulted in the discovery of 261 metabolites in 5 *Serratula* and 21 *Klasea* species (Table 1). To date, the largest number of compounds has been found in *K. centauroides* (*S. centauroides*) (123 compounds) as well as in *S. coronata* subsp. *coronata* (*S. manshurica* Kitag., *S. wolffii* Andrae) (57 compounds) and in *K. centauroides* subsp. *centauroides* (*S. komarovii*) (32 compounds).

From 1967 to 2022, compounds **1–261** were identified for two genera, including monoterpene **1**, sesquiterpenes (**2**–**48**), sterols (**49**–**60**), triterpene alcohols (**61**, **62**), ecdysteroids (**63**–**148**), phenols (**149**, **150**), hydroxycinnamates (**151**–**158**), flavonoids (**159**–**190**) and other phenolics (**191**, **192**), thiophenes (**193**–**195**), fatty acids (**196**–**230**), glycerolglycolipids (**231**–**233**), cerebrosides (**234**–**236**), amino acids (**237**–**247**), alkanes (**248**–**255**), and other groups (**256**–**261**) [18–77] (Table 2). The largest groups of metabolites are ecdysteroids, which include 86 compounds (ca. 33% of total compound), followed by the sesquiterpenes (47 comp.; ca. 18%), fatty acids (35 comp.; ca. 13%), and flavonoids (32 comp.; ca. 12%) (Figure 2).

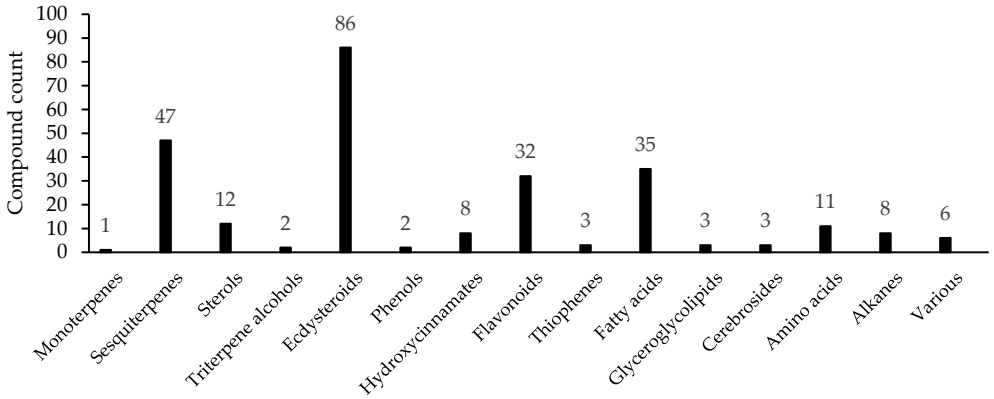


Figure 2. Total count of compounds found in *Serratula* and *Klasea*.

Table 1. Synopsis of *Serratula* (*S.*) and *Klasea* (*K.*) species included in the review and total count of compounds found.

Species (Synonyms)	Compound Count
Serratula species	
S. coronata L.	**30**
S. coronata subsp. *coronata* = syn. *S. manshurica* Kitag., *S. martini* Vaniot, *S. wolffii* Andrae	**57**
S. kirghisorum Iljin	**2**
S. tinctoria L.	**31**
S. tinctoria subsp. *tinctoria* = syn. *S. inermis* Gilib., *S. pinnata* Kit., *S. pumila* Thore ex DC	**4**
Klasea species	
K. algida (Iljin) Hidalgo = syn. *S. algida* Iljin, *S. dshungarica* Iljin	**3**
K. cardunculus (Pall.) Holub = syn. *S. cardunculus* (Pall.) Schischk., *S. nitida* Fisch. ex Spreng	**1**
K. centauroides (L.) Cass. ex Kitag. = syn. *S. centauroides* L.	**123**
K. centauroides subsp. *centauroides* = syn. *S. komarovii* Iljin, *S. pectinata* Turcz. ex Herder	**32**
K. centauroides subsp. *strangulata* (Iljin) L.Martins = syn. *S. strangulata* Iljin	**22**
K. chinensis (S.Moore) Kitag. = syn. *S. chinensis* S.Moore	**26**
K. erucifolia (L.) Greuter & Wagenitz = syn. *S. erucifolia* (L.) Boriss., *S. xeranthemoides* M.Bieb	**16**
K. flavescens subsp. *cichoracea* (L.) Greuter & Wagenitz = syn. *S. cichoracea* (L.) DC	**8**
K. hakkiarica (P.H.Davis) Greuter & Wagenitz = syn. *S. hakkiarica* P.H.Davis	**15**
K. lasiocephala (Bornm.) Greuter & Wagenitz = syn. *S. lasiocephala* Bornm	**15**
K. latifolia (Boiss.) L.Martins = syn. *S. latifolia* Boiss	**9**
K. lycopifolia (Vill.) Á.Löve & D.Löve = syn. *S. lycopifolia* (Vill.) Wettst., *S. nitida* Besser	**3**
K. lyratifolia (Schrenk) L.Martins = syn. *S. lyratifolia* Schrenk ex Fisch. & C.A.Mey., *S. rugulosa* Iljin	**5**
K. pinnatifida (Cav.) Talavera = syn. *S. pinnatifida* Poir	**2**
K. procumbens (Regel) Holub = syn. *S. procumbens* Regel	**2**
K. quinquefolia (Willd.) Greuter & Wagenitz = *S. quinquefolia* Willd	**4**
K. radiata (Waldst. & Kit.) Á.Löve & D.Löve = syn. *S. radiata* (Waldst. & Kit.) DC	**8**
K. radiata subsp. *biebersteiniana* (Grossh.) Greuter = syn. *S. radiata* subsp. *biebersteiniana* Grossh	**14**
K. radiata subsp. *gmelinii* (Tausch) L.Martins = *S. gmelinii* Tausch	**5**
K. radiata subsp. *radiata* = *S. bracteifolia* (Iljin) Stankov, *S. heterophylla* Vill, *S. isophylla* Claus	**3**
K. sogdiana (Bunge) L.Martins = syn. *S. sogdiana* Bunge	**4**

Table 2. Compounds **1–261** found in *Serratula* (*S.*) and *Klasea* (*K.*) plants.

No	Compound [a]	Species (Organ) [b]	Ref.
	Monoterpenes		
1	Geranyl acetate	*K. centauroides* (h)	[18]
	Sesquiterpenes		
2	Alantolactone	*K. latifolia* (ae)	[19]
3	*cis*-α-Bergamotene	*K. centauroides* (h)	[18]
4	*trans*-α-Bergamotene	*K. centauroides* (h)	[18]
5	Bicyclogermacrene	*K. centauroides* (h)	[18]
6	(*Z*)-α-Bisabolene	*K. centauroides* (h)	[18]
7	(6*S*,7*R*)-Bisabolone	*K. centauroides* (h)	[18]
8	*trans*-Cadina-1,4-diene	*K. centauroides* (h)	[18]
9	α-Cadinene	*K. centauroides* (h)	[18]
10	δ-Cadinene	*K. centauroides* (h)	[18]
11	α-Calacorene	*K. centauroides* (h)	[18]
12	Carabrone	*K. latifolia* (ae)	[19]

Table 2. *Cont.*

No	Compound [a]	Species (Organ) [b]	Ref.
13	Caryophyllene	*S. coronata* subsp. *coronata* (r) *K. centauroides* (h, r)	[20] [18]
14	Caryophyllene oxide	*S. coronata* subsp. *coronata* (r) *K. centauroides* (h, r)	[20] [18]
15	Centaurepensin	*K. centauroides* subsp. *strangulata* (rz,w)	[22]
16	Centaurepensin 17-*O*-(*p*-hydroxyphenylethanol)	*K. centauroides* subsp. *strangulata* (w)	[21]
17	α-Copaene	*K. centauroides* (h)	[18]
18	Costic acid	*K. latifolia* (ae)	[19]
19	β-Elemene	*K. centauroides* (h)	[18]
20	γ-Elemene	*K. centauroides* (h)	[18]
21	Eudesma-4(15),7-dien-1β-ol	*K. centauroides* (h, r)	[18]
22	γ-Eudesmol	*K. centauroides* (h)	[18]
23	(*E*,*E*)-α-Farnesene	*K. centauroides* (h)	[18]
24	(*E*)-β-Farnesene	*K. centauroides* (h, r)	[18]
25	Germacrene B	*K. centauroides* (h)	[18]
26	Germacrene D	*S. coronata* subsp. *coronata* (r)	[20]
27	Hexahydroxyfarnesyl	*K. centauroides* (h)	[18]
28	4α-Hydroxy-1β-hydroperoxyguaia-10(14),11(13)-dien-12,8β-olide	*K. latifolia* (ae)	[19]
29	4α-Hydroxy-10α-hydroperoxyguaia-1,11(13)-dien-12,8β-olide	*K. latifolia* (ae)	[19]
30	4α-Hydroxy-10β-hydroperoxyguaia-1,11(13)-dien-12,8β-olide	*K. latifolia* (ae)	[19]
31	Humulene	*K. centauroides* (h, r)	[18]
32	Humulen-6,7-epoxide	*K. centauroides* (h, r)	[18]
33	Isospathulenol	*K. centauroides* (h)	[18]
34	Ivalin	*K. latifolia* (ae)	[19]
35	Junenol	*K. centauroides* (h, r)	[18]
36	Mint oxide	*K. centauroides* (h, r)	[18]
37	Mint sulfide	*K. centauroides* (r)	[18]
38	*E*-Nerolidol	*K. centauroides* (h)	[18]
39	Pseudoivalin	*K. latifolia* (ae)	[19]
40	Salviadienol	*K. centauroides* (h, r)	[18]
41	Salvial-4(14)-en-1-one	*K. centauroides* (h, r)	[18]
42	Selina-4,11-diene	*K. centauroides* (h)	[18]
43	7-*epi*-α-Selinene	*K. centauroides* (h)	[18]
44	β-Selinene	*K. centauroides* (h, r)	[18]
45	*E*-Sesquilavandulol	*K. centauroides* (h)	[18]
46	Spathulenol	*K. centauroides* (h, r)	[18]
47	Valencene	*K. centauroides* (h)	[18]
48	*epi*-Zonarene	*K. centauroides* (h)	[18]
	Sterols		
49	Campesterol	*S. tinctoria* (r)	[23]

Table 2. *Cont.*

No	Compound [a]	Species (Organ) [b]	Ref.
		K. centauroides (h)	[24]
50	Cholesterol	*S. tinctoria* (r)	[23]
51	Desmosterol	*S. tinctoria* (r)	[23]
52	Lathosterol	*S. tinctoria* (r)	[23]
53	24-Methylene-cholesterol	*S. tinctoria* (r)	[23]
54	β-Sitosterol	*S. tinctoria* (r)	[23]
55	β-Sitosterol acetate	*K. centauroides* (h, r)	[24]
56	γ-Sitosterol	*K. centauroides* (h, r)	[24]
57	Sitostanol	*S. tinctoria* (r)	[23]
58	Stigmasterol	*S. tinctoria* (r) *K. centauroides* (h, r)	[23] [24]
59	Stigmastanol	*S. tinctoria* (r)	[23]
60	Stigmast-4-en-3-one	*K. centauroides* (h)	[24]
	Triterpene alcohols		
61	α-Amyrin	*K. centauroides* (h)	[24]
62	β-Amyrin	*K. centauroides* (h)	[24]
	Ecdysteroids		
63	*epi*-Abutasterone	*K. chinensis* (r)	[25]
64	*epi*-Abutasterone 24-*O*-acetate	*K. chinensis* (r)	[26]
65	Ajugasterone C	*S. coronata* (l, s) *S. coronata* subsp. *coronata* (h) *K. flavescens* subsp. *cichoracea* (f)	[27,28] [29,30] [31]
66	Ajugasterone C 2-*O*-acetate	*S. coronata* (j)	[32]
67	Ajugasterone C 3-*O*-acetate	*S. coronata* (j)	[32]
68	Ajugasterone C 11-*O*-acetate	*S. coronata* (j)	[32]
69	Ajugasterone C 20,22-monoacetonide	*S. coronata* (j) *S. coronata* subsp. *coronata* (h)	[33] [29]
70	Ajugasterone C 20,22-ethylidene	*S. coronata* (j)	[33]
71	22-*epi*-Ajugasterone C	*K. flavescens* subsp. *cichoracea* (f)	[31]
72	Ajugasterone D	*S. coronata* subsp. *coronata* (h) *K. chinensis* (r)	[30] [25]
73	Atrotosterone C	*K. chinensis* (r)	[34]
74	Carthamosterone	*K. chinensis* (r)	[25,34]
75	Calonisterone	*S. coronata* (j)	[32]
76	Coronatasterone	*K. chinensis* (r)	[25]
77	Dacryhainansterone	*S. coronata* (l) *S. coronata* subsp. *coronata* (h)	[28] [30]
78	24(28)-Dehydromakisterone	*K. centauroides* (h)	[35]
79	22-Dehydro-20-desoxymakisterone C	*S. coronata* subsp. *coronata* (r)	[36]
80	2-Deoxy-3-*epi*-4β,20-dihydroxycedysone	*S. coronata* (h)	[37]

Table 2. *Cont.*

No	Compound [a]	Species (Organ) [b]	Ref.
81	2-Deoxy-20-hydroxyecdysone	*K. centauroides* (f, h, l, st) *K. centauroides* subsp. *centauroides* (l,r,s,st)	[35,38] [39]
82	3-*epi*-2-Deoxy-20-hydroxyecdysone	*S. coronata* subsp. *coronata* (r)	[40]
83	22-Deoxy-20-hydroxyecdysone	*S. coronata* subsp. *coronata* (h)	[30]
84	22-Deoxy-20,21-dihydroxyecdysone	*S. coronata* subsp. *coronata* (h)	[30]
85	22-Deoxy-20,21-didehydroecdysone	*S. coronata* subsp. *coronata* (r)	[36]
86	25-Deoxy-11,20-dihydroxyecdysone	*K. centauroides* subsp. *strangulata* (l, r, rz, s)	[22,41,42]
87	25,26-Didehydroponasterone A	*K. chinensis* (r)	[34]
88	20,22-Didehydrotaxisterone	*S. coronata* subsp. *coronata* (r)	[43]
89	Ecdysone	*S. coronata* subsp. *coronata* (h) *K. lycopifolia* (h) *K. radiata* (h) *K. radiata* subsp. *gmelinii* (h)	[29,30] [44] [44] [44]
90	Gerardiasterone	*S. tinctoria* (h)	[45]
91	Herkesterone	*S. coronata* subsp. *coronata* (h)	[30,46]
92	1-Hydroxy-22-desoxy-20,21-didehydroecdysone	*S. coronata* subsp. *coronata* (r)	[36]
93	25-Hydroxydacryhainansterone	*S. coronata* subsp. *coronata* (h)	[30]
94	20-Hydroxyecdysone	*S. coronata* (s) *S. coronata* subsp. *coronata* (h) *S. kirghisorum* (f, h) *S. tinctoria* (r) *S. tinctoria* subsp. *tinctoria* (f) *K. algida* (h) *K. centauroides* (f, h, l, r, st) *K. centauroides* subsp. *centauroides* (l, r, s, st) *K. centauroides* subsp. *strangulata* (l, r, rz, s) *K. chinensis* (r) *K. carduncullus* (f, h) *K. ericifolia* (f, h) *K. flavescens* subsp. *cichoracea* (f) *K. procumbens* (h) *K. quinquefolia* (f, j, l, st) *K. lycopifolia* (h) *K. radiata* (f, l, st) *K. radiata* subsp. *gmelinii* (f, l, st) *K. sogdiana* (f)	[27] [29,30] [47,48] [49] [17] [44,47] [35,38,50] [39] [22,41,42] [25,34] [48] [48,51] [31] [44] [48,52] [44] [48] [48] [53]
95	20-Hydroxyecdysone 20,22-monoacetonide	*S. coronata* (j) *S. coronata* subsp. *coronata* (h) *K. centauroides* (h) *K. centauroides* subsp. *strangulata* (rz, w) *K. chinensis* (r)	[33] [29,30] [35] [22,42] [25]
96	20-Hydroxyecdysone 2,3;20,22-diacetonide	*S. coronata* subsp. *coronata* (h)	[29]
97	20-Hydroxyecdysone 20,22-ethylidene	*S. coronata* (j)	[33]
98	20-Hydroxyecdysone 2-*O*-$^{\beta D}$Glc*p*	*K. chinensis* (r)	[25]

Table 2. *Cont.*

No	Compound [a]	Species (Organ) [b]	Ref.
99	20-Hydroxyecdysone 2-*O*-$^{\beta D}$Gal*p*	*K. chinensis* (r)	[26]
100	20-Hydroxyecdysone 25-*O*-$^{\beta D}$Glc*p*	*K. chinensis* (r)	[25]
101	20-Hydroxyecdysone 2-*O*-acetate	*S. coronata* (j) *S. tinctoria* (r) *K. chinensis* (r)	[33] [49] [25]
102	20-Hydroxyecdysone 3-*O*-acetate	*S. coronata* (j) *S. tinctoria* (r) *K. chinensis* (r)	[33] [49] [25,34]
103	20-Hydroxyecdysone 3-*O*-acetate 2-*O*-$^{\beta D}$Glc*p*	*K. chinensis* (r)	[26]
104	20-Hydroxyecdysone 3-*O*-acetate 2-*O*-$^{\beta D}$Gal*p*	*K. chinensis* (r)	[26]
105	20-Hydroxyecdysone 22-*O*-acetate	*S. coronata* (j) *S. tinctoria* (r) *K. centauroides* (h)	[33,54] [49] [35]
106	20-Hydroxyecdysone 2,22-di-*O*-acetate	*S. tinctoria* (r)	[49]
107	20-Hydroxyecdysone 3,22-di-*O*-acetate	*S. tinctoria* (r)	[49]
108	20-Hydroxyecdysone 20,22-butylidene acetal	*K. chinensis* (r)	[25,34]
109	3-*epi*-20-Hydroxyecdysone	*S. coronata* subsp. *coronata* (h)	[30]
110	5α-20-Hydroxyecdysone	*S. coronata* subsp. *coronata* (h)	[30]
111	14-*epi*-20-Hydroxyecdysone	*S. coronata* subsp. *coronata* (h)	[30]
112	22-*epi*-20-Hydroxyecdysone	*S. coronata* subsp. *coronata* (h) *S. tinctoria* (h)	[30] [45]
113	11α-Hydroxypoststerone	*S. coronata* subsp. *coronata* (h)	[30,46]
114	11α-11-Hydroxyshidasterone	*S. coronata* subsp. *coronata* (r)	[55]
115	24-(2-Hydroxyethyl)-20-hydroxyecdysone	*K. centauroides* subsp. *strangulata* (w)	[42]
116	5β-Hydroxyrubrosterone	*S. tinctoria* (r)	[49]
117	1-Hydroxy-20,22-didehydrotaxisterone	*S. coronata* subsp. *coronata* (r)	[43]
118	Isovitexirone	*S. coronata* subsp. *coronata* (h) *K. centauroides* (f, l, st)	[30] [35]
119	Inokosterone	*K. centauroides* (f, l, st) *K. lycopifolia* (h) *K. quinquefolia* (j) *K. radiata* (h) *K. radiata* subsp. *gmelinii* (h)	[35] [44] [52] [44] [44]
120	Inokosterone 26-*O*-acetate	*S. coronata* (j)	[33]
121	Integristerone A	*S. coronata* (s) *S. coronata* subsp. *coronata* (h) *K. centauroides* (f, h, l, st) *K. centauroides* subsp. *centauroides* (l,r,s,st) *K. ericifolia* (f)	[27] [29] [35,38] [39] [51]
122	Makisterone A	*S. coronata* subsp. *coronata* (h)	[30]
123	Makisterone C	*S. coronata* (j, l) *S. coronata* subsp. *coronata* (h) *S. tinctoria* (r) *K. centauroides* (h)	[28,33] [30] [49] [35]

Table 2. *Cont.*

No	Compound [a]	Species (Organ) [b]	Ref.
124	24-Methyleneshidasterone	*S. coronata* subsp. *coronata* (r) *K. chinensis* (r)	[56] [25,34]
125	22-Oxo-20-hydroxyecdysone	*S. tinctoria* (r)	[49]
126	(2β,3α,5β,22*R*)-2,3,20,22,25-Pentahydroxycholest-7-en-6-one	*S. coronata* subsp. *coronata* (r)	[55]
127	(2β,3α,5β,14β,22*R*)-2,3,20,22,25-Pentahydroxycholest-7-en-6-one	*S. coronata* subsp. *coronata* (r)	[55]
128	Podecdysone C	*S. coronata* subsp. *coronata* (h) *K. chinensis* (r)	[30] [34]
129	Polypodine B	*S. coronata* (s) *S. coronata* subsp. *coronata* (h) *S. tinctoria* (r) *K. chinensis* (r) *K. quinquefolia* (j)	[27] [29,30] [49] [25] [52]
130	Polypodine B 20,22-monoacetonide	*K. chinensis* (r)	[25]
131	Ponasterone A	*S. coronata* subsp. *coronata* (r)	[55]
132	Ponasterone A 22-*O*-$^{\beta D}$Api*f*	*S. coronata* subsp. *coronata* (r)	[40]
133	Poststerone	*S. tinctoria* (r)	[49]
134	3-*epi*-Poststerone	*S. tinctoria* (r)	[49]
135	Pterosterone	*S. coronata* subsp. *coronata* (h) *S. tinctoria* (r)	[29,30] [49]
136	Rubrosterone	*S. tinctoria* (r)	[49]
137	3-*epi*-Rubrosterone	*S. tinctoria* (r)	[49]
138	Serfurosterone A	*S. coronata* subsp. *coronata* (r)	[57]
139	Serfurosterone B	*S. coronata* subsp. *coronata* (r)	[57]
140	Shidasterone	*K. chinensis* (r)	[25,34]
141	3-*epi*-Shidasterone	*S. coronata* subsp. *coronata* (r)	[40]
142	Sogdisterone	*K. sogdiana* (f)	[58]
143	Stachysterone B	*S. coronata* subsp. *coronata* (r)	[56]
144	Stachysterone B 14,15-α-epoxide	*S. coronata* subsp. *coronata* (r)	[56]
145	Stachysterone C	*K. chinensis* (r)	[34]
146	Taxisterone	*S. coronata* (j)	[54]
147	Turkesterone	*S. coronata* subsp. *coronata* (h)	[30]
148	Viticosterone E	*S. coronata* (j) *S. tinctoria* (r) *K. centauroides* (h) *K. procumbens* (h) *K. sogdiana* (l)	[33] [49] [59] [44] [60]

Table 2. *Cont.*

No	Compound [a]	Species (Organ) [b]	Ref.
	Phenols		
149	Arbutin	*K. centauroides* (h)	[59]
		K. centauroides subsp. *centauroides* (l, st)	[61]
		K. erucifolia (l)	[15]
		K. quinquefolia (h, j)	[52,62]
		K. lyratifolia (l)	[63]
		K. radiata (l)	[62]
		K. radiata subsp. *radiata* (l)	[15]
		K. radiata subsp. *gmelinii* (l)	[62]
		K. sogdiana (l)	[64]
150	7-Isobutyryloxy-8,9-epoxy-thymol-isobutyrate	*K. latifolia* (ae)	[19]
	Hydroxycinnamates		
151	Caffeic acid	*K. centauroides* (h)	[47]
		K. algida (h)	[47]
152	1-*O*-Caffeoylquinic acid	*K. centauroides* (h)	[59]
153	3-*O*-Caffeoylquinic acid	*S. tinctoria* (l, st)	[65]
154	4-*O*-Caffeoylquinic acid	*K. centauroides* (h)	[59]
155	5-*O*-Caffeoylquinic acid	*S. kirghisorum* (h)	[47]
		S. tinctoria (l, st)	[65]
		K. centauroides (h)	[47,59]
		K. algida (h)	[47]
156	1,5-Di-*O*-caffeoylquinic acid	*K. centauroides* (h)	[59]
157	3,5-Di-*O*-caffeoylquinic acid	*K. centauroides* (h)	[59]
158	4,5-Di-*O*-caffeoylquinic acid	*K. centauroides* (h)	[59]
	Flavones		
159	Chrysin 7-*O*-$^{\beta D}$Glc*p*	*K. centauroides* (h)	[47]
160	Apigenin	*S. coronata* (h)	[66]
		S. coronata subsp. *coronata* (h)	[67]
		S. tinctoria (f)	[16]
		S. tinctoria subsp. *tinctoria* (f)	[16]
		K. flavescens subsp. *cichoracea* (f)	[68]
161	Apigenin 7-*O*-$^{\beta D}$GlcA*p*	*S. coronata* subsp. *coronata* (h)	[67]
		K. centauroides (h)	[59]
		K. centauroides subsp. *centauroides* (h)	[69]
162	Acacetin	*K. flavescens* subsp. *cichoracea* (f)	[68]
163	Genkwanin	*K. flavescens* subsp. *cichoracea* (f)	[68]
164	Luteolin	*S. coronata* (h)	[66]
		S. coronata subsp. *coronata* (h)	[67]
		S. tinctoria (f, st)	[16,65]
		S. tinctoria subsp. *tinctoria* (f)	[16]
		K. centauroides (h, r)	[70]
		K. centauroides subsp. *centauroides* (h)	[69]
		K. flavescens subsp. *cichoracea* (f)	[68]
165	Luteolin 7-*O*-$^{\beta D}$Glc*p*	*K. centauroides* (h)	[47]
166	Luteolin 7-*O*-$^{\beta D}$GlcA*p*	*S. coronata* subsp. *coronata* (h)	[67]
		K. centauroides subsp. *centauroides* (h)	[69]

Table 2. *Cont.*

No	Compound [a]	Species (Organ) [b]	Ref.
167	Luteolin 4′-*O*-$^{\beta D}$Glc*p*	*S. coronata* (h) *S. tinctoria* (l, st)	[66,71] [11]
168	Luteolin 4′-*O*-$^{\beta D}$GlcA*p*	*S. coronata* (h)	[71]
169	Diosmetin	*S. tinctoria* (l, st)	[65]
170	Chrysoeriol 7-*O*-$^{\beta D}$GlcA*p*	*K. centauroides* (h) *K. centauroides* subsp. *centauroides* (h)	[59] [69]
	Flavonols		
171	Kaempferol	*K. lyratifolia* (l)	[63]
172	Kaempferol 3-*O*-(6′′-$^{\alpha L}$Rha*p*)-$^{\beta D}$Glc*p* (nicotoflorin)	*K. lyratifolia* (l)	[63]
173	Kaempferol 3-*O*-methyl ester (kaempferide)	*S. heterophilla* (r) *S. coronata* (r) *S. coronata* subsp. *coronata* (h, r) *K. pinnatifida* (r) *K. radiata* subsp. *gmelinii* (r) *K. radiata* subsp. *radiata* (r)	[14] [14] [20,67] [14] [14] [14]
174	Kaempferol 4′-*O*-methyl ester	*K. centauroides* subsp. *strangulata* (w)	[21]
175	Kaempferol 4′-*O*-methyl ester 7-*O*-$^{\beta D}$Glc*p* (mumemin)	*K. centauroides* subsp. *strangulata* (w)	[21]
176	Kaempferol 7,4′-di-*O*-methyl ester	*K. centauroides* subsp. *strangulata* (l, r, rz, s)	[21,41]
177	Quercetin	*S. coronata* subsp. *coronata* (h) *K. centauroides* (h, r) *K. centauroides* subsp. *centauroides* (h) *K. lyratifolia* (l)	[67] [70] [69] [63]
178	Quercetin 3-*O*-(6′′-$^{\alpha L}$Rha*p*)-$^{\beta D}$Glc*p* (rutin)	*K. centauroides* (h, r) *K. lyratifolia* (l)	[70] [63]
179	Quercetin 4′-*O*-$^{\beta D}$Glc*p*	*S. coronata* (h)	[66,71]
180	Quercetin 4′-*O*-$^{\beta D}$GlcA*p*	*S. coronata* (h) *S. coronata* subsp. *coronata* (h)	[71] [67]
181	Quercetin 3-*O*-methyl ester	*S. coronata* (h) *S. coronata* subsp. *coronata* (h) *S. tinctoria* (l, st) *S. tinctoria* subsp. *tinctoria* (f) *K. centauroides* subsp. *centauroides* (h) *K. flavescens* subsp. *cichoracea* (f)	[66] [67] [11] [72] [69] [68]
182	Quercetin 3-*O*-methyl ester 4′-*O*-$^{\beta D}$GlcA*p*	*S. coronata* subsp. *coronata* (h)	[67]
183	6-Hydroxykaempferol 4′-*O*-methyl ester	*K. centauroides* subsp. *strangulata* (w)	[21]
184	6-Hydroxykaempferol 4′-*O*-methyl ester 7-*O*-$^{\beta D}$Glc*p*	*K. centauroides* subsp. *strangulata* (w)	[21]
185	6-Hydroxykaempferol 4′-*O*-methyl ester 7-*O*-$^{\beta D}$Gal*p*	*K. centauroides* subsp. *strangulata* (w)	[21]
186	6-Hydroxykaempferol 6,4′-di-*O*-methyl ester	*K. centauroides* subsp. *strangulata* (w)	[21]
187	6-Hydroxykaempferol 6,4′-di-*O*-methyl ester 7-*O*-$^{\beta D}$Glc*p*	*K. centauroides* subsp. *strangulata* (w)	[21]
	Isoflavones		
188	Genistein	*K. centauroides* subsp. *strangulata* (w)	[21]
189	5,7-Dihydroxy-4′-methoxyisoflavone (biochanin A)	*K. centauroides* subsp. *strangulata* (l, r, s)	[41]
190	5,6,7-Trihydroxy-4′-methoxy-isoflavone	*K. centauroides* subsp. *strangulata* (w)	[21]

Table 2. *Cont.*

No	Compound [a]	Species (Organ) [b]	Ref.
	Various phenolics		
191	Strangusin A	*K. centauroides* subsp. *strangulata* (w)	[73]
192	Strangusin B	*K. centauroides* subsp. *strangulata* (w)	[73]
	Thiophenes		
193	5-(1,2-Dihydroxyethyl)-2-[hepten-(5)-diin-(1,3)-yl]-thiophene	*K. radiata* (r)	[74]
194	5-(1,2-Diacetoxyethyl)-2-[hepten-(5)-diin-(1,3)-yl]-thiophene	*K. radiata* (r)	[74]
195	5-(1-Hydroxy-2-acetoxyethyl)-2-[hepten-(5)-diin-(1,3)-yl]-thiophene	*K. radiata* (r)	[74]
	Fatty acids		
196	9:0 (pelargonic acid)	*K. erucifolia* (h)	[75]
197	10:0 (capric acid)	*K. erucifolia* (h) *K. lasiocephala* (h)	[75] [75]
198	12:0 (lauric acid)	*K. centauroides* (h, r) *K. erucifolia* (h) *K. hakkiarica* (h) *K. lasiocephala* (h) *K. radiata* subsp. *biebersteiniana* (h)	[18] [75] [75] [75] [75]
199	14:0 (myristic acid)	*K. centauroides* (h, r) *K. erucifolia* (h) *K. hakkiarica* (h) *K. lasiocephala* (h) *K. radiata* subsp. *biebersteiniana* (h)	[18] [75] [75] [75] [75]
200	15:0 (pentadecanoic acid)	*K. centauroides* (r) *K. erucifolia* (h) *K. hakkiarica* (h) *K. lasiocephala* (h) *K. radiata* subsp. *biebersteiniana* (h)	[18] [75] [75] [75] [75]
201	16:0 (palmitic acid)	*S. coronata* subsp. *coronata* (r) *K. centauroides* (h, r) *K. erucifolia* (h) *K. hakkiarica* (h) *K. lasiocephala* (h) *K. radiata* subsp. *biebersteiniana* (h)	[20] [18] [75] [75] [75] [75]
202	17:0 (margaric acid)	*K. centauroides* (h, r) *K. erucifolia* (h) *K. lasiocephala* (h) *K. radiata* subsp. *biebersteiniana* (h)	[18] [75] [75] [75]
203	18:0 (stearic acid)	*K. centauroides* (h, r) *K. erucifolia* (h) *K. hakkiarica* (h) *K. lasiocephala* (h) *K. radiata* subsp. *biebersteiniana* (h)	[18] [75] [75] [75] [75]
204	19:0 (nonadecanoic acid)	*K. centauroides* (h, r)	[18]
205	20:0 (arachidic acid)	*K. centauroides* (h, r) *K. erucifolia* (h) *K. hakkiarica* (h) *K. lasiocephala* (h) *K. radiata* subsp. *biebersteiniana* (h)	[18] [75] [75] [75] [75]

Table 2. *Cont.*

No	Compound [a]	Species (Organ) [b]	Ref.
206	21:0 (heneicosanoic acid)	*K. centauroides* (h) *K. hakkiarica* (h) *K. lasiocephala* (h)	[18] [75] [75]
207	22:0 (behenic acid)	*K. centauroides* (h, r) *K. hakkiarica* (h) *K. lasiocephala* (h) *K. radiata* subsp. *biebersteiniana* (h)	[18] [75] [75] [75]
208	23:0 (tricosanoic acid)	*K. centauroides* (h, r) *K. lasiocephala* (h)	[18] [75]
209	24:0 (lignoceric acid)	*K. centauroides* (h, r) *K. hakkiarica* (h) *K. lasiocephala* (h) *K. radiata* subsp. *biebersteiniana* (h)	[18] [75] [75] [75]
210	2-OH-24:0 (2-hydroxytetracosanoic acid)	*K. centauroides* (h, r)	[18]
211	25:0 (pentacosanoic acid)	*K. centauroides* (h)	[18]
212	26:0 (cerotic acid)	*K. centauroides* (h, r)	[18]
213	27:0 (carboceric acid)	*K. centauroides* (h)	[18]
214	28:0 (montanic acid)	*K. centauroides* (h)	[18]
215	29:0 (nonacosanoic acid)	*K. centauroides* (h)	[18]
216	30:0 (melissic acid)	*K. centauroides* (h)	[18]
217	14:1n5 (myristoleic acid)	*K. centauroides* (h)	[18]
218	16:1n7 (palmitoleic acid)	*K. erucifolia* (h) *K. radiata* subsp. *biebersteiniana* (h)	[75] [75]
219	16:1n9 (hypogeic acid)	*K. centauroides* (h, r)	[18]
220	17:1 (heptadecenoic acid)	*K. centauroides* (h)	[18]
221	18:1n9 (oleic acid)	*K. centauroides* (h) *K. erucifolia* (h) *K. hakkiarica* (h) *K. lasiocephala* (h) *K. radiata* subsp. *biebersteiniana* (h)	[18] [75] [75] [75] [75]
222	20:1n9 (gondoic acid)	*K. centauroides* (h) *K. hakkiarica* (h)	[18] [75]
223	18:2n6 (linoleic acid)	*S. coronata* subsp. *coronata* (r) *K. centauroides* (h, r) *K. erucifolia* (h) *K. hakkiarica* (h) *K. lasiocephala* (h) *K. radiata* subsp. *biebersteiniana* (h)	[20] [18] [75] [75] [75] [75]
224	18:3n3 (α-linolenic acid)	*S. coronata* subsp. *coronata* (r) *K. centauroides* (h, r) *K. hakkiarica* (h) *K. radiata* subsp. *biebersteiniana* (h)	[20] [18] [75] [75]
225	18:3n6 (γ-linolenic acid)	*K. centauroides* (h, r)	[18]
226	18:4n3 (stearidonic acid)	*K. centauroides* (h)	[18]
227	20:2n6 (eicosadienoic acid)	*K. centauroides* (h, r)	[18]
228	20:4n6 (arachidonic acid)	*K. hakkiarica* (h)	[75]

Table 2. *Cont.*

No	Compound [a]	Species (Organ) [b]	Ref.
229	22:2n6 (docosahexaenoic acid)	*K. centauroides* (h, r)	[18]
230	24:1n9 (nervonic acid)	*K. centauroides* (r) *K. erucifolia* (h) *K. hakkiarica* (h) *K. lasiocephala* (h) *K. radiata* subsp. *biebersteiniana* (h)	[18] [75] [75] [75] [75]
	Glyceroglycolipids		
231	1,2-Di-*O*-(9*Z*,12*Z*,15*Z*-octadecatrienoyl)-3-*O*-(6-amine-6-deoxy-α-D-glucosyl)-glycerol (strangulatoside A)	*K. centauroides* subsp. *strangulata* (rz)	[22]
232	1,2-Di-*O*-(9*Z*,12*Z*,15*Z*-octadecatrienoyl)-3-*O*-(6-*p*-hydroxy-phenyl-propionamido-6-deoxy-α-D-glucosyl)-glycerol (strangulatoside B)	*K. centauroides* subsp. *strangulata* (rz)	[22]
233	1,2-Di-*O*-(9*Z*,12*Z*,15*Z*-octadecatrienoyl)-3-*O*-[α-D-glucose(1→6)-β-D-allose]-glycerol (strangulatoside C)	*K. centauroides* subsp. *strangulata* (rz)	[22]
	Cerebrosides		
234	1-*O*-β-D-Glucopyranosyl-(2*S*,3*R*,8*E*)-2-[(2′*R*)-2-hydroxylpalmitoylamino]-8-octadecene-1,3-diol	*K. chinensis* (r)	[76]
235	1-*O*-β-D-Glucopyranosyl-(2*S*,3*S*,4*R*,8*E*)-2-[(2′*R*)-2-hydroxybehenoyl-amino]-8-octadecene-1,3,4-triol	*K. chinensis* (r)	[76]
236	1-*O*-β-D-Glucopyranosyl-(2*S*,3*S*,4*R*,8*E*)-2-[(2′*R*)-2-hydroxypalmitoyl-amino]-8-octadecene-1,3,4-triol (aralia cerebroside)	*K. chinensis* (r)	[76]
	Amino acids		
237	Alanine	*K. centauroides* (h)	[77]
238	Arginine	*K. centauroides* (h, r)	[77]
239	Histidine	*K. centauroides* (r)	[77]
240	Glycine	*K. centauroides* (h, r)	[77]
241	Lysine	*K. centauroides* (h, r)	[77]
242	Methionine	*K. centauroides* (h)	[77]
243	Phenylalanine	*K. centauroides* (h, r)	[77]
244	Proline	*K. centauroides* (h, r)	[77]
245	Serine	*K. centauroides* (h, r)	[77]
246	Tyrosine	*K. centauroides* (h, r)	[77]
247	Valine	*K. centauroides* (h, r)	[77]
	Alkanes		
248	Tricosane	*K. centauroides* (h)	[18]
249	Pentacosane	*K. centauroides* (h, r)	[24]
250	Heptacosane	*K. centauroides* (h, r)	[18,24]
251	Octacosane	*K. centauroides* (h, r)	[24]
252	Nonacosane	*K. centauroides* (h)	[18]
253	Docosane	*K. centauroides* (h, r)	[24]
254	Triacontane	*K. centauroides* (h, r)	[24]

Table 2. *Cont.*

No	Compound [a]	Species (Organ) [b]	Ref.
255	Hentriacontane	*K. centauroides* (h)	[18]
	Other groups		
256	Tridec-1-ene	*K. centauroides* (r)	[18]
257	Hexadecanol	*K. centauroides* (h, r)	[18]
258	2*E*,4*E*-Heptadienal	*K. centauroides* (r)	[18]
259	Cuparene	*K. centauroides* (h)	[18]
260	Tetradeca-2,12-diene-4,6,8,10-tetrayne	*K. radiata* (r)	[74]
261	Trideca-12-ene-2,4,6,8,10-pentayne	*S. coronata* (r) *K. pinnatifida* (r) *K. radiata* subsp. *radiata* (r)	[14] [14] [14]

[a] Abbreviation used: $^{\beta D}$Gal*p*—β-D-galactopyranose; $^{\beta D}$Glc*p*—β-D-glucopyranose; $^{\beta D}$GlcA*p*—β-D-glucuronopyranose; $^{\alpha L}$Rha*p*—α-L-rhamnopyranose. [b] Plant part: f—flowers; h—herb; l—leaves; r—roots; rz—rhizome; s—seed; st—stems; w—whole plant.

3.1. Mono-, Sesquiterpenes, Sterols and Triterpene Alcohols

One monoterpene geranyl acetate (**1**) and forty-seven sesquiterpenes (**2**–**48**) were detected in essential oils of herbs and roots of *K. centauroides* [18], aerial part of *K. latifolia* [19], roots of *S. coronata* subsp. *coronata* [20] and *K. centauroides* subsp. *strangulata* [21,22]. Non-volatile sesquiterpenes were alantolactone (**2**), carabrone (**12**), costic acid (**18**), three guaianolides **28**–**30**, ivalin (**34**), and pseudoivalin (**39**) from *K. latifolia* [19], and cetaurepensin (**15**) and its ester **16** from *K. centauroides* subsp. *strangulata* [21,22] (Figure 3).

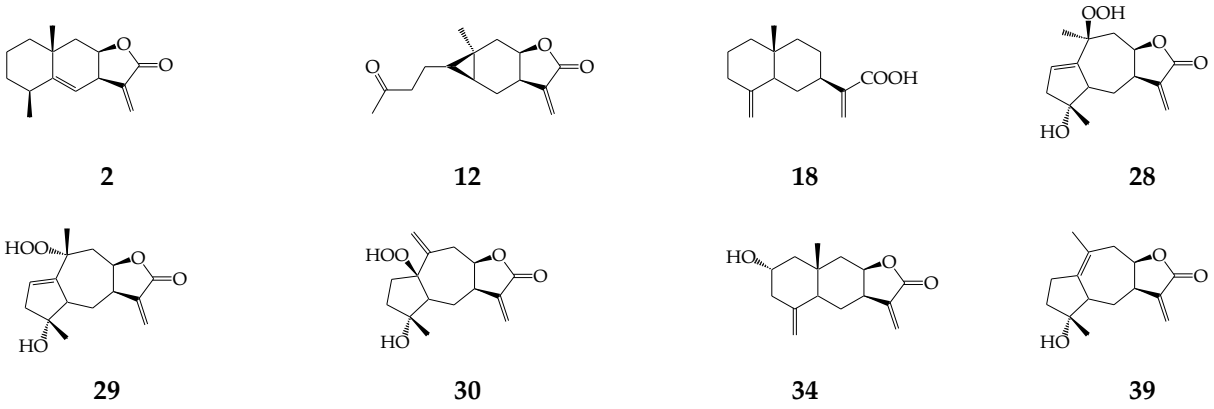
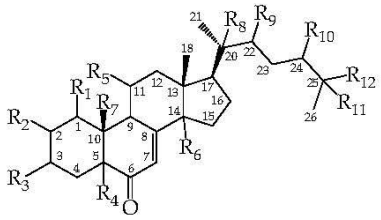


Figure 3. Non-volatile sesquiterpenes (**2**), (**12**), (**18**), (**28**–**30**), (**34**), and (**39**).

Sterols of *S. tinctoria* [23] and *K. centauroides* [24] are derivatives of cholestane (**50**–**52**), ergostane (**49**, **53**), and stigmastane (**54**–**60**), and two triterpene alcohols include α- (**61**) and β-amyrins (**62**) [24].

3.2. Ecdysteroids

To date, 86 ecdysteroids have been isolated from *Serratula* and *Klasea* species (**63**–**148**) (Figure 4). Most compounds have structures with complete side chains, and six compounds are characterized by C-20–C-22 bond breaks (**113**, **116**, **133**, **134**, **136**, and **137**). The presence of a hydroxyl group, free or substituted, at the C-3 position of the steroid nucleus, was noted for all compounds.



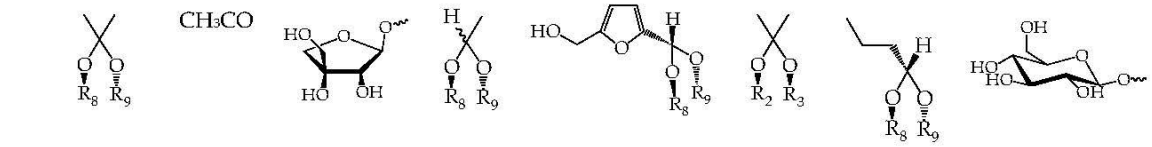
No	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8	R_9	R_{10}	R_{11}	R_{12}
63	H	β-OH	β-OH	β-H	H	α-OH	β-CH_3	β-OH	α-OH	β-OH	OH	CH_3
64	H	β-OH	β-OH	β-H	H	α-OH	β-CH_3	β-OH	α-OH	β-OAc	OH	CH_3
65	H	β-OH	β-OH	β-H	α-OH	α-OH	β-CH_3	β-OH	α-OH	H	H	CH_3
66	H	β-OAc	β-OH	β-H	α-OH	α-OH	β-CH_3	β-OH	α-OH	H	H	CH_3
67	H	β-OH	β-OAc	β-H	α-OH	α-OH	β-CH_3	β-OH	α-OH	H	H	CH_3
68	H	β-OH	β-OH	β-H	α-OAc	α-OH	β-CH_3	β-OH	α-OH	H	H	CH_3
69	H	β-OH	β-OH	β-H	α-OH	α-OH	β-CH_3	A		H	H	CH_3
70	H	β-OH	β-OH	β-H	α-OH	α-OH	β-CH_3	B		H	H	CH_3
71	H	β-OH	β-OH	β-H	α-OH	α-OH	β-CH_3	β-OH	β-OH	H	H	CH_3
73	H	β-OH	β-OH	β-H	α-OH	α-OH	β-CH_3	β-OH	α-OH	=CH_2	OH	CH_3
76	H	H	α-OH	β-H	H	α-OH	β-CH_3	β-OH	α-OH	H	OH	CH_3
78	H	β-OH	β-OH	β-H	H	α-OH	β-CH_3	β-OH	α-OH	=CH_2	OH	CH_3
79	H	β-OH	β-OH	β-H	α-OH	α-OH	β-CH_3	H	C=O	H	H	CH_3
80	H	H	α-OH	β-H	H	α-OH	β-CH_3	β-OH	α-OH	H	OH	CH_3
81	H	H	β-OH	β-H	H	α-OH	β-CH_3	β-OH	α-OH	H	OH	CH_3
82	H	β-OH	α-OH	β-H	H	α-OH	β-CH_3	β-OH	H	H	OH	CH_3
83	H	β-OH	β-OH	β-H	H	α-OH	β-CH_3	β-OH	H	H	OH	CH_3
86	H	β-OH	β-OH	β-H	α-H	α-OH	β-CH_3	β-OCH_3	α-OH	H	H	CH_3
87	H	β-OH	β-OH	β-H	H	α-OH	β-CH_3	β-OH	α-OH	H	H	=CH_2
89	H	β-OH	β-OH	β-H	H	α-OH	β-CH_3	H	α-OH	H	OH	CH_3
94	H	β-OH	β-OH	β-H	H	α-OH	β-CH_3	β-OH	α-OH	H	OH	CH_3
95	H	β-OH	β-OH	β-H	H	α-OH	β-CH_3	A		H	OH	CH_3
96	H	D		β-H	H	α-OH	β-CH_3	A		H	OH	CH_3
97	H	β-OH	β-OH	β-H	H	α-OH	β-CH_3	B		H	OH	CH_3
98	H	β-OGlc	β-OH	β-H	H	α-OH	β-CH_3	β-OH	α-OH	H	OH	CH_3
99	H	β-OGal	β-OH	β-H	H	α-OH	β-CH_3	β-OH	α-OH	H	OH	CH_3
100	H	β-OH	β-OH	β-H	H	α-OH	β-CH_3	β-OH	α-OH	H	OGlc	CH_3
101	H	β-OAc	β-OH	β-H	H	α-OH	β-CH_3	β-OH	α-OH	H	OH	CH_3
102	H	β-OH	β-OAc	β-H	H	α-OH	β-CH_3	β-OH	α-OH	H	OH	CH_3
103	H	β-OGlc	β-OAc	β-H	H	α-OH	β-CH_3	β-OH	α-OH	H	OH	CH_3
104	H	β-OGal	β-OAc	β-H	H	α-OH	β-CH_3	β-OH	α-OH	H	OH	CH_3
105	H	β-OH	β-OH	β-H	H	α-OH	β-CH_3	β-OH	α-OAc	H	OH	CH_3
106	H	β-OAc	β-OH	β-H	H	α-OH	β-CH_3	β-OH	α-OAc	H	OH	CH_3
107	H	β-OH	β-OAc	β-H	H	α-OH	β-CH_3	β-OH	α-OAc	H	OH	CH_3
108	H	β-OH	β-OH	β-H	H	α-OH	β-CH_3	E		H	OH	CH_3
109	H	β-OH	α-OH	β-H	H	α-OH	β-CH_3	β-OH	α-OH	H	OH	CH_3
110	H	β-OH	β-OH	α-H	H	α-OH	β-CH_3	β-OH	α-OH	H	OH	CH_3
111	H	β-OH	β-OH	β-H	H	β-OH	β-CH_3	β-OH	α-OH	H	OH	CH_3
112	H	β-OH	β-OH	β-H	H	α-OH	β-CH_3	β-OH	β-OH	H	OH	CH_3
115	H	β-OH	β-OH	β-H	H	α-OH	β-CH_3	β-OH	α-OH	CH_2CH_2OH	OH	CH_3
118	H	β-OH	β-OH	β-H	α-OH	α-OH	β-CH_3	β-OH	α-OH	H	H	=CH_2
119	H	β-OH	β-OH	β-H	H	α-OH	β-CH_3	β-OH	α-OH	H	H	CH_2OH
120	H	β-OH	β-OH	β-H	H	α-OH	β-CH_3	β-OH	α-OH	H	H	OAc
121	β-OH	β-OH	β-OH	β-H	H	α-OH	β-CH_3	β-OH	α-OH	H	OH	CH_3
122	H	β-OH	β-OH	β-H	H	α-OH	β-CH_3	β-OH	α-OH	β-CH_3	OH	CH_3
123	H	β-OH	β-OH	β-H	H	α-OH	β-CH_3	β-OH	α-OH	C_2H_5	OH	CH_3
125	H	β-OH	β-OH	β-H	H	α-OH	β-CH_3	β-OH	C=O	H	OH	CH_3
126	H	β-OH	α-OH	β-H	H	α-H	β-CH_3	β-OH	β-OH	H	OH	CH_3
127	H	β-OH	α-OH	β-H	H	β-H	β-CH_3	β-OH	β-OH	H	OH	CH_3
128	H	β-OH	β-OH	β-H	H	α-OH	β-CH_3	β-OH	α-OH	H	OH	CH_2OH
129	H	β-OH	β-OH	β-OH	H	α-OH	β-CH_3	β-OH	α-OH	H	OH	CH_3
130	H	β-OH	β-OH	β-OH	H	α-OH	β-CH_3	A		H	OH	CH_3
131	H	β-OH	β-OH	β-H	H	α-OH	β-CH_3	β-OH	α-OH	H	H	CH_3
132	H	β-OH	β-OH	β-H	H	α-OH	β-CH_3	β-OH	α-OApi	H	H	CH_3

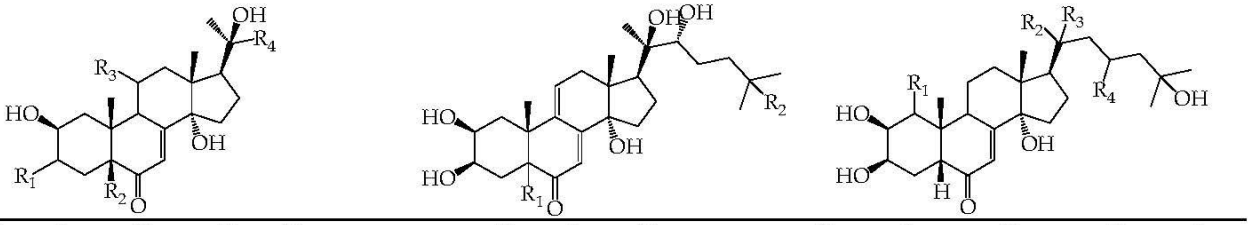
Figure 4. *Cont.*

135	H	β-OH	β-OH	β-H	H	α-OH	β-CH_3	β-OH		α-OH	α-OH	H	CH_3
138	H	β-OH	β-OH	β-H	H	α-OH	β-CH_3		C		H	OH	H
139	H	β-OH	β-OH	β-H	α-OH	α-OH	β-CH_3		C		H	H	CH_3
142	H	β-OH	β-OH	β-H	H	α-OH	β-CH_2OH	β-OH		α-OH	H	OH	CH_3
146	H	β-OH	β-OH	β-H	H	α-OH	β-CH_3	β-OH		H	H	OH	CH_3
147	H	β-OH	β-OH	β-H	α-OH	α-OH	β-CH_3	β-OH		α-OH	H	OH	CH_3
148	H	β-OH	β-OH	β-H	H	α-OH	β-CH_3	β-OH		α-OH	H	Ac	CH_3

Substituents

A Ac Api B C D E Glc

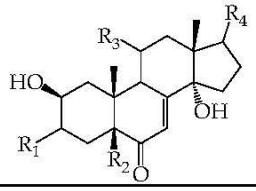




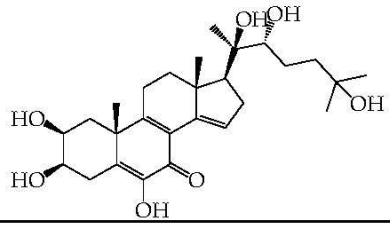
No	R_1	R_2	R_3	R_4
72	β-OH	β-OH	H	F
74	β-OH	H	H	G
114	β-OH	H	α-OH	F
124	β-OH	H	H	I
140	β-OH	H	H	F
141	α-OH	H	H	H

No	R_1	R_2
77	β-H	H
91	β-OH	OH
93	β-H	OH

No	R_1	R_2	R_3	R_4
84	H	α-CH_2OH	β-OH	H
85	H	=CH_2	H	H
90	H	α-CH_3	β-OH	α-OH
92	β-OH	=CH_2	H	H



No	R_1	R_2	R_3	R_4
113	β-OH	H	α-OH	β-$COCH_3$
116	β-OH	OH	H	C=O
133	β-OH	H	H	β-$COCH_3$
134	α-OH	H	H	β-$COCH_3$
136	β-OH	H	H	C=O
137	α-OH	H	H	C=O



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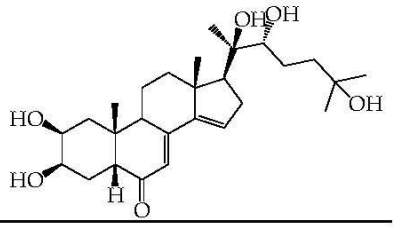

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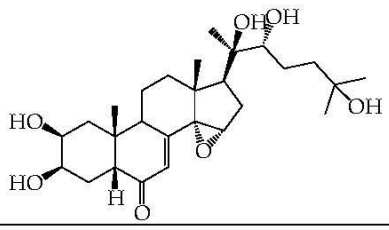

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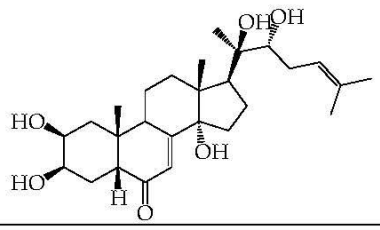

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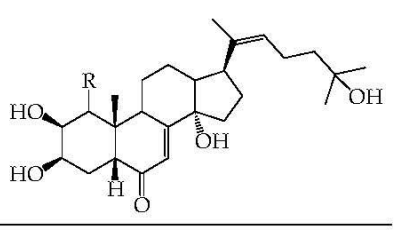


No	R
88	H
117	β-OH

Figure 4. *Cont.*

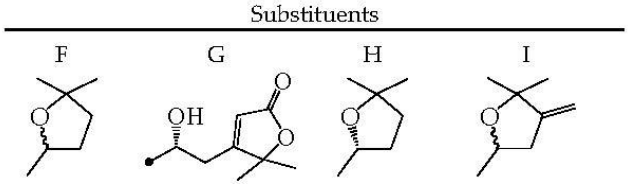


Figure 4. Ecdysteroids **66**–**148**.

The frequently encountered positions of the hydroxyl group also include C-2 (82 comp.), C-14 (76 comp.), C-20 (64 comp.), C-22, and C-25 (54 comp. each). Components with a hydroxy function at positions C-1 (2 comp.), C-24 (3 comp.), C-5 (5 comp.), and C-11 (14 comp.) are rare. The keto group at C-6 is an obligatory structural feature of all phytoecdysteroids, except calonisterone (**75**) from *S. coronata* [32] has a hydroxyl in this position. Component **75** also differs from other compounds in the presence of an unsaturated Δ^{5-6} bond, which is uncharacteristic of other compounds with an unsaturated Δ^{7-8} bond. The presence of the Δ^{9-11} dehydro function was found in herkesterone (**91**), dacryhainansterone (**77**), and its 25-hydroxy derivative (**93**), while stachysterone B (**143**) has an unsaturated Δ bond[14–15]. The presence of a large number of hydroxyl groups in the structures of phytoecdysteroids indicates the possibility for the synthesis of conjugates, esters, and other derivatives in plants. The formation of monoesters with acetic acid was revealed for ajugasterone C (**65**) at positions C-2 (**66**), C-3 (**67**), and C-11 (**68**), for inokosterone (**119**) at position C-26 (**120**), as well as for 20-hydroxyecdysone (**94**) at positions C-2 (**101**), C-3 (**102**), C-22 (**105**), and C-25 (**148**). Two 20-hydroxyecdysone diacetates were isolated from *S. tinctoria* containing acyl groups at C-2 and C-22 (**106**) and C-3 and C-22 (**107**) [49]. The existence of 1,2-diol fragments in the structures of ajugasterone C (**65**), polypodin B (**129**), and 20-hydroxyecdysone (**94**) at C2–C3 and C20–C22 allows the existence of isopropylidene ketals in the form of monoacetonides **69**, **95**, and **130** and diacetonide **96** found in *S. chinensis* [25], *S. coronata* [29,30,33], and *S. strangulata* [42]. Ethylidene-substituted ajugasterone C (**70**) and 20-hydroxyecdysone (**97**) were identified as components of *S. tinctoria* [33], while 20,22-*O*-butylidene-acetal of 20-hydroxyecdysone (**108**) was found in *S. chinensis* [25,34].

The side chain of some compounds may contain a furan ring attached via an ethylidene group to the C-20–C-22 diol fragment, as in serfusterone A (**138**) and serfusterone B (**139**) from *S. coronata* [57]. In ajugasterone D (**72**), shidasterone (**140**), and its derivatives **114**, **124**, and **141** from *S. chinensis* [25,34] and *S. coronata* [40,55,56], the furan fragment is present at C-22, as in carthamosterone (**74**) from *S. chinensis* at C-24 [25,34]. The only 14,15-epoxide of stachysterone B (**144**) was found in *S. coronata* [56]. Glycosides of phytoecdysteroids remain a rare group of derivatives for the genera *Serratula* and *Klasea*. The isolations of ponasterone A 22-*O*-apioside (**132**) from *S. coronata* [40] and 2-*O*- (**98**), 25-*O*-glucosides 20-hydroxyecdysone (**100**) [25], 2-*O*-galactoside 20-hydroxyecdysone (**99**), 2-*O*-glucoside (**103**), and 2-*O*-galactoside (**104**) of 20-hydroxyecdysone 3-*O*-acetate from *S. chinensis* [26] have been found. In general, the phytoecdysteroids *Serratula* and *Klasea* are characterized by the presence of a complete side chain and a large number of hydroxyl groups (5–7) both in the steroid core and in the side chain.

The content of ecdysteroids varied in plant organs of *Serratula* and *Klasea* species (Table 3). A high level of 20-hydroxyecdysone (190.1 mg/g) and polypodine B (35.8 mg/g) was detected in *S. coronata* extract [78], and 20-hydroxyecdysone was quantified in *S. coronata* subsp. *coronata* leaves (1.0–8.5 mg/g) and stems (0.2–3.4 mg/g) [79,80] and in *S. tinctoria* leaves (1.6–13.4 mg/g) [79]. Three *Klasea* species showed a high content of 20-hydroxyecdysone in leaves (8.8–16.8 mg/g) [35,38], stems (4.5–14.2 mg/g) [35,38], and seeds (4.7–5.5 mg/g) [39,41]. The minor *Klasea* ecdysteroids are integristerone A (0.02–2.20 mg/g) [35,38,39], 2-desoxy-20-hydroxyecdysone (0.1–2.9 mg/g) [35,38,39], and inokosterone (0.9–2.5 mg/g) [35,59].

Table 3. Ecdysteroid content in *Serratula* (*S.*) and *Klasea* (*K.*) species [a].

Species	20-Hydroxyecdysone	Integristerone A	2-Desoxy-20-hydroxyecdysone	Polypodine B	Inokosterone
S. coronata	18.4 mg/g (s) [27] 190.1 mg/g (e) [78]			35.8 mg/g (e) [78]	
S. coronata subsp. *coronata*	1.0–8.5 mg/g (l) [79,80] 0.2–3.4 mg/g (st) [80]				
S. tinctoria	1.6–13.4 mg/g (l) [79]				
K. centauroides	1.5–6.5 mg/g (f) [35,38] 10.1 mg/g (h) [50] 8.8–16.8 mg/g (l) [35,38] 0.5 mg/g (r) [50] 4.5–14.2 mg/g (st) [35,38] 27.4 mg/g (e) [59]	0.1–1.3 mg/g (f) [35,38] 2.2 mg/g (h) [50] 0.1–1.6 mg/g (l) [35,38] 0.1 mg/g (r) [50] 0.1–1.3 mg/g (st) [35,38]	0.9–1.1 mg/g (f) [35,38] 1.8 mg/g (h) [50] 1.0–2.9 mg/g (l) [35,38] 0.1 mg/g (r) [50] 1.0–3.2 mg/g (st) [35,38]		0.9 mg/g (f) [35] 2.5 mg/g (l) [35] 1.1 mg/g (st) [35] 5.7 mg/g (e) [59]
K. centauroides subsp. *centauroides*	0.7 mg/g (f) [39] 0.1–3.1 mg/g (l) [39] 0.6–1.5 mg/g (r) [39] 4.7 mg/g (s) [39] 0.1–2.9 mg/g (st) [39]	23–150 µg/g (l) [39] 30–94 µg/g (r) [39] 20–24 µg/g (st) [39]	0.1–0.4 mg/g (l) [39] 0.3–0.5 mg/g (r) [39] 0.8 mg/g (s) [39] 0.1–0.2 mg/g (st) [39]		
K. centauroides subsp. *strangulata*	0.7 mg/g (l) [41] 0.6 mg/g (r) [41] 5.5 mg/g (s) [41]				

[a] Sample: f—flowers; l—leaves; r—roots; s—seeds; st—stems; e—extract.

3.3. Distribution of Ecdysteroids in the Genera Serratula and Klasea

Data on the presence of phytoecdysteroids in the genus *Serratula* are known for % species, as well as for 14 species of the genus *Klasea*. Literature reports indicate that *S. coronata* subsp. *coronata* (*S. wolffii*, *S. manshurica*) is the most studied species in which 42 compounds were found (Table 4).

The probable reason for this interest is the availability of raw materials, which are widely distributed in Europe, European Russia, Siberia, and the Far East. From *S. chinensis*, *S. coronata*, and *S. tinctoria*, 23, 21, and 18 compounds were isolated, respectively. For the majority of species studied, information on the presence of ecdysteroids is limited to the presence of 20-hydroxyecdysone (**94**) and two to three other compounds. Such information cannot be considered sufficient for understanding the biological functions of these compounds for a plant or revealing the chemotaxonomic features of their accumulation within the genus; therefore, additional research is needed in this area. Considering the distribution of individual compounds among species, the most common is 20-hydroxyecdysone (**94**) found in all studied species. Inokosterone (**119**), polypodin B (**129**), and viticosterone E (**148**) were found in five species; ecdysone (**89**), integristerone A (**121**), and makisterone C (**123**) were found in four species; ajugasterone C (**65**), 20-hydroxyecdysone 20,22-monoacetonide (**95**), and 20-hydroxyecdysone 2-*O*-, 3-*O*- and 22-*O*-acetates (**101**, **102**, **105**) were found in three species.

Table 4. Ecdysteroid distribution on *Serratula* and *Klasea* species.

Species	Total Count	Compound Numbers
	Serratula	
S. coronata	21	**65–70, 75, 77, 80, 94, 95, 97, 101, 102, 105, 120, 121, 123, 129, 149, 148**
S. coronata subsp. *coronata*	42	**65, 69, 72, 77, 79, 82–85, 88, 89, 91–96, 109–114, 117, 118, 121–124, 126–129, 131, 132, 135, 138, 139, 141, 143, 144, 147**
S. kirghisorum	1	**94**
S. tinctoria	18	**90, 94, 101, 102, 105–107, 112, 116, 123, 125, 129, 133–137, 148**
S. tinctoria subsp. *tinctoria*	1	**94**
	Klasea	
K. algida	1	**94**
K. cardunculus	1	**94**
K. centauroides	10	**78, 81, 94, 95, 105, 118, 119, 121, 123, 148**
K. centauroides subsp. *centauroides*	3	**81, 94, 121**
K. centauroides subsp. *strangulata*	4	**86, 94, 95, 115**
K. chinensis	23	**63, 64, 72–74, 76, 87, 94, 95, 98–104, 108, 124, 128–130, 140, 145**
K. ericifolia	2	**94, 121**
K. flavescens subsp. *cichoracea*	3	**94, 65, 71**
K. lycopifolia	3	**89, 94, 119**
K. procumbens	2	**94, 148**
K. quinquefolia	3	**94, 119, 129**
K. radiata	3	**89, 94, 119**
K. radiata subsp. *gmelinii*	3	**89, 94, 119**
K. sogdiana	3	**94, 142, 148**

3.4. Phenols and Hydroxycinnamates

Arbutin (hydroquinone *O*-glucoside; **149**), a rare Asteraceae metabolite, which was detected in only nine *Klasea* species [15,62–64] and never in *Serratula*, was also found in other Centaureinae members, such as *Centaurea* [41] and *Stizolophus* [81] (Figure 5). The known data demonstrated the high level of arbutin in *K. centauroides* subsp. *centauroides* leaves (3.3%) and stems (0.5%) [61] and in *K. centauroides* herb extract (2.5%) [59]. One thymol derivative, **150**, was isolated from the *K. latifolia* herb [19]. The known hydroxycinnamates of *Serratula* and *Klasea* include caffeic acid (**151**) and caffeoylquinic acids (**152–158**) found in *S. tinctoria* [65] and three klaseas [47,59].

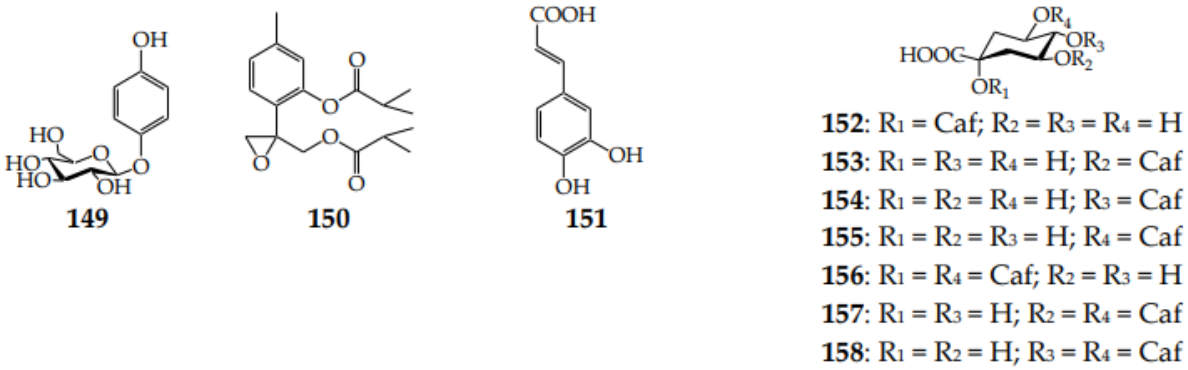
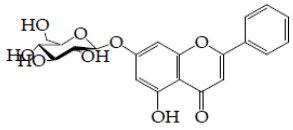


Figure 5. Phenols **149** and **150** and hydroxycinnamates **151–158**. Caf–caffeoyl.

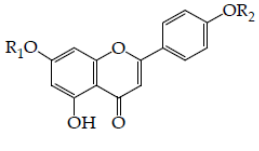
3.5. Flavonoids

Three groups of flavonoids, including flavones (**159–170**), flavonols (**171–187**), and isoflavones (**188–190**), are distributed in different organs of four serratulas and seven klaseas (Figure 6). Flavones are derivatives of chrysin (**159**) [47], apigenin (**160**, **161**) [16,67,68], acacetin (**162**) [68], genkwanin (**163**) [68], luteolin (**164–168**) [67,70], diosmetin (**169**) [65], and chrysoeriol (**170**) [69] in the form of aglycones (6 comp.) and *O*-glycosides (7 comp.). All

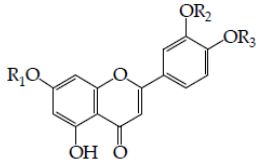
glycosides have one carbohydrate (monoglycosides) that is β-D-glucose or β-D-glucuronic acid attached at the C-7 or C-4′ position of aglycone. The most common flavone is luteolin (**164**), found in three *Serratula*, and three *Klasea*, followed by the apigenin (**160**) and apigenin 7-*O*-glucuronide detected in four and three species, respectively. The highest number of flavones have been found in *K. centauroides* (5 comp.), with four found in *S. coronata* subsp. *coronata*, *K. centauroides* subsp. *centauroides*, and *K. flavescens* subsp. *cichoriacea*, three found in *S. tinctoria*, and two found in *S. coronata* and *S. tinctoria* subsp. *tinctoria*. The chemodiversity of seventeen flavonols include derivatives of kaempferol (**171**, **172**) [63], its methyl esters at the C-3 (kaempferide, **173**) [14], C-4′ (**174**, **175**) [21] and C-7/C-4′ positions (**176**) [21], quercetin (**177**–**180**) [70] and 3-*O*-methyl ester (**181**, **182**) [11], 6-hydroxykaempferol 4′-*O*-methyl ester (**183**–**185**) [21], and 6,4′-di-*O*-methyl ester (**186**, **187**) [21].



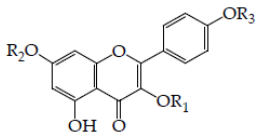
159



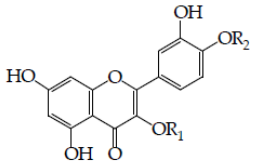
160: $R_1 = R_2 = H$
161: $R_1 = {}^{\beta D}GlcAp$; $R_2 = H$
162: $R_1 = CH_3$; $R_2 = H$
163: $R_1 = H$; $R_2 = CH_3$



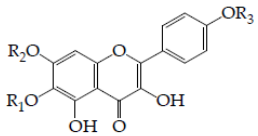
164: $R_1 = R_2 = R_3 = H$
165: $R_1 = {}^{\beta D}Glcp$; $R_2 = R_3 = H$
166: $R_1 = {}^{\beta D}GlcAp$; $R_2 = R_3 = H$
167: $R_1 = R_2 = H$; $R_3 = {}^{\beta D}Glcp$
168: $R_1 = R_2 = H$; $R_3 = {}^{\beta D}GlcAp$
169: $R_1 = R_2 = H$; $R_3 = CH_3$
170: $R_1 = R_3 = H$; $R_2 = CH_3$



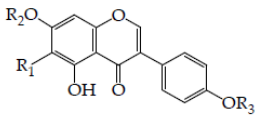
171: $R_1 = R_2 = R_3 = H$
172: $R_1 = (6''\text{-}O\text{-}{}^{\alpha L}Rhap)\text{-}{}^{\beta D}Glcp$; $R_2 = R_3 = H$
173: $R_1 = CH_3$; $R_2 = R_3 = H$
174: $R_1 = R_2 = H$; $R_3 = CH_3$
175: $R_1 = {}^{\beta D}Glcp$; $R_2 = H$; $R_3 = CH_3$
176: $R_1 = H$; $R_2 = R_3 = CH_3$



177: $R_1 = R_2 = H$
178: $R_1 = (6''\text{-}O\text{-}{}^{\alpha L}Rhap)\text{-}{}^{\beta D}Glcp$; $R_2 = H$
179: $R_1 = H$; $R_2 = {}^{\beta D}Glcp$
180: $R_1 = H$; $R_2 = {}^{\beta D}GlcAp$
181: $R_1 = CH_3$; $R_2 = H$
182: $R_1 = CH_3$; $R_2 = {}^{\beta D}GlcAp$



183: $R_1 = R_2 = H$; $R_3 = CH_3$
184: $R_1 = H$; $R_2 = {}^{\beta D}Glcp$; $R_3 = CH_3$
185: $R_1 = H$; $R_2 = {}^{\beta D}Galp$; $R_3 = CH_3$
186: $R_1 = R_3 = CH_3$; $R_2 = H$
187: $R_1 = R_3 = CH_3$; $R_2 = {}^{\beta D}Glcp$



188: $R_1 = R_2 = R_3 = H$
189: $R_1 = R_2 = H$; $R_3 = CH_3$
190: $R_1 = OH$; $R_2 = H$; $R_3 = CH_3$

Figure 6. Flavonoids **159**–**190**. ${}^{\beta D}Galp$–β-D-galactopyranose; ${}^{\beta D}Glcp$–β-D-glucopyranose; ${}^{\beta D}GlcAp$–β-D-glucuronopyranose; ${}^{\alpha L}Rhap$–α-L-rhamnopyranose.

Seven glycosides are monoglycosides with β-D-glucose (**175**, **179**, **184**, and **187**), β-D-galactose (**185**), and β-D-glucouronic acid (**180** and **182**) at the C-7 and C-4′ positions, and two biosides **172** and **178** containing rutinose moiety were found. From *K. centauroides* subsp. *strangulata*, eight compounds were isolated, and five flavonols were detected in *S. coronata* subsp. *coronata*; however, in other species, no more than two compounds were found. Non-glycosidic quercetin 3-*O*-methyl ester and quercetin have been described in five and four species, respectively. Additionally, three isoflavones have been mentioned for the whole plant of *K. centauroides* subsp. *strangulata* [21,41]. The total contents of flavonoids in wild *S. coronata* leaves and stems are 6.7–8.3% and 0.5–0.9%, respectively [71]; in *S. tinctoria* leaves, they are 1.2–1.6% [11], and in *K. centauroides* subsp. *centauroides* leaves, flowers, and stems, they are 9.0%, 4.6%, and 2.0%, respectively [69]. The dominant flavonoids in *K. centauroides* subsp. *centauroides* after HPLC quantification are apigenin-7-*O*-glucuronide (**161**) in flowers (1.1%), and luteolin-7-*O*-glucuronide (**166**) in leaves (4.9%) and stems (1.2%) [69].

3.6. Other Groups

Lignan strangusin A (**191**) and phenolic glycoside strangusin B (**192**) have been isolated from the whole herb of *K. centauroides* subsp. *strangulata* [73]. The lipophilic nature metabolites include thiophenes **193**–**195** from *K. radiata* roots [74], fatty acids (**196**–**230**) from *S. coronata* subsp. *coronata* [20] and five klaseas [18,75], three rare glycerolipids strangulatosides A (**231**), B (**232**), and C (**233**) from *K. centauroides* subsp. *strangulata* rhizomes [22], rare cerebrosides **234**–**236** from *K. chinensis* roots [76], alkanes **248**–**255** found in essential oils of *K. centauroides* [18,24] and other groups (**256**–**261**) (Figure 7). Additionally, 11 amino acids were quantified in the herb and roots of *K. centauroides* [77].

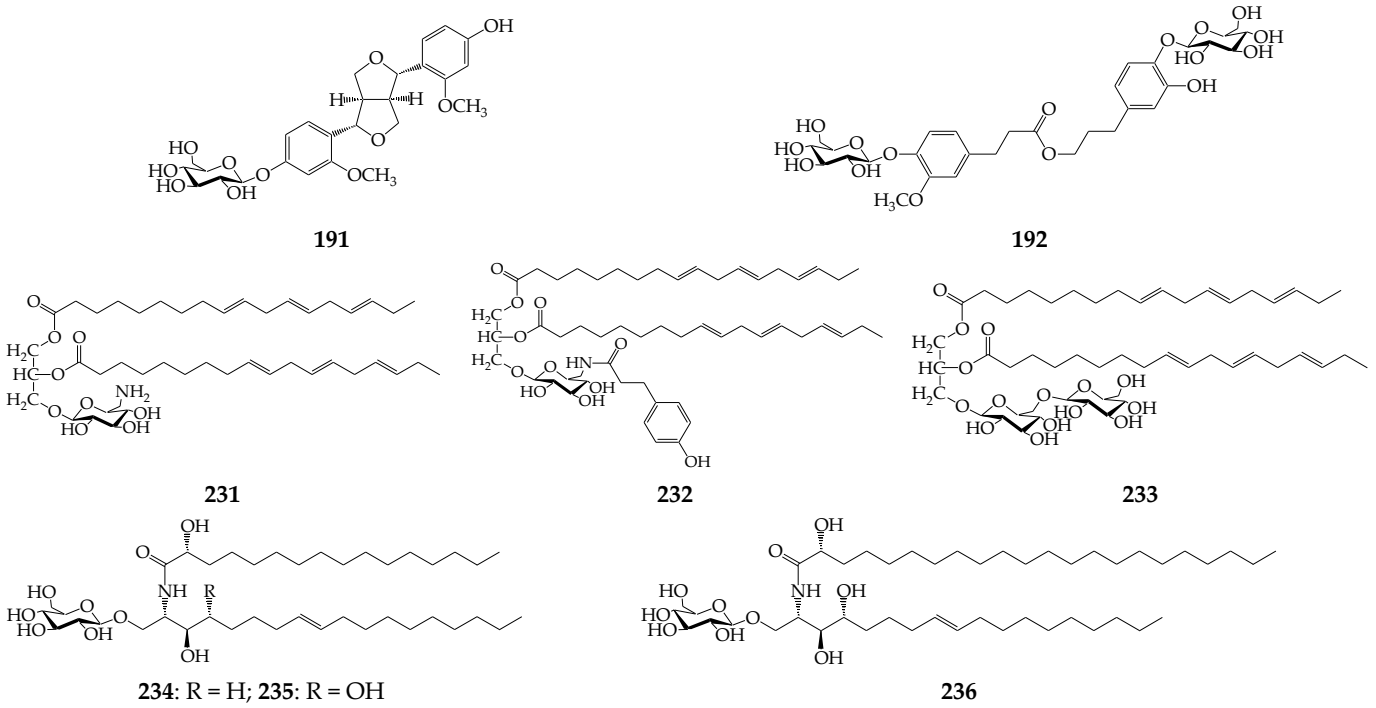


Figure 7. Strangusin A (**191**), strangusin B (**192**), glycerolipids (**231**–**233**), and cerebrosides (**234**–**236**).

4. Extraction and Separation of Ecdysteroids and Flavonoids of *Serratula* и *Klasea*

Despite the diversity of metabolites found in *Serratula* and *Klasea*, the real highlights are ecdysteroids and flavonoids, featuring the most frequently isolated and separated compounds with proven data about their bioactivity, making them valuable metabolites (Figure 2). Sesquiterpenes and fatty acids have been characterized after a routine chromatographic procedure by gas chromatography-mass spectrometry (GC-MS) and have been described elsewhere. For other compounds, it is too early to draw conclusions about the features of isolation and separation.

4.1. Ecdysteroids

The general isolation procedure for *Serratula* and *Klasea* ecdysteroids includes the steps of extracting plant materials, followed by liquid–liquid/solid-phase extraction and/or purification of the resulting extract to obtain target-enriched fractions for which chromatographic separation is performed (Table 5). Herb and roots used for the extraction and the main solvents are low-molecular-weight alcohols (ethanol and methanol) as well as water. In rare cases, extraction is performed from freshly squeezed plant juice to prevent the thermal degradation of compounds [32,33,52,54]. Depending on the tasks set, the extraction temperature can vary from 0 °C [38] to the boiling point of the extractant [53,55,56,60]. After extraction and additional concentration, the aqueous residue is subjected to liquid–liquid extraction by lipophilic organic solvents (e.g., petroleum ether and hexane) to remove interfering lipophilic components.

Table 5. Extraction conditions of ecdysteroid from *Serratula* and *Klasea* plant material.

Species	Source, Solvent, Extraction Conditions *	Ref.
S. coronata	Leaves → H_2O-extr. (1:10; 50 °C) → LLE EtOAc–MeOH (4:1)/H_2O → EtOAc–MeOH-extr. RP-APC (Diasorb 130 C_{16} T), prep. RP-HPLC (Diasorb 130 C_{16} T)	[28]
	Herb → EtOH-extr. (1:6) → LLE $CHCl_3$/H_2O, BuOH/H_2O → BuOH-extr. NP-APC (Al_2O_3, SiO_2)	[29]
	Herb juice → LLE EtOAc/H_2O → EtOAc-extr. NP-APC (SiO_2), prep. TLC (SiO_2)	[32,33,54]
	Herb → MeOH-extr. (1:10; 20 °C) → dissol. MeOH → mixing with Me_2CO → LLE Hex/H_2O → water phase NP-APC (SiO_2, polyamide), prep. NP-HPLC (Zorbax SIL), RP-HPLC (Zorbax-ODS), APC Sephadex LH-20	[30]
	Roots → MeOH-extr. (1:10; 20 °C) → RP-APC (octadecyl silica), prep. NP-HPLC (Zorbax SIL), RP-HPLC (Zorbax SB C18)	[36,40,49,57,58]
S. tinctoria	Herb → MeOH-extr. (boiling) → LLE Benz/H_2O → LLE Benz-extr./50% MeOH → MeOH-extr. mixing with Me_2CO → NP-APC (Al_2O_3, SiO_2), prep. RP-TLC (RP-18 $F_{254}S$)	[45]
	Roots → MeOH-extr. (1:17; boiling) → LLE Benz/H_2O → LLE Benz.-extr./50% MeOH → MeOH-extr. NP-APC (Al_2O_3, SiO_2, Sephadex LH-20, polyamide), prep. NP-HPLC (Zorbax SIL), RP-HPLC (Spherisorb®-50DS2)	[49]
K. centauroides	Roots, herb → 70% EtOH-extr. (1:25–1:50; 0 °C) → SPE → NP-APC (SiO_2), RP-HPLC (LiChrospher PR-18), RP-HPLC (LiChrospher PR-18)	[35,38]
K. chinensis	Roots → 95% EtOH-extr. (20 °C) → LLE PE/H_2O, $CHCl_3$/H_2O, BuOH/H_2O → BuOH-extr. NP-APC (SiO_2, Sephadex LH-20), RP-HPLC (Diaion HP-20)	[34]
K. erucifolia	Flowers → MeOH-extr. (20 °C) → LLE Hex/H_2O, BuOH/H_2O → BuOH-extr. NP-APC (Al_2O_3, SiO_2)	[51]
K. quinquefolia	Herb juice → LLE EtOAc/H_2O → EtOAc-extr. NP-APC (Al_2O_3, SiO_2)	[52]
K. sogdiana	Flowers → EtOH-extr. (boiling) → NP-APC (Al_2O_3, SiO_2)	[53]
	Leaves → MeOH-extr. (1:6; boiling) → LLE PE/H_2O, BuOH/H_2O → BuOH-extr. NP-APC (polyamide), LP-RP-CC (octadecyl silica), prep. NP-HPLC (SiO_2)	[55,60]

* APC—atmospheric pressure chromatography; CC—column chromatography; dissol.—dissolving; extr.—extract; filtr—filtration; LLE—liquid–liquid extraction (upper solvent/lower solvent); LP—low pressure; NP—normal-phase; prep.—preparative; RP—reversed-phase; SPE—solid phase extraction; TLC—thin layer chromatography. Solvents: Benz—benzene; BuOH—*n*-butanol; $CHCl_3$—chloroform; EtOAc—ethyl acetate; EtOH—ethanol; Hex—hexane; MeOH—methanol; PE—petroleum ether.

Liquid–liquid extraction of target compounds is performed, as a rule, with ethyl acetate or *n*-butanol. In rare cases, multistage purification schemes of plant extracts are used, including multiple precipitations of ballast components from a methanol solution using acetone [30]. As an additional stage of purification, the procedure of liquid–liquid extraction of ecdysteroids by benzene followed by re-extraction of the organic phase with 50% methanol can be applied [49]. As the final stage of the purification, the solid-phase extraction [38] or ion exchange [34] leads to better results.

To isolate separate compounds from the mixture, it is not enough to use extraction procedures. An obligatory step is a chromatographic separation, various variants of which are widely used for the study of *Serratula* and *Klasea* ecdysteroids (Table 6).

Table 6. Chromatographic conditions used for the separation of *Serratula* и *Klasea* ecdysteroids.

Sorbent, Column	Eluent	Ref.
Atmospheric Pressure Chromatography		
Al_2O_3	$CHCl_3$-MeOH (30:1)	[55,60]
	$CHCl_3$-MeOH (10:1)	[51]
	$CHCl_3$-MeOH (2:1, 15:1)	[29]
	$CHCl_3$-MeOH	[28]
	$CHCl_3$-MeOH (95:5 → 90:10); CH_2Cl_2-EtOH (90:10 → 70:30); $CHCl_3$-EtOH (90:10 → 60:40)	[30]
	EtOAc-EtOH-H_2O (80:10:2)	[56]
	EtOAc-MeOH-H_2O (85:10:5)	[49]
SiO_2	$CHCl_3$-EtOH (90:10)	[53]
	$CHCl_3$-MeOH (90:10)	[34]
	$CHCl_3$-MeOH (20:1)	[32]
	$CHCl_3$-MeOH (10:1)	[52]
	$CHCl_3$-MeOH (5:1)	[54]
	$CHCl_3$-MeOH (25:1), $CHCl_3$-MeOH (10:1 → 5:1)	[33]
	$CHCl_3$-MeOH (25:1, 9:1, 4:1); $CHCl_3$-MeOH-H_2O (4:1:0.1)	[29]
	$CHCl_3$-MeOH-H_2O (60:32:6)	[51]
	CH_2Cl_2; CH_2Cl_2-EtOH (98:2 → 80:20)	[56]
	CH_2Cl_2-EtOH (90:10 → 50:50)	[49]
	EtOAc-MeOH-H_2O (85:10:5); CH_2Cl_2; CH_2Cl_2-EtOH (98:2 → 90:10); MeOH	[30]
	MeOH-H_2O (55:45)	[40]
	MeOH-H_2O (50:40)	[57,58]
	MeOH-H_2O (45:55)	[45]
Sephadex LH-20	MeOH-EtOAc (50:50), MeOH	[56]
	EtOAc-MeOH-H_2O (16:2:1); EtOAc-MeOH (2:1)	[30]
Polyamide	H_2O	[36,40,49,56–58]
	H_2O-MeOH (100:0 → 0:100)	[30]
Kovasil C_{18}	MeOH-H_2O (30:70 → 60:40)	[30]
Superclean C_{18}	EtOH-H_2O (60:40)	[38]
Thin Layer Chromatography		
NP-SiO_2	$CHCl_3$-EtOH (4:1)	[53,55,60]
	$CHCl_3$-MeOH (4:1)	[51]
	$CHCl_3$-MeOH (5:1)	[32,52,54]
	$CHCl_3$-MeOH (8:1)	[33]
	$CHCl_3$-MeOH (25:1)	[29]
	CH_2Cl_2-EtOH (85:15), EtOAc-MeOH-NH_3 (85:10:5), EtOAc-EtOH-H_2O (80:10:2)	[49,56]
	CH_2Cl_2-EtOH (8:2), Toluene-Me_2CO-EtOH-NH_3 (100:140:32:9), CH_2Cl_2-MeOH-C_6H_6 (25:5:3), EtOAc-EtOH-H_2O (16:2:1)	[30]

Table 6. *Cont.*

Sorbent, Column	Eluent	Ref.
RP-SiO_2	MeOH-H_2O (65:35)	[49]
	MeOH-H_2O (4:6), MeCN-H_2O (35:65), 0.1% TFA in MeCN-H_2O (35:65), Tetrahydrofuran-H_2O (45:55)	[30]
Cy-SiO_2	Hexane-Me_2CO (6:4), MeCN-H_2O (2:8)	[30]
	Preparative NP-HPLC	
Zorbax-SIL (250 mm × 9.4 mm × 5 μm)	CH_2Cl_2-iPrOH-H_2O (125:25:2, 125:15:1)	[33,56]
	CH_2Cl_2-iPrOH-H_2O (125:40:3); CH_2Cl_2-iPrOH-H_2O (125:25:2); Cyclohexane-iPrOH-H_2O (80:40:3).	[49]
	Cyclohexane-iPrOH-H_2O (100:40:3)	[40]
Zorbax SIL (250 mm × 4.6 mm × 5 μm)	CH_2Cl_2-iPrOH-H_2O (125:50:5; 125:40:3; 125:30:2; 125:25:2), Cyclohexane-iPrOH-H_2O (100:40:3)	[30,36,49,57]
	Preparative RP-HPLC	
Diasorb 130 C_{16} T (250 mm × 15 mm × 7.5 μm)	H_2O-MeOH-BuOH (45:30:1); MeOH-H_2O (45:55)	[28]
Reprosil-Pur C_{18}-AQ (250 mm × 10 mm × 10 μm)	MeCN-H_2O	[32]
Separon C_{18} (125 mm × 25 mm × 10 μm)	MeOH-H_2O (60:40)	[54]
Separon C_{18} (250 mm × 10 mm × 5 μm)	MeOH-H_2O (60:40)	[52]
Zorbax SB-C_{18} (250 mm × 4.6 mm × 5 μm)	MeCN-H_2O (23:77)	[30]
	MeCN-H_2O (35:65)	[40,49,58]
	MeOH-H_2O (80:20)	[36]
	Analytic NP-HPLC	
Zorbax-SIL (250 mm × 4.6 mm × 5 μm)	Isooctane-iPrOH-H_2O (100:30:2)	[56]
	Cyclohexane-iPrOH-H_2O (100:30:2)	[33]
	CH_2Cl_2-iPrOH-H_2O (125:50:5; 125:40:3; 125:30:2; 125:25:2), Cyclohexane-iPrOH-H_2O (100:40:3)	[30]
	Analytic RP-HPLC	
Separon C_{18} (125 mm × 4 mm × 5 μm)	MeOH-H_2O (60:40)	[54]
Spherisorb 5ODS2 (250 mm × 4.6 mm × 5 μm)	MeCN-0.1% TFA in H_2O (20:80 → 70:30; 23:77) MeOH-H_2O (60:40, 50:50)	[56] [33]
Zorbax ODS (250 mm × 4.6 mm × 5 μm)	MeCN-H_2O (20:80)	[38]
	MeCN-H_2O (23:77)	[30]

Atmospheric pressure chromatography (APC), as the main large-scale separation method, is realized on various sorbents, including alumina, normal- and reverse-phase silica gel, polyamide, and Sephadex LH-20. For separation on alumina, two-component solvent systems are often used, which are mixtures of chloroform and methanol/ethanol, and are less often three-component systems, including ethyl acetate and low-molecular-weight alcohols. Silica gel, as the most commonly used sorbent for APC of ecdysteroids, allows elution with mixtures of chloroform or dichloroethane with alcohols, as well as water–methanol solvent systems. To perform the separation on the epoxy-modified dextran Sephadex LH-20, one-component (methanol), two-component (methanol–ethyl acetate), and three-component systems (ethyl acetate–methanol–water) are used. The possibility of

gradient elution with water–alcohol mixtures is a distinctive feature of APC on polyamide and reversed-phase silica gel.

Thin layer chromatography (TLC), as both a detection (analysis) and a separation method, is widely used to isolate the ecdysteroids of *Serratula* and *Klasea*. The use of TLC variants on normal-phase (NP) silica gel and its modifications, such as reversed-phase (RP) and cyano-derivatized layers, are well known. The compositions of the solvent systems used on NP-silica gel are close to those used in APC, including mixtures of chloroform with alcohols, as well as complex alkaline systems containing an ammonia solution, allowing more selective separation of individual components. For TLC on RP-silica gel, two-component systems are used, which are mixtures of water with methanol, acetonitrile, and tetrahydrofuran, while for TLC on cyano-derivatized-silica gel, mixtures of hexane and acetone can be used.

The proximity of the physicochemical and chromatographic properties of *Serratula* ecdysteroids, which make it difficult to isolate individual compounds, has led to using the various HPLC options, including its preparative mode. The normal-phase sorbent Zorbax-SIL has performed well in the process of ecdysteroid separation for *S. tinctoria* [45,49] and *S. coronata* [30,33,36,40,57,58]. The use of the isocratic mode for solvent systems containing dichloroethane/cyclohexane mixed with aqueous solutions of isopropanol made it possible to satisfactorily separate more than 30 compounds.

Traditional variants of preparative HPLC have been realized on RP-silica gel columns, and the Zorbax SB-C18 column has been used most often as a tool for the isolation of *S. coronata* ecdysteroids [30,33,36,40,57,58]. The positive results obtained with the use of Diasorb 130 C_{16} T [28], Reprosil-Pur C_{18}-AQ [32], and Separon C_{18} [52,54] columns are also worth noting. For RP-HPLC, the use of mixtures of methanol and acetonitrile with water as eluents is common. An analytical version of HPLC was implemented on columns with normal (Zorbax-SIL) [30,33,56] and reversed-phase Separon C_{18} (Spherisorb 5ODS2, Zorbax ODS) [30,38,54,56] using mixtures of cyclohexane/dichloroethane/isooctane with isopropanol as eluents for NP-silica gels and mixtures of methanol/acetonitrile with water for RP-silica gels.

The presented information demonstrates the breadth of options for the chromatographic separation of *Serratula* and *Klasea* ecdysteroids, which explains the large number of compounds isolated from the genera.

4.2. Flavonoids

The extraction procedure of flavonoids of the herb and roots of *Serratula* and *Klasea* plants may include treatment by lipophilic solvents, such as ethyl ether–petroleum ether mixture [14] or methanol/ethanol infusion [21,68], boiling [67,71], or sonication [11] (Table 7). The resulting extracts have been subjected to liquid–liquid extraction by low- and medium-polarity solvents for purification and isolation of the target compounds in most cases [67–69] or re-crystallized from the alcohols to isolate the dominant component [67]. Finally, the enriched fractions can be separated by chromatographic techniques using atmospheric pressure, thin-layer, and high-performance chromatography (Table 8).

Table 7. Extraction conditions of flavonoids from *Serratula* and *Klasea* plant material.

Species	Source, Solvent, Extraction Conditions *	Ref.
S. coronata	Roots → Et_2O-PE-extr. (1:2) → pecip.	[14]
	Herb → 50% MeOH-extr. (US) → MeOH-extr. NP-APC (polyamide, Sephadex LH-20), prep. TLC (polyamide)	[66]
	Leaves, stems → 70% EtOH-extr. (boiling) → LLE CCl_4/H_2O, EtOAc/H_2O, BuOH/H_2O → BuOH-extr. NP-APC (SiO_2)	[71]
S. coronata subsp. *coronata*	Leaves, flowers → 70% EtOH-extr. (boiling) → LLE CCl_4/H_2O, EtOAc/H_2O, BuOH/H_2O → BuOH-extr. recry.	[67]

Table 7. *Cont.*

Species	Source, Solvent, Extraction Conditions *	Ref.
S. tinctoria	Leaves → 30% EtOH-extr. (1:10, US) → LLE Benz/H_2O → Water phase MPLC (cellulose), NP-APC (Sephadex LH-20)	[11]
K. centauroides subsp. *centauroides*	Leaves, flowers → 70% EtOH-extr. (boiling) → LLE CCl_4/H_2O, EtOAc/H_2O, BuOH/H_2O → BuOH-extr. NP-APC (SiO_2), prep. RP-HPLC (Discovery C18)	[69]
K. centauroides subsp. *strangulata*	Whole plant → EtOH-extr. (20 °C) → LLE PE/H_2O, EtOAc/H_2O, BuOH/H_2O → EtOAc-extr. NP-APC (SiO_2)	[21]
K. flavescens subsp. *cichoracea*	Flowers → 80% EtOH-extr. (20 °C) → LLE PE/H_2O, $CHCl_3/H_2O$, EtOAc/H_2O → EtOAc-extr. prep. TLC (SiO_2)	[68]
K. lyratifolia	Leaves → MeOH-extr. (20 °C) → MeOH-extr. PC, NP-APC (Sephadex LH-20)	[63]
K. radiata subsp. *gmelinii*	Roots → Et_2O-PE-extr. (1:2) → pecip.	[14]

* extr.—extract; HPLC—high-performance liquid chromatography; recry.—recrystallization; LLE—liquid–liquid extraction (upper solvent/lower solvent); MPLC—medium-pressure liquid chromatography; NP—normal-phase; pecip.—precipitation; PC—paper chromatography; prep.—preparative; RP—reversed-phase; S—solvent; TLC—thing layer chromatography; US—sonication. Solvents: Benz—benzene; BuOH—*n*-butanol; $CHCl_3$—chloroform; CCl_4—tetrachloromethane; EtOAc—ethyl acetate; EtOH—ethanol; Et_2O—ethyl ether; MeOH—methanol; PE—petroleum ether.

Table 8. Chromatographic conditions used for the separation of *Serratula* and *Klasea* flavonoids.

Sorbent, Column	Eluent	Ref.
Atmospheric Pressure Chromatography		
Cellulose	EtOH-H_2O (90:10 → 70:30)	[11]
SiO_2	Et_2O-PE (5:1) $CHCl_3$-Me_2CO, Hexane-EtOAc CCl_4-EtOH (100:0 → 0:100)	[21] [68] [69,71]
Sephadex LH-20	70% EtOH MeOH; CH_2Cl_2:MeOH (8:2)	[63] [66]
Polyamide	H_2O-MeOH (100:0 → 0:100); EtOAc-MeOH (100:0 → 50:50)	[66]
Thin Layer Chromatography		
Cellulose	BuOH-AcOH-H_2O (4:1:5); 15% AcOH; BuOH-EtOH-H_2O (4:1:2.2); AcOH-conc.HCl-H_2O (30:3:10)	[63]
Analytic RP-HPLC		
GLC Mastro C18 (150 × 2.1 mm, 3 µm; Shimadzu, Kyoto, Japan)	0.5% HCOOH in water (A), 0.5% HCOOH in MeCN (B); gradient: 0–2 min 5–6% B, 2–9 min 6–11% B, 9–15 min 11–25% B, 15–20 min 25–55% B, 20–25 min 55–5% B	[59]
Kromasil 100-5-C18 (250 × 4.6 mm, 5 µm; Kromasil, Göteborg, Sweden)	MeOH-H_2O-H_3PO_4 (400:600:5)	[70]
PerfectSil Target ODS-3 (250 × 4.6 mm, 5 µm; MZ-Analysentechnik GmbH, Mainz, Germany)	0.1% TFA (A), MeCN-iPrOH (B); gradient: 0–45 min 15–35% B	[47]
Simpak CLC-ODS (150 × 6 mm, 5 µm; Shimadzu, Columbia, MA, USA)	MeCN-H_2O-H_3PO_4 (22:78:0.1), (35:65:0.2)	[63]
Supelco Discovery C18 (250 × 4.6 mm, 5 µm; Thermo Fisher Scientific, Waltham, MA, USA)	1% AcOH (A), MeOH (B); gradient: 0–10 min 20% B, 10–56 min 80% B, 56–60 min 20% B	[67,69,71]

Table 8. *Cont.*

Sorbent, Column	Eluent	Ref.
Symmetry C18 (150 × 2.1 mm, 5 µm; Waters, Milford, MA, USA)	H_2O (A), MeCN (B); gradient: 0–30 min 15–45% B	[63]
Zorbax SB-Phenyl (150 × 4.6 mm, 3.5 µm; Agilent Technologies, Santa-Clara, CA, USA)	0.15% HCOOH in H_2O (A), MeOH (B); gradient: 0–15 min 40–60% B, 15–20 min 60–70% B, 20–27 min 70–100% B, 27–30 min 100% B	[65]

Separation of *Serratula* and *Klasea* flavonoids by APC has been realized on cellulose [11], silica [21,68,71], Sephadex LH-20 [63,66], and polyamide sorbents [66], as well as preparative thin-layer chromatography on the cellulose if necessary [66]. Thus, although there was far less interest in flavonoids than in ecdysteroids, more than thirty compounds were successfully isolated and characterized. Additionally, some high-performance assays were applied to the profiling and quantitative analysis of *Serratula* and *Klasea* flavonoids. All known HPLC methods used reversed-phase sorbents (packed in 150-mm [59,63,65] and 250-mm columns [47,69–71]) and various combinations of high-polarity solvents (such as water [63] and organic acid solutions [47,59,65]) and medium-polarity solvents (such as acetonitrile [47,59] and methanol [67,71]). The elution mode is isocratic [63,70] or gradient [47,59,67,69,71]. Traditionally, the methods of flavonoid separation used for *Serratula* and *Klasea* plants are similar to the known methodological approach applied in flavonoid chemistry.

5. Bioactivity of *Serratula* and *Klasea*

The earliest mentions of the bioactivity of *Serratula* that we were able to find were inaccessible papers from the 1990s that demonstrated the genoprotective [82], immunostimulant [83], and anti-ulcer potential of *S. coronata* extracts [84]. Later, these studies were slightly expanded for total extracts and individual compounds [12,31,42,59,66,68,70,78,85–93] (Table 9). Pharmacological in vitro and in vivo animal studies of methanol, ethanol, and water extracts showed that *S. coronata* and *K. centauroides* have various activities, such as stress-protective [59], antioxidative [66], anxyolitic [70], adaptogenic [85], aldose reductase inhibitory [86], anti-ishemic [89], antihypoxic, and neuroprotective effects [90]. The only human experiment showed the antiseborrheic dermatitis effect of methanol extract of *S. coronata* herb [78]. The ecdysteroid fraction of the *S. coronata* herb containing 20-hydroxyecdysone as a dominant component proved to be an antihypoxic, adaptogenic, termoprotective [12], and cardioprotective agent [87]. Pure ecdysteroids and flavonoids isolated from *S. coronata*, *K. centauroides* subsp. *strangulata*, and *K. flavescens* subsp. *cichoracea* have shown antioxidant [31,42,68], stress-protective [92], and antibacterial effects [31,93].

Table 9. Bioactivity data of *Serratula* and *Klasea* extracts and pure compounds.

Extract, Compound	Assay, Model	Dose *	Positive Control	Result	Ref.
		Serratula species			
50% MeOH extracts of *S. coronata*, *S. coronata* subsp. *coronata*, *S. tinctoria* herb	In vitro: enzyme-independent lipid peroxidation of brain homogenate, enzyme-dependent lipid peroxidation of rat liver microsomes	0–20 μg/mL	Vitamin E	Antioxidant effect	[66]
Methanol extract of *S. coronata* herb	In vivo: seborrheic dermatitis of human	8 mg/human	Lekobaza® (Fagron, Kraków, Poland)	Antiseborrheic dermatitis effect	[78]
Water extract of *S. coronata* herb	In vivo: electric shock of Wistar rats	5–15 mg/kg; i.p.	-	Adaptogenic effect	[85]
Methanol extract of *S. coronata* flowers	In vitro: rat lens aldose reductase inhibition	0.1–10 μg/mL	3,3′-Tetramethy-leneglutaric acid	Aldose reductase inhibition	[86]
Ecdysteroid fraction of *S. coronata* herb	In vivo: normal pressure hypoxia of rats	20 mg/kg; i.p.	*Rhaponticum carthamoides* extract	Antihypoxic effect	[12]
	In vivo: swimming duration, immobilization stress of rats	20 mg/kg; i.p.		Adaptogenic effect	[12]
	In vivo: hypo- and hyperthermia of rats	20 mg/kg; i.p.		Termoprotective effect	[12]
	In vivo: chronic cardiac failure of rats	20 mg/kg; i.p.		Cardioprotective effect	[87]
	In vivo: survival of *Drosophila melanogaster*	0.2–1 μM	Fenugreek extract, dioscin	Adaptogenic, geroprotective effects	[88]
		Klasea species			
Ethanol extract of *K. centauroides* herb	In vivo: elevated plus maze test, light/dark test, Vogel test	50–150 mg/kg; p.o.	*Rhaponticum carthamoides* extract	Anxyolitic effect	[70]
	In vivo: acute/chromic emotional stress of Wistar rats	25–200 mg/kg; p.o.		Stress-protective effect	[59]
Ethanol extract of *K. centauroides* leaves	In vivo: bilateral occlusion of the carotid arteries of Wistar rats	50–200 mg/kg; p.o.		Anti-ishemic effect	[89]
	In vivo: hypobaric hypoxia/reoxigenation of Wistar rats	50–100 mg/kg; p.o.		Antihypoxic, neuroprotective effect	[90]
	In vivo: positive reinforcement of Wistar rats	50–200 mg/kg; p.o.		Anxyolitic effect	[91]

Table 9. *Cont.*

Extract, Compound	Assay, Model	Dose *	Positive Control	Result	Ref.
		Ecdysteroids			
20-Hydroxyecdysone	In vivo: pulse heat stress of housefly larvae	2×10^{-7} M	-	Stress-protective effect	[92]
20-Hydroxyecdysone, 25-deoxy-11,20-dihydroxyecdysone, 20-hydroxyecdysone-20,22-monoacetonide, 24-(2-hydroxyethyl)-20-hydroxyecdysone	In vitro: human eritrocite oxidation hemolysis induced by AAPH; Fe^{2+}- cysteine-induced lipid peroxidation of liver microsome	0–3.2 mM	Glutatione reduced	Medium antioxidant effect	[42]
Ajugasterone C, 22-*epi*-ajugasterone C	In vitro: DPPH test	0–300 μg/mL	Myricetin	Low antioxidant effect	[31]
Ecdysone, 20-hydroxyecdysone, 20-hydroxyecdysone 2-*O*-acetate, inokosterone	In vitro: serial dilutions method, *Staphylococcus aureus*, *Escherichia coli*, *Proteus rettgeri*, *P. morgani*, *P. vulgaris*, *Bacillus cereus*, *B. subtilis*, *Micrococcus luteus*, *Pseudomonas aeruginosa*, *Candida tropicalis*, *C. utilis*, *C. pelliculosa*, *C. albicans*, *C. rugosa*, *Saccharomyces cerevisiae*, *Rhodotorula dracilis*, *Erwinia caratovora*, *Alternaria alternata*, *Fusarium solani*, *Aspergillus niger*, *Penicillium expansum*	0–1000 μg/mL	-	Low or null antibacterial effect	[93]
Ajugasterone C, 22-*epi*-ajugasterone C	In vitro: serial dilutions method, *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Serratia* sp., *Pseudomonas aurogenosa*, *Candida albicans*	0–1000 μg/mL	Gentamicin, streptomycin, nystatin	Medium antibacterial effect	[31]
		Flavonoids			
3-Methylquercetin, apigenin, acacetin, luteolin, genkwanin	In vitro: DPPH test	0–50 μg/mL	Quercetin	Antioxidant effect	[68]

* p.o.–per os, oraly; i.p.–intraperitonealy.

6. Conclusions

Plant species of the *Serratula* and *Klasea* genera are a source of various groups of biologically active and economically valuable natural compounds with a chemodiversity of approximately 300 compounds. Despite this, to date, it is not possible to make conclusions about the chemical differentiation of *Serratula* and *Klasea* using the features of the chemical composition due to insufficient scientific information. Acceptance of 20-hydroxyecdysone, found in most of the studied species (in 19 of 26 studied), as a chemical marker of the genera cannot be considered correct because this compound is present in all ecdysteroid-containing plants. The distribution of other compounds does not allow the creation of an adequate chemical picture for these genera. It is necessary to note the complete absence of chemical information about the carbohydrate components (including polysaccharides) of both genera and the poor knowledge of flavonoids, which are rich in species of the Asteraceae family, as well as non-volatile sesquiterpenes, which are characteristic of plants belonging to the Cardueae tribe, including *Serratula* and *Klasea*. Because some species (*K. centauroides* and others) are used as food and functional products, in-depth studies of nutrients and their safety in humans are needed. In this regard, the relevance of the further in-depth study of the metabolites of *Serratula* and *Klasea* species is beyond doubt. Among the *Serratula* and *Klasea* plants, there are still few objects used for the industrial production of medicinal substances; only *S. coronata* is used to manufacture drugs containing 20-hydroxyecdysone and other ecdysteroids. Given the good natural resources of some species of *Klasea*, as well as the possibility of their cultivation in artificial conditions, it is necessary to expand the range of industrial plants. For the industrial species *S. coronata*, there is no information on the processing of waste products from the production of ecdysteroid-containing substances and the use of the plant's industrial waste, which should remain after the end of industrial cycles. Regarding the methods of isolating and separating the metabolites of *Serratula* and *Klasea*, they are diverse and allow the required level of selectivity to be achieved. The use of massive and multistage schemes for the chromatographic separation of total fractions is justified in most cases because this leads to the isolation of new compounds and the refinement of the chemical composition of individual species. However, there is still little information about the quantitative content of individual groups of compounds, especially those that are important as target bioactive agents. Extracts and individual compounds of *Serratula* and *Klasea* require an extended and in-depth study of biological activity, as well as the study of the mechanisms of biological effects. To date, spot studies of bioactivity have been realized due to adaptogenic and anti-stress effects. There are no data on the effect of *Serratula* and *Klasea* preparations on the immune, cardiovascular, excretory, and other systems of humans or on the safety and possibility of mutagenic effects. When summarizing data on the metabolites of the genera *Serratula* and *Klasea*, it should be clarified that despite the gaps in scientific knowledge and the need for further research, plants of both genera are promising sources of drugs and possible food products. Although the history of the study of these plants began in the 20th century, it can be confidently stated that great achievements in the field of studying metabolites, their methods of separation, and their biological activity are still ahead.

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