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Review

The Ethnopharmacological Uses, Metabolite Diversity, and Bioactivity of *Rhaponticum uniflorum* (*Leuzea uniflora*): A Comprehensive Review

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Abstract: *Rhaponticum uniflorum* (L.) DC. (*syn*. *Leuzea uniflora* (L.) Holub) is a plant species of the Compositae (Asteraceae) family that is widely used in Asian traditional medicines in China, Siberia, and Mongolia as an anti-inflammatory and stimulant remedy. Currently, *R. uniflorum* is of scientific interest to chemists, biologists, and pharmacologists, and this review includes information from the scientific literature from 1991 to 2022. The study of the chemodiversity of *R. uniflorum* revealed the presence of 225 compounds, including sesquiterpenes, ecdysteroids, triterpenes, sterols, thiophenes, hydroxycinnamates, flavonoids, lignans, nucleosides and vitamins, alkanes, fatty acids, and carbohydrates. The most studied groups of substances are phenolics (76 compounds) and triterpenoids (69 compounds). Information on the methods of chromatographic analysis of selected compounds, as well as on the quantitative content of some components in various organs of *R. uniflorum*, is summarized in this work. It has been shown that the extracts and some compounds of *R. uniflorum* have a wide range of biological activities, including anti-inflammatory, antitumor, immunostimulatory, anxiolytic, stress-protective, actoprotective, antihypoxic, anabolic, hepatoprotective, inhibition of PPARγ receptors, anti-atherosclerotic, and hypolipidemic. Published research on the metabolites and bioactivity of *R. uniflorum* does not include clinical studies of extracts and pure compounds; therefore, an accurate study of this traditional medicinal plant is needed.

Keywords: *Rhaponticum uniflorum*; Compositae (Asteraceae); ecdysteroids; flavonoids; thiophenes; HPLC; anti-inflammatory activity; neuroprotection

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1. Introduction

Rhaponticum Vaill. is a small genus from the tribe Cynareae of the Asteraceae family that is distributed mainly in tropical and subtropical regions of Europe, Asia, and Africa. In total, more than 20 species belong to the genus and are distributed in a narrow strip in the Northern hemisphere from the Atlantic coast to the Pacific Ocean [1]. Close to *Rhaponticum* are the Mediterranean monotypic genus *Leuzea* and the small Asian genus *Stemmacantha*, which, combined, include approximately 10 species. Many species of *Rhaponticum* are of economic importance, and some have been introduced into cultivation as ornamental or medicinal plants. *R. carthamoides* (also known as Maral root) is widespread from Central Asia to Siberia and Xinjiang; it is a medicinal plant and a source of ecdysteroids; it is recommended as part of combination therapy for asthenia, physical and mental overwork, impotency, and during convalescence [2]. North African endemic species *R. acaule* is used as an aperitif, cholagogue, depurative, digestive, stomachic, and tonic in North and Central Tunisia [3]. Creeping knapweed or *R. repens* is a traditional medicine in Central Asia; it is applied as an emetic, antiepileptic, and anti-malaria remedy [4].

One-flowered leuzea or *Rhaponticum uniflorum* (L.) DC. (synonyms—*R. dauricum* Turcz., *R. monanthum* (Georgi) Worosch., *Centaurea monanthos* Georgi, *C. grandiflora* Pall., *C. membranaceae* Lam., *Serratula uniflora* Spreng., *Leuzea daurica* Bge., and *L. uniflora* (L.)

Holub.) has received considerable attention in recent years. There are some scientific study reviews dedicated to *R. carthamoides* [2] and the genus *Rhaponticum* [5]; however, the issues of *R. uniflorum* are not fully covered. Therefore, the aim of this work is to summarize scientific information about *R. uniflorum* regarding the chemical composition of the herb and roots, as well as methods of analysis and biological activity.

Botanically, *R. uniflorum* is a low- or medium-height plant (20–60-cm tall) with straight, simple, felted stems [1,2]. Its leaves are rough on both sides, with adpressed cobwebby pubescence, pinnately divided into 8–12 pairs of dentate or entire obtuse lobes. The basal and lower leaves are petiolate, and the upper ones are sessile. Single inflorescences (3–5-cm wide) have outer and middle leaflets that are adpressed, leathery, light-brown, bare, broadly ovate, contain shiny appendages, and are split at the top into uneven lobes. Flower corolla is slightly funnel-shaped and has a coloration ranging from pale pink to red. The rhizome is thick, long, and vertical, with a loose, tuberous-fibrous surface and a few thin roots. Flowers are collected in late spring and early summer, and the roots are dug up in early autumn (Figure 1). In nature, *R. uniflorum* is scattered on meadow-steppe mountain slopes, along sandy riverbanks, and in the forests of Eastern Siberia and the Russian Far East, as well as in Northern Mongolia, Northeastern China, and Korea [6].

a **b** **c**

Figure 1. *Rhaponticum uniflorum* (L.) DC. (one-flowered leuzea) in its natural habitat (Republic Buryatia, Ivolginskii District, Kluchi vicinity, mountain slope; (**a**)), and dried roots (*qizhou loulu*; (**b**)) and flowers (*louluhua*, *spyang-tser*; (**c**)).

2. Review Strategy

To produce a relevant review, international databases (e.g., Scopus, Web of Science, PubMed, and Google Scholar) were used. Because most studies have been performed by Chinese and Russian scientists, national electronic resources (e.g., Chinese research databases (Wanfang and CNKI Journals) and the Russian scientific database (eLibrary)) were included in the search. These resources contain relevant articles that are not indexed by international databases. Only original papers written in English, Chinese, and Russian, and published in journals prior to October 2022, were considered. An exception was made for the ethnopharmacological data collected from books. The search keywords used included plant names (e.g., "*Rhaponticum uniflorum*", "*Leuzea uniflora*", "*Stemmacantha uniflora*", "*Fornicium uniflorum*") and metabolite names. The list of *R. uniflorum* compounds includes secondary metabolites mostly correlated with ethnopharmacological uses and bioactivities of the plant, and, for a more complete picture, information about primary metabolites is also mentioned in this manuscript.

3. Ethnopharmacology

Ethnopharmacological uses of roots, flowers, and the herb of *R. uniflorum* were found in Asian traditional medicines (Table 1).

In traditional Chinese medicine, the roots of *R. uniflorum* (qizhou loulu) have been used as an anti-inflammatory, antipyretic, detoxifier, antitumor, and lactation agent [7], while flowers (louluhua) have the functions of relieving burning pain, clearing 'heat' (or 'fire'), and as a detoxifying remedy [8]. In the Buryatia Republic, in addition to *R. uniflorum* [9], under the name spyang-tser, flowers of *R. carthamoides*, as well as the flowers and roots of *Carduus crispus*, Guirão ex Nyman, and *Cirsium esculentum* (Siev.) C.A.Mey., are used to treat stomach inflammations, gastroenteritis, pneumonia, bronchitis, and tuberculosis [10]. In Tibetan medicine, spyang-tser plants are prescribed for cleansing wounds and ulcers, indigestion, and other diseases of the stomach [11], lung diseases [12], and to treat skin diseases (boils, carbuncles), mastitis, and rheumatoid arthritis [13]. In Mongolian folk medicine, the *R. uniflorum* herb (khonkhor zul, spyang-tser, spyang-tser-dmar-po) is used as a water decoction, as an anti-inflammatory remedy, and to increase the vitality of the body [14]. In Korea, young buds of *R. uniflorum* are a food product, and the roots (nuro) are used to treat chronic gastritis as an anti-inflammatory, detoxifier, antipyretic, and analgesic agent [15]. Roots and flowers of *R. uniflorum* are traditional Chinese remedies recorded in the Chinese pharmacopeia and the "Drug Standard of the Ministry of Public Health of the People's Republic of China" [16].

Table 1. Traditional medical uses of *R. uniflorum*.

Plant Part	Locality	Traditional Use	Ref.
Roots	China	Anti-inflammatory, antipyretic, detoxifier, antitumor, lactation remedy	[7]
Flowers	China	Relieving burning pain, clearing heat, detoxifying remedy	[9]
	Buryatia	Anti-inflammatory remedy at stomach deseases, gastroenteritis, pneumonia, bronchitis, tuberculosis	[10,11]
	Tibet	Remedy for cleansing wounds and ulcers, indigestion, stomach and lung diseases, to treat skin diseases (boils, carbuncles), mastitis, rheumatoid arthritis	[12–14]
Herb	Mongolia	Anti-inflammatory remedy, increasing the vitality of the body	[15]
Buds	Korea	Anti-inflammatory, detoxifier, antipyretic, and analgesic agent	[8]

4. Metabolite Diversity

More than 200 compounds (**1**–**225**) have been detected in various organs of *R. uniflorum*, including sesquiterpenes (**1**–**14**), diterpenes (**15**–**17**), triterpenes (**18**–**86**), thiophenes (**87**–**98**), hydroxycinnamates (**99**–**108**), flavonoids (**109**–**162**), lignans (**163**–**170**), various phenolics (**171**–**174**), amino acids (**175**–**187**), nucleosides and vitamins (**188**–**195**), alkanes (**196**–**199**), fatty acids (**200**–**217**), and carbohydrates (**218**–**225**) (Table 2).

4.1. Sesquiterpenes

Fourteen sesquiterpenes (**1**–**14**) have been identified in *R. uniflorum*, including eudesmane **1**, germacranolide **2**, and guaianes **3**–**14** [17–20] (Figure 2). Rhaponticol {7α,8α,12-trihydroxy-eudesma-4(15)-11(13)-diene, **1**}, isolated from roots of *R. uniflorum* [17], is the only eudesmane found in the *Rhaponticum* genus, and it is non-typical for the Rhaponticum group (Centaureinae subtribe). This sesquiterpene type is characteristic of other members of the tribe, including the genus *Centaurea* (Centaurea group) and, less commonly, for the Mediterranean species *Cheirolophus* and *Phonus* (Carthamus group) [20].

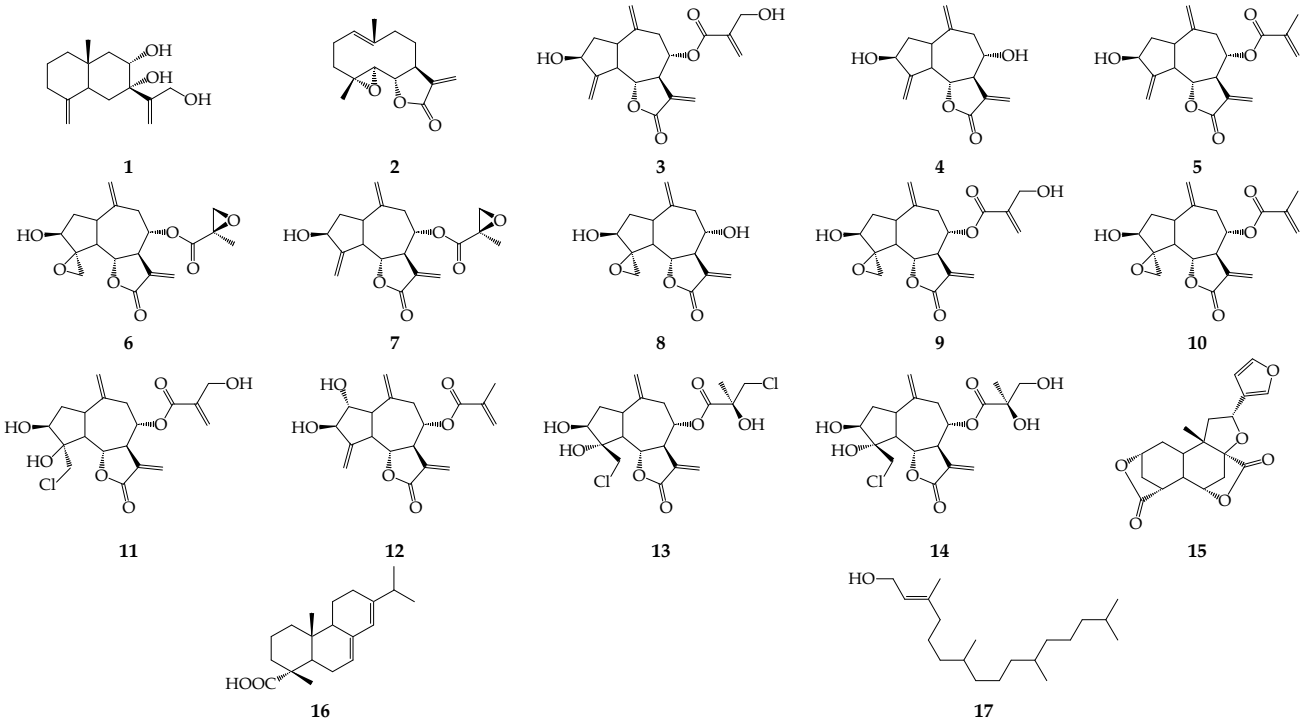


Figure 2. Sesquiterpenes **1–14** and diterpenes **15–17**.

Table 2. Compounds **1–225** found in *R. uniflorum*.

No	Compound	Formula	MW *	Herb	Leaves	Flowers	Seeds	Roots
	Sesquiterpenes							
1	Rhaponticol	$C_{15}H_{24}O_3$	252					[17]
2	Parthenolide	$C_{15}H_{20}O_3$	248			[9]		
3	Cynaropicrin	$C_{19}H_{22}O_6$	364	[18]	[19]	[19]	[19]	[19]
4	Cynaropicrin, desacyl-	$C_{15}H_{18}O_4$	262		[19]			
5	Cynaropicrin, 4′-deoxy- (aguerin B)	$C_{19}H_{22}O_5$	330	[18]	[19]	[19]	[19]	[19]
6	Repin	$C_{19}H_{22}O_7$	362		[19]			
7	Repin, 15-desoxy- (salograviolide C)	$C_{17}H_{20}O_6$	320	[18]	[19]			[19]
8	Repin, 8-desacyl-	$C_{15}H_{18}O_5$	278		[19]			
9	Janerin	$C_{19}H_{22}O_7$	362		[19]			
10	Janerin, 19-desoxy-	$C_{19}H_{22}O_6$	346		[19]			
11	Janerin, chloro-	$C_{19}H_{23}ClO_7$	398.5		[19]			
12	Repdiolide	$C_{19}H_{22}O_6$	346		[19]			
13	Chlorohyssopifolin A (centaurepensin, hyrcanin)	$C_{19}H_{24}Cl_2O_7$	435		[19]			[20]
14	Chlorohyssopifolin E	$C_{19}H_{25}ClO_8$	416		[19]			
	Diterpenes							
15	Diosbulbin B	$C_{19}H_{20}O_6$	344					[21]
16	Abietic acid	$C_{20}H_{30}O_2$	302			[9]		
17	Phytol	$C_{20}H_{40}O$	296	[6]				
	Triterpenes							
18	Ajugasteron C	$C_{27}H_{44}O_7$	480	[6]	[22]			[23–25]
19	Ajugasteron C 20,22-acetonide	$C_{30}H_{48}O_7$	520		[22]			[23–25]
20	Ajugasteron C 2,3;20,22-diacetonide	$C_{33}H_{52}O_7$	560		[22]			[23,24,26]
21	5-Deoxycaladasterone (dacryhainansterone)	$C_{27}H_{42}O_6$	462		[22]	[27]		

Table 2. *Cont.*

No	Compound	Formula	MW *	Herb	Leaves	Flowers	Seeds	Roots
22	5-Deoxycaladasterone (dacryhainansterone) 20,22-acetonide	$C_{30}H_{46}O_6$	502		[22]	[27]		[16,17]
23	2-Deoxyecdysone	$C_{27}H_{44}O_5$	448		[22]			
24	25-Deoxyecdysone	$C_{27}H_{44}O_5$	448		[22]			
25	2-Deoxy-20-hydroxyecdysone	$C_{27}H_{44}O_6$	464	[28]	[22]		[29]	[28]
26	Ecdysone	$C_{27}H_{44}O_6$	464	[6]				
27	11α-Hydroxyecdysone	$C_{27}H_{44}O_7$	480					[23]
28	20-Hydroxyecdysone	$C_{27}H_{44}O_7$	480	[7,28,30]	[22]	[27]	[29]	[7,23–25,31,32]
29	20-Hydroxyecdysone 2-*O*-acetate	$C_{29}H_{46}O_8$	522		[22]			
30	20-Hydroxyecdysone 3-*O*-acetate	$C_{29}H_{46}O_8$	522		[22]	[27]		
31	20-Hydroxyecdysone 25-*O*-acetate (viticosterone E)	$C_{29}H_{46}O_8$	522	[6]				
32	20-Hydroxyecdysone 20,22-acetonide	$C_{30}H_{48}O_7$	520	[6]	[22]	[27]		
33	20-Hydroxyecdysone 2,3;20,22-diacetonide	$C_{33}H_{52}O_7$	560		[22]			
34	20-Hydroxyecdysone 3-*O*-glucoside	$C_{33}H_{54}O_{12}$	642					[6]
35	20-Hydroxyecdysone 25-*O*-glucoside	$C_{33}H_{54}O_{12}$	642					[6]
36	20-Hydroxyecdysone 2-*O*-cinnamate	$C_{36}H_{50}O_8$	610		[33]			
37	29-Hydroxy-24(28)-dehydromakisterone C	$C_{29}H_{46}O_8$	522		[22]			
38	Inokosterone (callinecdysone A)	$C_{27}H_{44}O_7$	480		[22]	[27]		
39	Inokosterone 20,22-acetonide	$C_{30}H_{48}O_7$	520		[22]			
40	Inokosterone 20,22-acetonide 25-*O*-acetate	$C_{32}H_{50}O_8$	562		[22]			
41	Integristerone A	$C_{27}H_{44}O_8$	496	[28]	[22]			[28]
42	Integristerone A 20,22-acetonide	$C_{30}H_{48}O_8$	536		[22]	[27]		
43	Makisterone C (podecdysone A, lemmasterone)	$C_{29}H_{48}O_7$	508		[22]			
44	Makisterone C 20,22-acetonide	$C_{32}H_{52}O_7$	548		[27]	[27]		
45	Polypodine B	$C_{27}H_{44}O_8$	496		[22]			
46	Polypodine B 20,22-acetonide	$C_{30}H_{48}O_8$	536		[27]			
47	Polypodine B 2-*O*-cinnamate	$C_{36}H_{50}O_9$	626		[33]			
48	Ponasterone A	$C_{27}H_{44}O_6$	464		[22]			
49	Rapisterone C	$C_{29}H_{48}O_7$	508					[23]
50	Rhapontisterone (punisterone)	$C_{27}H_{44}O_8$	496	[7]	[22]			[7,23,31,32]
51	Rhapontisterone R_1	$C_{29}H_{42}O_9$	534					[32]
52	Rubrosterone	$C_{19}H_{26}O_5$	334	[6]				
53	Turkesterone	$C_{27}H_{44}O_8$	496	[7,30]	[22]			[7,31]
54	Turkesterone 20,22-acetonide	$C_{30}H_{48}O_8$	536		[22]			
55	Turkesterone 2-*O*-cinnamate	$C_{36}H_{50}O_9$	626		[33]			
56	Uniflorsterone	$C_{27}H_{44}O_7$	480					[34]
57	Roburic acid	$C_{30}H_{48}O_2$	440			[9]		
58	Urs-12-en-3-one (α-amyrenone)	$C_{30}H_{48}O$	424					[35]
59	Urs-12-en-3β-ol (α-amyrin)	$C_{30}H_{50}O$	426	[35]				[35]
60	3-Oxo-urs-12-en-24-oic acid methyl ester	$C_{31}H_{48}O_3$	468	[35]				
61	3β-Hydroxy-urs-12-en-28-oic acid (ursolic acid)	$C_{30}H_{48}O_3$	456	[35]				[25,36,37]

Table 2. *Cont.*

No	Compound	Formula	MW *	Herb	Leaves	Flowers	Seeds	Roots
62	3β-Hydroxy-urs-12,18(19)-dien-28-oic acid 28-*O*-glucoside	$C_{36}H_{56}O_8$	616					[25]
63	3β-Hydroxy-urs-12,18(19)-dien-28-oic acid 3-*O*-arabinoside-28-*O*-glucoside	$C_{41}H_{64}O_{12}$	748					[25]
64	3β-Hydroxy-urs-12,18(19)-dien-28-oic acid 3,28-di-*O*-glucoside	$C_{42}H_{66}O_{13}$	778					[38]
65	3β-Hydroxy-urs-9(11),12-dien-28-oic acid 3-*O*-arabinoside-28-*O*-glucoside (unifloroside)	$C_{41}H_{64}O_{12}$	748					[39]
66	3β-Hydroxy-urs-12,19(29)-dien-28-oic acid 28-*O*-glucoside	$C_{36}H_{56}O_8$	616					[25]
67	3β-Hydroxy-urs-12,19(29)-dien-28-oic acid 3,28-di-*O*-glucoside	$C_{42}H_{66}O_{13}$	778					[38]
68	3β,19α-Dihydroxy-urs-12-en-28-oic acid (pomolic acid)	$C_{30}H_{48}O_4$	472					[25,40]
69	Pomolic acid 28-*O*-glucoside	$C_{36}H_{58}O_9$	634					[25,39]
70	Pomolic acid 3-*O*-arabinoside-28-*O*-glucoside (ziyuglycoside I)	$C_{41}H_{66}O_{13}$	766					[25,39]
71	Pomolic acid 3-*O*-arabinoside (ziyuglycoside II)	$C_{35}H_{56}O_8$	604					[25,39]
72	3-Oxo-19α-hydroxy-urs-12-en-28-oic acid	$C_{30}H_{46}O_4$	470					[25,36,40]
73	2α,3β,19α-Trihydroxy-urs-12-en-28-oic acid (tormentic acid)	$C_{30}H_{48}O_5$	488					[36]
74	Tormentic acid 28-*O*-glucoside (rosamutin, rosamultin)	$C_{36}H_{58}O_{10}$	650					[25,39]
75	2α,3β,19α-Trihydroxy-urs-12-en-23,28-dioic acid 28-*O*-glucoside (sauvissimoside R_1)	$C_{36}H_{56}O_{12}$	680					[25,39]
76	2α,3α,19α-Trihydroxy-urs-12-en-28-oic acid	$C_{30}H_{48}O_5$	488					[18,29]
77	2α,3α,19α,25-Tetrahydroxy-urs-12-en-28-oic acid	$C_{30}H_{48}O_6$	504					[40]
78	2α,3α,19α,25-Tetrahydroxy-urs-12-en-23,28-dioic acid	$C_{30}H_{46}O_8$	534					[25]
79	Olean-12-en-3β-ol (β-amyrin)	$C_{30}H_{50}O$	426	[35]				[35]
80	3β-Hydroxy-olean-12-en-28-oic acid (oleanolic acid)	$C_{30}H_{48}O_3$	456					[41]
81	2α,3β,19α-Trihydroxy-olean-12-en-28-oic acid (arjunic acid)	$C_{30}H_{48}O_5$	488					[36]
82	β-Sitosterol	$C_{29}H_{50}O$	414	[35]				[40,41]

Table 2. *Cont.*

No	Compound	Formula	MW *	Herb	Leaves	Flowers	Seeds	Roots
83	β-Sitosterol 28-*O*-glucoside (daucosterol)	$C_{35}H_{60}O_6$	576					[25]
84	Stigmasterol	$C_{29}H_{48}O$	412	[35]				[41]
85	Stigmastan-3,5-diene	$C_{29}H_{48}$	396	[35]				[35]
86	Stigmast-4-en-3-on	$C_{29}H_{48}O$	412					[35]
	Thiophenes							
87	Arctinal	$C_{12}H_8OS_2$	232					[17,41]
88	Arctinone b	$C_{13}H_{10}OS_2$	246					[17,41,42]
89	Arctinone b, 7-chloro-	$C_{13}H_9ClOS_2$	280.5					[41,42]
90	Arctinol b	$C_{13}H_{12}O_2S_2$	264					[17]
91	Arctic acid	$C_{12}H_8O_2S_2$	248					[17,25,40]
92	2,2′-Dithiophene, 5-methoxy-	$C_9H_8OS_2$	196					[41]
93	2,2′-Dithiophene, 5-methoxy-5′-(1-propynyl)-	$C_{12}H_{10}OS_2$	234					[41]
94	2,2′-Dithiophene, 5-(4-acetoxy-1-butynyl)-	$C_{14}H_{12}O_2S_2$	276					[41]
95	Rhaponthienylenol	$C_{13}H_{14}O_3S_2$	282					[6]
96	Rhapontiynethiophene A	$C_{11}H_7ClS_2$	238.5					[42]
97	Rhapontiynethiophene B	$C_{13}H_{10}O_2S$	230					[42]
98	Thiophene, 2-(pentadiynyl-1,3)-5-(3,4-dihydroxy-butynyl-1)-	$C_{13}H_{10}O_2S$	230					[17]
	Hydroxycinnamates							
99	Cinnamic acid	$C_9H_8O_2$	148			[9]		
100	Cinnamaldehyde	C_9H_8O	132			[9]		
101	4-*O*-Caffeoylquinic acid	$C_{16}H_{18}O_9$	354	[43]			[29]	
102	5-*O*-Caffeoylquinic acid	$C_{16}H_{18}O_9$	354	[43]		[9]	[29]	
103	1,3-Di-*O*-caffeoylquinic acid	$C_{25}H_{24}O_{12}$	516	[43]				
104	1,5-Di-*O*-caffeoylquinic acid	$C_{25}H_{24}O_{12}$	516	[43]				
105	3,4-Di-*O*-caffeoylquinic acid	$C_{25}H_{24}O_{12}$	516	[43]			[29]	
106	3,5-Di-*O*-caffeoylquinic acid	$C_{25}H_{24}O_{12}$	516	[30]		[9]	[29]	
107	4,5-Di-*O*-caffeoylquinic acid	$C_{25}H_{24}O_{12}$	516				[29]	
108	Isoferuoyl serotonin	$C_{20}H_{20}N_2O_4$	352				[29]	
	Flavonoids							
109	Apigenin	$C_{15}H_{10}O_5$	270		[33]	[16]		
110	Apigenin 7-*O*-glucoside (cosmosiin)	$C_{21}H_{20}O_{10}$	432		[33]	[16]		
111	Apigenin 7-*O*-glucuronide	$C_{21}H_{18}O_{11}$	446		[33]	[16]		
112	Apigenin 6-*C*-glucoside (isovitexin)	$C_{21}H_{20}O_{10}$	432		[33]			
113	Apigenin 8-*C*-glucoside (vitexin)	$C_{21}H_{20}O_{10}$	432		[33]	[9]		
114	Apigenin 6,8-di-*C*-glucoside (vicenin-2)	$C_{27}H_{30}O_{15}$	594			[16]		
115	6-Methoxyapigenin (hispidulin)	$C_{16}H_{12}O_6$	300		[33]			
116	Luteolin	$C_{15}H_{10}O_5$	286			[16]	[29]	
117	Luteolin 7-*O*-glucoside (cynaroside)	$C_{21}H_{20}O_{11}$	448		[33]			
118	Luteolin 7-*O*-(6″-*O*-cinnamoyl)-glucoside	$C_{30}H_{26}O_{12}$	578		[33]		[29]	
119	Luteolin 7-*O*-(2″-*O*-caffeoyl)-glucoside (rhaunoside G)	$C_{30}H_{26}O_{14}$	610		[33]			
120	Luteolin 7-*O*-(6″-*O*-caffeoyl)-glucoside	$C_{30}H_{26}O_{14}$	610		[33]			
121	Luteolin 7-*O*-glucuronide	$C_{21}H_{18}O_{12}$	462		[33]			
122	Luteolin 7-*O*-rutinoside (scolymoside)	$C_{27}H_{30}O_{15}$	594		[33]			

Table 2. *Cont.*

No	Compound	Formula	MW *	Herb	Leaves	Flowers	Seeds	Roots
123	Luteolin 3′-*O*-glucoside (dracocephaloside)	$C_{21}H_{20}O_{11}$	448		[33]			
124	Luteolin 4′-*O*-glucoside	$C_{21}H_{20}O_{11}$	448		[33]			
125	Luteolin 6-*C*-glucoside (isoorientin)	$C_{21}H_{20}O_{11}$	448		[33]			
126	Luteolin 8-*C*-glucoside (orientin)	$C_{21}H_{20}O_{11}$	448		[33]			
127	Luteolin 6,8-di-*C*-glucoside (lucenin-2)	$C_{27}H_{30}O_{16}$	610		[33]			
128	3′-Methoxyluteolin (chrysoeriol)	$C_{16}H_{12}O_6$	300		[33]	[30]		
129	6-Hydroxyluteolin	$C_{15}H_{10}O_6$	302		[33]			
130	6-Hydroxyluteolin 7-*O*-glucoside	$C_{21}H_{20}O_{12}$	464		[33]		[29]	
131	6-Hydroxyluteolin 7-*O*-(6″-*O*-cinnamoyl)-glucoside (rhaunoside B)	$C_{30}H_{26}O_{13}$	594		[33]		[29]	
132	6-Hydroxyluteolin 7-*O*-(2″-*O*-caffeoyl)-glucoside (rhaunoside A)	$C_{30}H_{26}O_{15}$	626					
133	6-Hydroxyluteolin 7-*O*-(6″-*O*-caffeoyl)-glucoside (spicoside A)	$C_{30}H_{26}O_{15}$	626		[33]			
134	6-Hydroxyluteolin 7-*O*-rutinoside	$C_{27}H_{30}O_{16}$	610		[33]			
135	6-Hydroxyluteolin 4′-*O*-glucoside (rhaunoside C)	$C_{21}H_{20}O_{12}$	464		[33]			
136	6-Methoxyluteolin (nepetin)	$C_{16}H_{12}O_7$	316		[33]			
137	6-Methoxyluteolin 7-*O*-glucoside (nepitrin)	$C_{22}H_{22}O_{12}$	478		[33]			
138	6-Methoxyluteolin 7-*O*-(6″-*O*-cinnamoyl)-glucoside (rhaunoside E)	$C_{31}H_{28}O_{13}$	608		[33]			
139	6-Methoxyluteolin 7-*O*-(6″-*O*-caffeoyl)-glucoside (rhaunoside D)	$C_{31}H_{28}O_{15}$	640		[33]			
140	6-Methoxyluteolin 7-*O*-rutinoside	$C_{28}H_{32}O_{16}$	624		[33]			
141	6-Methoxyluteolin 3′-*O*-glucoside (rhaunoside F)	$C_{22}H_{22}O_{12}$	478		[33]			
142	6-Methoxyluteolin 4′-*O*-glucoside	$C_{22}H_{22}O_{12}$	478		[33]			
143	6,8-Dihydroxyluteolin 7-*O*-glucoside (zeravschanoside)	$C_{21}H_{20}O_{13}$	480		[33]			
144	5,6,7,4′-Tetrahydroxy-3′-methoxyflavone (nodifloretin)	$C_{16}H_{12}O_7$	316		[33]			
145	5,6,7,3′-Tetrahydroxy-4′-methoxyflavone	$C_{16}H_{12}O_7$	316		[33]			
146	Kaempferol	$C_{15}H_{10}O_6$	286			[30]		
147	Kaempferol 3-*O*-rhamnoside (quercitrin)	$C_{21}H_{20}O_{11}$	448			[30]		
148	6-Hydroxykaempferol	$C_{15}H_{10}O_7$	302		[33]			
149	6-Hydroxykaempferol 7-*O*-glucoside	$C_{21}H_{20}O_{12}$	464		[33]			
150	6-Hydroxykaempferol 7-*O*-(6″-*O*-caffeoyl)-glucoside	$C_{30}H_{26}O_{15}$	626		[33]			

Table 2. *Cont.*

No	Compound	Formula	MW *	Herb	Leaves	Flowers	Seeds	Roots
151	6-Methoxykaempferol 7-*O*-glucoside	$C_{22}H_{22}O_{12}$	478		[33]			
152	Quercetin	$C_{15}H_{10}O_7$	302			[30]		
153	Quercetin 3-*O*-rhamnoside (quercitrin)	$C_{21}H_{20}O_{11}$	448			[9]		
154	Quercetin 3-*O*-glucoside (isoquercitrin)	$C_{21}H_{20}O_{12}$	464			[9]		
155	Quercetin 3-*O*-rutinoside (rutin)	$C_{27}H_{30}O_{16}$	610			[9]		
156	6-Hydroxyquercetin (quercetagetin)	$C_{15}H_{10}O_8$	318		[33]			
157	6-Hydroxyquercetin 7-*O*-glucoside (quercetagitrin)	$C_{21}H_{20}O_{13}$	480		[33]			
158	6-Hydroxyquercetin 7-*O*-(6″-*O*-caffeoyl)-glucoside	$C_{30}H_{26}O_{16}$	642		[33]			
159	6-Methoxyquercetin 7-*O*-glucoside (patulitrin)	$C_{22}H_{22}O_{13}$	494		[33]			
160	3′-Methoxyquercetin (isorhamnetin)	$C_{16}H_{12}O_6$	300		[33]	[9]		
161	4′-Methoxyquercetin (diosmetin)	$C_{16}H_{12}O_6$	300			[30]		
162	Catechin	$C_{15}H_{14}O_6$	190					[25]
	Lignans							
163	Hemislin B					[30]		
164	Hemislin B *O*-glucoside					[30]		
165	Arctigenin	$C_{21}H_{24}O_6$	372			[9]		
166	Arctigenin *O*-glucoside (arctiin)	$C_{27}H_{34}O_{11}$	534			[9]		
167	Carthamogenin	$C_{21}H_{22}O_6$	370				[29]	
168	Carthamoside	$C_{27}H_{32}O_{11}$	532				[29]	
169	6″-*O*-Acetyl carthamoside	$C_{29}H_{34}O_{12}$	574				[29]	
170	Tracheloside	$C_{27}H_{34}O_{12}$	550				[29]	
	Other phenolics							
171	3,5-Dimethoxy-4-hydroxybenzaldehyde (syringaldehyde)	$C_9H_{10}O_4$	182			[9]		
172	3,3′,4-Tri-*O*-methyl-ellagic acid	$C_{17}H_{12}O_8$	344					[25]
173	Coumarin	$C_9H_6O_2$	146			[9]		
174	Ligustilide	$C_{12}H_{14}O_2$	190			[9]		
	Amino acids							
175	Alanin	$C_3H_7NO_2$	89	[44]				[44]
176	Arginin	$C_6H_{14}N_4O_2$	174	[44]				[44]
177	Glycine	$C_2H_5NO_2$	75	[44]				[44]
178	Histidin	$C_6H_9N_3O_2$	155					[44]
179	Lysine	$C_6H_{14}N_2O_2$	146	[44]				[44]
180	Leucin	$C_6H_{13}NO_2$	131	[44]				
181	Methionine	$C_5H_{11}NO_2S$	149					[44]
182	Phenylalanine	$C_9H_{11}NO_2$	165	[44]				[44]
183	Proline	$C_5H_9NO_2$	115	[44]				[44]
184	Serine	$C_3H_7NO_3$	105	[44]				[44]
185	Tyrosine	$C_9H_{11}NO_3$	181	[44]				[44]
186	Threonine	$C_4H_9NO_3$	119	[44]				[44]
187	Valin	$C_5H_{11}NO_2$	117					[44]
	Nucleosides and vitamins							
188	Cordycepin (3′-deoxyadenosine)	$C_{10}H_{13}N_5O_3$	251			[9]		
189	Thiamine (vitamin B_1)	$C_{12}H_{17}N_4OS^+$	265	[45]				[45]
190	Riboflavine (vitamin B_2)	$C_{17}H_{20}N_4O_6$	376	[45]				[45]
191	Pantothenic acid (vitamin B_5)	$C_9H_{17}NO_5$	219	[45]				[45]
192	Nicotinic acid (niacin, vitamin B_3)	$C_6H_5NO_2$	123	[45]				[45]

Table 2. *Cont.*

No	Compound	Formula	MW *	Herb	Leaves	Flowers	Seeds	Roots
193	Nicotinamide	$C_6H_6N_2O$	122			[9]		
194	Pyridoxine (vitamin B_6)	$C_8H_{11}NO_3$	169	[45]				[45]
195	Folic acid (vitamin B_9)	$C_{19}H_{19}N_7O_6$	441					[45]
	Alkanes							
196	Pentacosane	$C_{25}H_{52}$	352	[35]				
197	Heptacosane	$C_{27}H_{56}$	380	[35]				
198	Octacosane	$C_{28}H_{58}$	394	[35]				
199	Nonacosane	$C_{29}H_{60}$	408	[35]				
	Fatty acids							
200	Tetradecanoic acid (myristic acid; 14:0)	$C_{14}H_{28}O_2$	228	[35]				[35]
201	Pentadecanoic acid (15:0)	$C_{15}H_{30}O_2$	242	[35]				[35]
202	Hexadecanoic acid (palmitic acid; 16:0)	$C_{16}H_{32}O_2$	256	[35]				[35]
203	Heptadecanoic acid (margaric acid; 17:0)	$C_{17}H_{34}O_2$	270	[35]				[35]
204	Octadecanoic acid (stearic acid; 18:0)	$C_{18}H_{36}O_2$	284	[35]				[35]
205	Icosanoic acid (arachic acid; 20:0)	$C_{20}H_{40}O_2$	312	[35]				[35]
206	Heneicosanoic acid (21:0)	$C_{21}H_{42}O_2$	326	[35]				
207	Docosanoic acid (behenic acid; 22:0)	$C_{22}H_{44}O_2$	340	[35]				[35]
208	Tricosanoic acid (23:0)	$C_{23}H_{46}O_2$	354	[35]				[35]
209	Tetracosanoic acid (lignoceric acid; 24:0)	$C_{24}H_{48}O_2$	368	[35]				[35]
210	Pentacosanoic acid (25:0)	$C_{25}H_{50}O_2$	382	[35]				[35]
211	Hexacosanoic acid (cerotic acid; 26:0)	$C_{26}H_{52}O_2$	396	[35]				
212	Octacosanoic acid (montanic acid; 28:0)	$C_{28}H_{56}O_2$	424	[35]				
213	Triacontanoic acid (melissic acid; 30:0)	$C_{30}H_{60}O_2$	452	[35]				
214	Hexadec-7-enoic acid (16:1*n*9)	$C_{16}H_{30}O_2$	254	[35]				[35]
215	Octadec-9-enoic acid (oleic acid; 18:1*n*9)	$C_{18}H_{34}O_2$	282					[35]
216	Octadeca-9,12-dienoic acid (linoleic acid; 18:2*n*6)	$C_{18}H_{32}O_2$	280	[35]				[35]
217	Octadeca-9,12,15-trienoic acid (linolenic acid; 18:3*n*3)	$C_{18}H_{30}O_2$	278	[35]		[9]		[35]
	Carbohydrates							
218	Glucose	$C_6H_{12}O_6$	180		[46]	[46]	[46]	[46]
219	Fructose	$C_6H_{12}O_6$	180		[46]	[46]	[46]	[46]
220	Sucrose	$C_{12}H_{22}O_{11}$	342		[46]	[46]	[46]	[46]
221	Kestose (1^F-β-fructofuranosyl sucrose)	$C_{18}H_{32}O_{16}$	504		[46]			[46]
222	Nystose (di-(1^F-β-fructofuranosyl) sucrose)	$C_{24}H_{42}O_{21}$	666		[46]			[46]
223	1^F-β-Fructofuranosyl nystose	$C_{30}H_{52}O_{26}$	828		[46]			[46]
224	Di-(1^F-β-fructofuranosyl) nystose	$C_{36}H_{62}O_{31}$	990		[46]			[46]
225	Tri-(1^F-β-fructofuranosyl) nystose	$C_{42}H_{72}O_{36}$	1152		[46]			[46]

* MW—Molecular weight.

Parthenolide (**2**), a typical feverfew component, has been found in *Centaurea* and *Stizolophus* genera [20], but it is the only germacranolide in the Rhaponticum group. Unlike

eudesmanes and germacranolides, guaianes are widely distributed in *Rhaponticum* species, especially cynaropicrine (**3**), and are identified in *R. uniflorum* [18] and in *R. carthamoides* (Willd.) Iljin, *R. exaltatum* (Willk.) Greuter, *R. pulchrum* Fisch. & C.A.Mey., *R. scariosum* subsp. *Rhaponticum* (L.) Greuter, and *R. serratuloides* (Georgi) Bobrov [20]. Structurally similar to **3**, sesquiterpenes **4**–**12** have been isolated from the herb and roots of *R. uniflorum* [18,19], as well as two chlorinated sesquiterpenes, i.e., chlorohyssopifolins A (**13**) and E (**14**) [19,20].

4.2. Diterpenes

The member of furanoid norditerpenes diosbulbin B (**15**) was found in *R. uniflorum* roots (Figure 2) [21]. This compound, first isolated from *Dioscorea bulbifera* L. [47], is a hepatotoxic agent that causes oxidative damage to hepatocyte membranes [48]. Additionally, abietane diterpenoid abietic acid (**16**) and acyclic diterpene alcohol phytol (**17**) have been detected in the flowers and herb of *R. uniflorum*.

4.3. Triterpenes

Various types of triterpenes were found in *R. uniflorum*, including ecdysteroids, triterpene acids, alcohols, ketones, and sterols. Ecdysteroids were first discovered in *R. uniflorum* in the early 1990s [31]. Since then, 39 compounds (**18**–**56**) of this group have been identified in the plant, of which 33 are in the herb (**18**–**26**, **28**–**33**, **36**–**48**, **50**, **52**–**55**) and 15 in the roots (**18**–**20**, **22**, **25**, **27**, **28**, **34**, **35**, **41**, **49**–**51**, **53**, **56**) (Figure 3). Almost all compounds contain a full side chain, except rubosterone (**16**). The number of hydroxyl groups in ecdysteroid structures can be 3 (**52**), 4 (**23**, **24**), 5 (**21**, **22**, **25**, **26**, **48**), 6 (**18**–**20**, **27**–**36**, **38**–**40**, **43**, **44**, **49**, **51**, **56**), and 7 (**37**, **41**, **42**, **45**–**47**, **50**, **53**–**55**), indicating the dominance of polyhydroxy compounds. The most common derivatives are 20-hydroxyedysone (**28**–**36**), ajugasterone C (**18**–**20**), inokosterone (**38**–**40**), polypodine B (**45**–**47**), and turkesterone (**53**–**55**). For individual components, acetates (**29**–**31**), acetonides (**19**, **22**, **32**, **39**, **42**, **44**, **46**, **54**), diacetonides (**20**, **33**), and acetonide-acetates (**40**) can be formed. Glycosides are a rare group of derivatives for *R. uniflorum* because only two compounds (**22** and **23**) have been identified in the roots of this species [6]. Ecdysteroids cinnamoyl esters **36**, **47**, and **55** found in the leaves of the plant deserve special attention [33]. Previously known compounds (**36** and **47**) were isolated only from the fern *Dacrydium intermedium* Kirk (*Lepidothamnus intermedius* (Kirk) Quinn, Podocarpaceae) [49,50]. The unusual structural compounds include rapontisteron R_1 (**51**) (which contains a furan ring in the side chain [32]) and uniflorsterone (**56**) (which contains a hydroxyl group in the atom C-23 [34]).

Comparing the chemodiversity of the ecdysteroids in *R. uniflorum* with that of the more-studied species *R. carthamoides* (in which more than 50 compounds of this class have been identified so far [20]), it can be assumed that there are many more compounds in the composition of the steroid metabolome of *R. uniflorum*.

Different organs of *R. uniflorum* are the sources of 25 non-ecdysteroid triterpenoids (**57**–**81**), including 23 compounds isolated from the roots and five components detected in the herb (**57**, **59**–**61**, **79**) (Figure 4). The only tetracyclic triterpene roburic acid (**57**), typical for *Gentiana* roots [51], was detected in the flowers of *R. uniflorum* [9]. The remaining compounds (**58**–**81**) were pentacyclic triterpenes. Ursans are the dominant structural type of *R. uniflorum* triterpenes (21 compounds), as opposed to oleanans, represented by fewer components (3 compounds). Triterpenoids of *R. uniflorum* can contain unsaturated bonds at C_9–C_{11}, C_{12}–C_{13}, C_{18}–C_{19}, C_{19}–C_{29}, hydroxyl groups at C_2, C_3, C_{19}, and C_{25} and carboxyl groups at C_{23} and C_{28}. Eleven compounds have been identified as mono- and di-glycosides, including fragments of β-D-glucose and/or α-L-arabinose at C_3 and/or C_{28}. Two alcohols, α- (**59**) and β-amyrins (**79**) [35], as well as two acids, 3-oxo-ursus-12-en-24-oic acid (as methyl ether, **60**) [35] and ursolic acid (**61**) [30], have been detected in the *R. uniflorum* herb. Triterpenoids of *R. uniflorum* roots are notable for their large structural diversity of the primary ursan skeleton, as well as their ability to form glycosides identified only in this part of the plant. The basic triterpene aglycones are 3β-hydroxy-urs-12,18(19)-

dien-28-oic acid as glycosides **62**–**64** [25,39], 3β-hydroxy-urs-12,19(29)-dien-28-oic acid as glycosides **66** and **67** [25,39], pomolic acid (3β,19α-dihydroxy-urs-12-en-28-oic acid, **68**) [25,41] and tormentic acid (2α,3β,19α-trihydroxy-urs-12-en-28-oic acid, **73**) [36]. Of note, the 3β-hydroxy functional group is typical for *R. uniflorum* triterpenoids, except in three compounds with a 3α-hydroxy functional group, including **76** [25,41], **77** [41], and **76** [25], isolated from the roots of *R. uniflorum* growing in China. A few oleanan derivatives include β-amyrin (**79**) [35], oleanolic acid (**80**) [40], and arjunic acid (**81**) [36]. Five stigmastane derivatives have been found in the *R. uniflorum* herb and roots, including β-sitosterol (**82**) and its glucosides daucosterol (**83**) [25,35,40,41], stigmasterol (**84**) [35,41], stigmastan-3,5-diene (**85**) [35], and stigmast-4-en-3-one (**86**) [35].

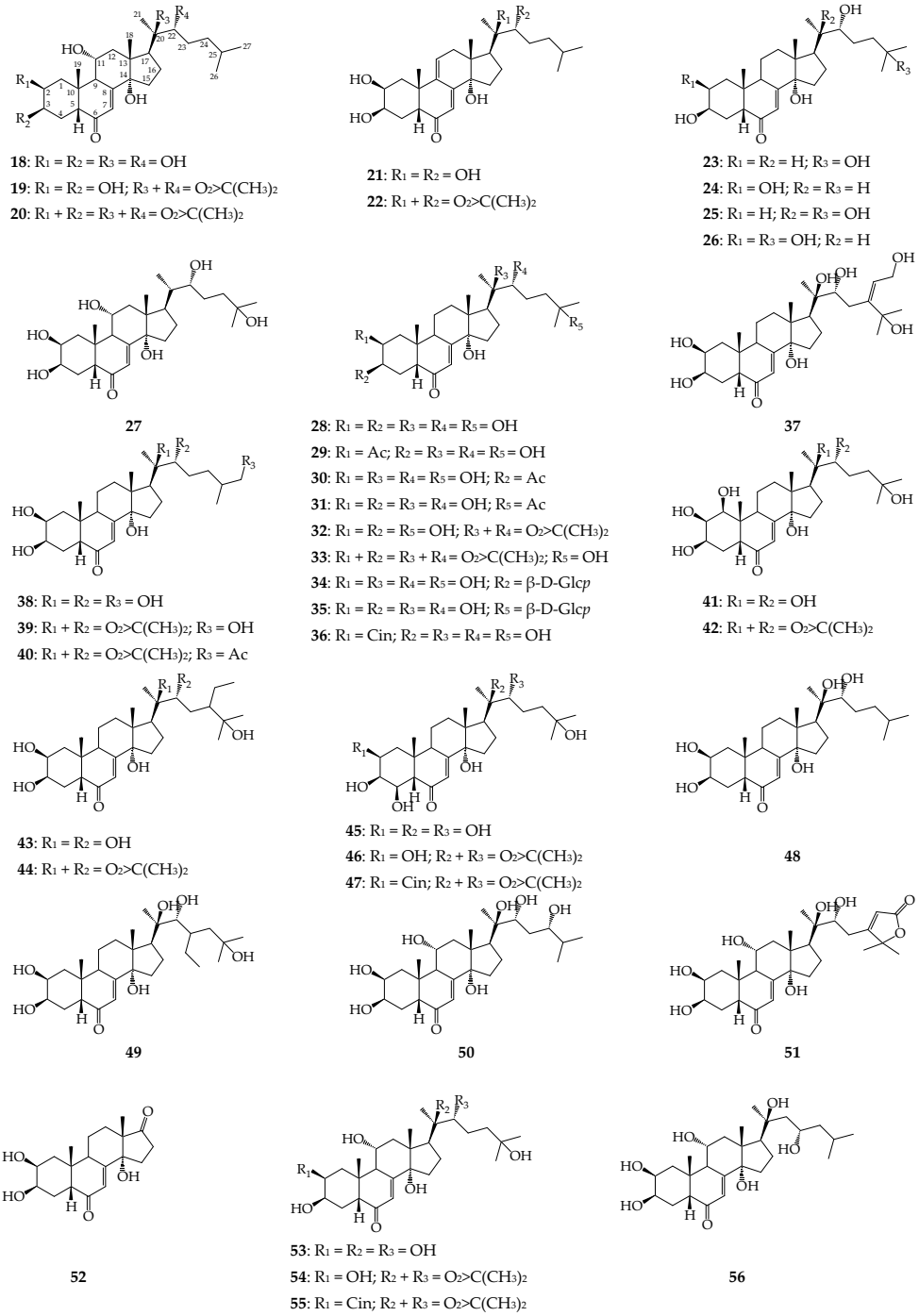


Figure 3. Ecdysteroids **18**–**56**. Ac–acetyl; Cin–cinnamoyl; β-D-Glc*p*–β-D-glucopyranose.

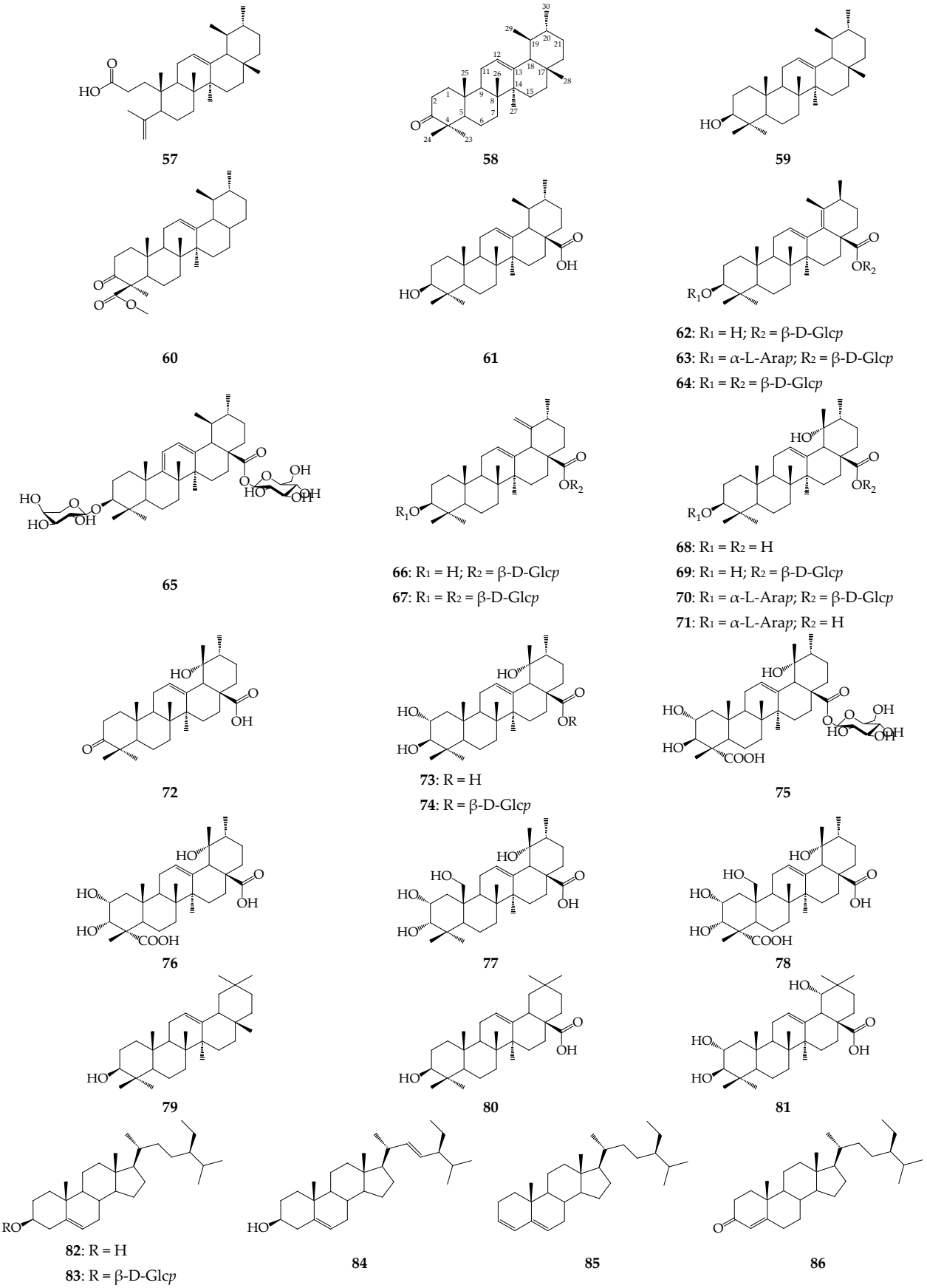


Figure 4. Triterpenes **57**–**86**. A-L-Ara*p*–α-L-arabinopyranose; β-D-Glc*p*–β-D-glucopyranose.

4.4. Thiophenes

Twelve thiophenes (**87**–**98**) have been isolated from the roots of *R. uniflorum*, including monomers (**97**, **98**) and dimeric derivatives of 2,2′-dithiophene (**87**–**96**) (Figure 5). Typical thiophenes of *R. uniflorum* are derivatives of 5′-(1-propynyl)-2,2′-dithiophene, with various substituents at position C_5, such as arctinal (**87**) [17,41], arctinone b (**88**) [17,41,42], and arctic acid (**91**) [17,25,40]. Two chlorinated thiophenes, 7-chloroarctinone b (**89**) [41,42] and rhapontiynethiophene A (**96**) [42], have been isolated from the roots of Chinese origin.

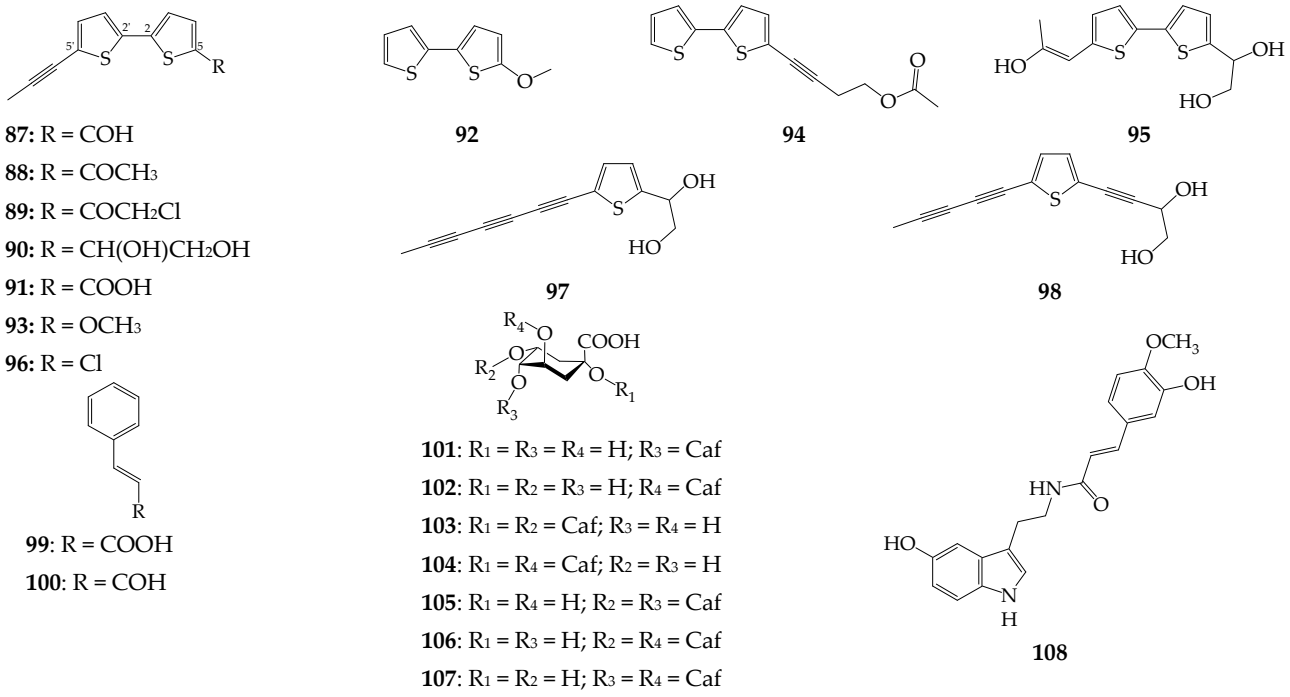


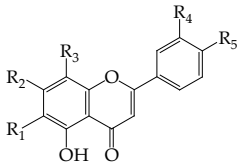
Figure 5. Thiophenes **87**–**98** and hydroxycinnamates **99**–**108**. Caf–caffeoyl.

4.5. Hydroxycinnamates

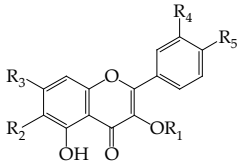
Cinnamic acid (**99**) and cinnamaldehyde (**100**) have been found in the *R. uniflorum* flowers [9], while seven caffeoylquinic acids (**101**–**107**) were found to be components of the herb and seeds (Figure 5) [29,30,43]. Feruloyl serotonin (**108**) was isolated from the seeds of *R. uniflorum* [29] and was previously found in *R. carthamoides* [52].

4.6. Flavonoids

Flavonoids are the largest group of *R. uniflorum* metabolites containing 53 compounds (**109**–**161**), including 37 flavones (**101**–**145**), 16 flavonols (**146**–**161**) and one catechin (**162**) (Figure 6) [9,16,29,30,33]. Flavone derivatives are present in most *O*- and *C*-glucosides of apigenin (6 compounds), luteolin (12 compounds), 6-hydroxyluteolin (7 compounds), and 6-methoxyluteolin (7 compounds). Glycoside moieties of flavone glycosides contain glucose, glucuronic acid, rutinose, and acylated carbohydrates as cinnamoyl/caffeoyl-glucose attached mainly at C_7 (18 compounds) and at $C_{3'}/C_{4'}$ (5 compounds). Glycosides of kaempferol, 6-hydroxykaempferol, quercetin, and 6-hydroxy/methoxy-quercetin are the main flavonols of *R. uniflorum*. The general structural patterns are very similar to flavones (carbohydrate nature, 7-*O*-glycosylation), and 3-*O*-glycosides have also been detected. The known data indicate that the greatest flavonoid diversity is specific to leaves, which contain 43 compounds [33], followed by the flowers (15 compounds) [9,30] and seeds (4 compounds) [29].



109: $R_1 = R_3 = R_4 = H$; $R_2 = R_5 = OH$
110: $R_1 = R_3 = R_4 = H$; $R_2 =$ *O*-β-D-Glc*p*; $R_5 = OH$
111: $R_1 = R_3 = R_4 = H$; $R_2 =$ *O*-β-D-GlcA*p*; $R_5 = OH$
112: $R_1 =$ β-D-Glc*p*; $R_2 = R_5 = OH$; $R_3 = R_4 = H$
113: $R_1 = R_4 = H$; $R_2 = R_5 = OH$; $R_3 =$ β-D-Glc*p*
114: $R_1 = R_3 =$ β-D-Glc*p*; $R_2 = R_5 = OH$; $R_4 = H$
115: $R_1 = OCH_3$; $R_2 = R_5 = OH$; $R_3 = R_4 = H$
116: $R_1 = R_3 = H$; $R_2 = R_4 = R_5 = OH$
117: $R_1 = R_3 = H$; $R_2 =$ *O*-β-D-Glc*p*; $R_4 = R_5 = OH$
118: $R_1 = R_3 = H$; $R_2 =$ *O*-(6″-*O*-Cin)-β-D-Glc*p*; $R_4 = R_5 = OH$
119: $R_1 = R_3 = H$; $R_2 =$ *O*-(2″-*O*-Caf)-β-D-Glc*p*; $R_4 = R_5 = OH$
120: $R_1 = R_3 = H$; $R_2 =$ *O*-(6″-*O*-Caf)-β-D-Glc*p*; $R_4 = R_5 = OH$
121: $R_1 = R_3 = H$; $R_2 =$ *O*-β-D-GlcA*p*; $R_4 = R_5 = OH$
122: $R_1 = R_3 = H$; $R_2 =$ *O*-(6″-*O*-α-L-Rha*p*)-β-D-Glc*p*; $R_4 = R_5 = OH$
123: $R_1 = R_3 = H$; $R_2 = R_5 = OH$; $R_4 =$ *O*-β-D-Glc*p*
124: $R_1 = R_3 = H$; $R_2 = R_4 = OH$; $R_5 =$ *O*-β-D-Glc*p*
125: $R_1 =$ β-D-Glc*p*; $R_2 = R_4 = R_5 = OH$; $R_3 = H$
126: $R_1 = H$; $R_2 = R_4 = R_5 = OH$; $R_3 =$ β-D-Glc*p*
127: $R_1 = R_3 =$ β-D-Glc*p*; $R_2 = R_4 = R_5 = OH$
128: $R_1 = R_3 = H$; $R_2 = R_5 = OH$; $R_4 = OCH_3$
129: $R_1 = R_2 = R_4 = R_5 = OH$; $R_3 = H$
130: $R_1 = R_4 = R_5 = OH$; $R_2 =$ *O*-β-D-Glc*p*; $R_3 = H$
131: $R_1 = R_4 = R_5 = OH$; $R_2 =$ *O*-(6″-*O*-Cin)-β-D-Glc*p*; $R_3 = H$
132: $R_1 = R_4 = R_5 = OH$; $R_2 =$ *O*-(2″-*O*-Caf)-β-D-Glc*p*; $R_3 = H$
133: $R_1 = R_4 = R_5 = OH$; $R_2 =$ *O*-(6″-*O*-Caf)-β-D-Glc*p*; $R_3 = H$
134: $R_1 = R_4 = R_5 = OH$; $R_2 =$ *O*-(6″-*O*-α-L-Rha*p*)-β-D-Glc*p*; $R_3 = H$
135: $R_1 = R_2 = R_4 = OH$; $R_3 = H$; $R_5 =$ *O*-β-D-Glc*p*
136: $R_1 = OCH_3$; $R_2 = R_4 = R_5 = OH$; $R_3 = H$
137: $R_1 = OCH_3$; $R_2 =$ *O*-β-D-Glc*p*; $R_4 = R_5 = OH$; $R_3 = H$
138: $R_1 = OCH_3$; $R_2 =$ *O*-(6″-*O*-Cin)-β-D-Glc*p*; $R_4 = R_5 = OH$; $R_3 = H$
139: $R_1 = OCH_3$; $R_2 =$ *O*-(6″-*O*-Caf)-β-D-Glc*p*; $R_4 = R_5 = OH$; $R_3 = H$
140: $R_1 = OCH_3$; $R_2 =$ *O*-(6″-*O*-α-L-Rha*p*)-β-D-Glc*p*; $R_4 = R_5 = OH$; $R_3 = H$
141: $R_1 = OCH_3$; $R_2 = R_5 = OH$; $R_3 = H$; $R_4 =$ *O*-β-D-Glc*p*
142: $R_1 = OCH_3$; $R_2 = R_4 = OH$; $R_3 = H$; $R_5 =$ *O*-β-D-Glc*p*
143: $R_1 = R_3 = R_4 = R_5 = OH$; $R_2 =$ *O*-β-D-Glc*p*
144: $R_1 = R_2 = R_5 = OH$; $R_3 = H$; $R_4 = OCH_3$
145: $R_1 = R_2 = R_4 = OH$; $R_3 = H$; $R_5 = OCH_3$



146: $R_1 = R_2 = R_4 = H$; $R_3 = R_5 = OH$
147: $R_1 =$ α-L-Rha*p*; $R_2 = R_4 = H$; $R_3 = R_5 = OH$
148: $R_1 = R_4 = H$; $R_2 = R_3 = R_5 = OH$
149: $R_1 = R_4 = H$; $R_2 = R_5 = OH$; $R_3 =$ *O*-β-D-Glc*p*
150: $R_1 = R_4 = H$; $R_2 = R_5 = OH$; $R_3 =$ *O*-(2″-*O*-Caf)-β-D-Glc*p*
151: $R_1 = R_4 = H$; $R_2 = OCH_3$; $R_3 =$ *O*-β-D-Glc*p*; $R_5 = OH$
152: $R_1 = R_2 = H$; $R_3 = R_4 = R_5 = OH$
153: $R_1 =$ α-L-Rha*p*; $R_2 = H$; $R_3 = R_4 = R_5 = OH$
154: $R_1 =$ β-D-Glc*p*; $R_2 = H$; $R_3 = R_4 = R_5 = OH$
155: $R_1 =$ *O*-(6″-*O*-α-L-Rha*p*)-β-D-Glc*p*; $R_2 = H$; $R_3 = R_4 = R_5 = OH$
156: $R_1 = H$; $R_2 = R_3 = R_4 = R_5 = OH$
157: $R_1 = H$; $R_2 = R_4 = R_5 = OH$; $R_3 =$ *O*-β-D-Glc*p*
158: $R_1 = H$; $R_2 = R_4 = R_5 = OH$; $R_3 =$ *O*-(2″-*O*-Caf)-β-D-Glc*p*
159: $R_1 = H$; $R_2 = OCH_3$; $R_3 =$ *O*-β-D-Glc*p*; $R_4 = R_5 = OH$
160: $R_1 = R_2 = H$; $R_3 = R_4 = OH$; $R_5 = OCH_3$
161: $R_1 = R_2 = H$; $R_3 = R_5 = OH$; $R_4 = OCH_3$

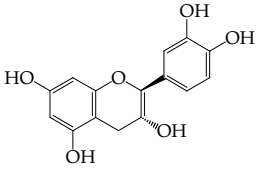


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Figure 6. Flavonoids **109**–**162**. Caf–caffeoyl; Cin–cinnamoyl; β-D-Glc*p*–β-D-glucopyranose; β-D-GlcA*p*–β-D-glucuronopyranose; α-L-Rha*p*–α-L-rhamnopyranose.

4.7. Lignans

Four lignans have been identified in the herbal part of *R. uniflorum*, which include those widely distributed in Asteraceae arctigenin (**164**), arctiin (**165**) [9], hemislin B (**162**), hemislin B O-glucoside (**163**) [30], found only in *Hemistepta lyrata* (Bunge) Bunge (Asteraceae) (Figure 7) [52]. Later, carthamogenin (**166**) and carthamoside (**167**), which are isomeric to **162** and **163** in the α-position of hydrogen at $C_{8'}$ [53], were isolated from the seeds of *R. uniflorum* together with the acetyl ester of **167** and tracheloside (**169**) [29].

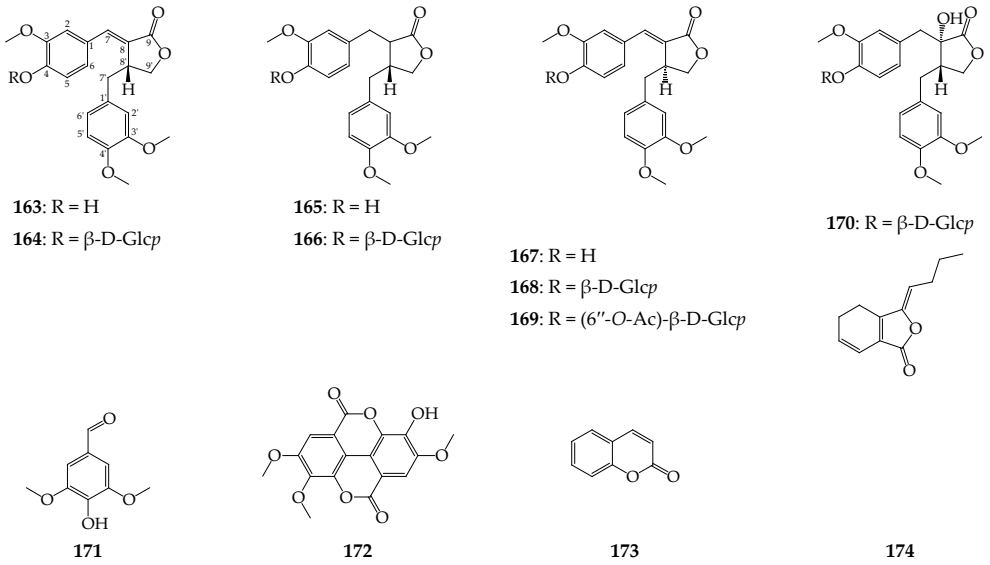

Figure 7. Lignans **163**–**170** and various phenolics **171**–**174**. Ac–acetyl; β-D-Glc*p*–β-D-glucopyranose.

4.8. Other Compounds

Among other phenolic components, catechin (**171**) and 3,3′,4-tri-O-methyl-ellagic acid (**172**) in the roots [13] and 3,5-dimethoxy-4-hydroxybanzaldehyde (**170**), coumarin (**173**), and ligustilide (**174**) in the flowers have been identified in *R. uniflorum* [9]. The presence of 13 amino acids (**175**–**187**), including essential amino acids, was found in *R. uniflorum* organs [44]. The main components of the free amino acids were alanine and glycine, while lysine and valine dominated among the bound amino acids. 3′-Deoxyadenosine (cordycepin, **188**) and nicotinamide (**193**) were detected in the flowers [9], and some vitamins (**189**–**192**, **194**, **195**) have been quantified in the herb and roots of *R. uniflorum* [45]. Additionally, four alkanes (**196**–**199**) and fatty acids (**200**–**217**) have been described as components of the whole plant [35]. The main components of the lipid fraction of *R. uniflorum* herb are linolenic acid (19.6%), palmitic acid (18.0%), and linoleic acid (13.4%). Root lipids of *R. uniflorum* are similar to the herb profile; however, the highest content was noted for linoleic acid (41.2%) and lower for palmitic acid (1.8%) and linolenic acid (8.3%). There is also information about essential oil composition in the flowers [54] and roots of *R. uniflorum* [55], including free carbohydrates (**218**–**225**) and polysaccharides [46].

5. Chromatographic Analysis of *R. uniflorum*

Despite the widespread use of *R. uniflorum* as a medicinal plant, only few methods for the quantitative analysis of this plant material using liquid chromatography are known (Table 3). To separate the main ecdysteroids of the herb and roots of *R. uniflorum* (**28**, **25, 41**, **50**, **53**), six variants of high performance liquid chromatography analysis on reversed-phase sorbents have been proposed, i.e., using the columns Ultrasphere ODS [7], Zorbax ODS [28], ProntoSIL 120-5 C18 [56], YMC-Pack C18 [57], GLC Mastro C18 [43], and Waters Acquity UPLC HSS T3 C18 [9] with 100–250-mm length [7,9,28] or 60-mm microcolumns [56]. Mixtures of methanol, acetonitrile, water, perchlorate buffer, and formic acid have been used as eluents to achieve separation in isocratic and gradient modes. The total duration of the analysis varied from 15 to 70 min. Analysis of the dominant components of *R. uniflorum* flowers has also been performed under reversed phase HPLC conditions using a mixture of phosphoric acid and acetonitrile [57]. The chosen analysis conditions allowed separation of six compounds, including **28**, **109**, **116**, **128**, **147**, and **163**.

According to the quantitative analysis of *R. uniflorum*, the content of individual compounds in different organs may vary (Table 4). The concentration of the dominant ecdysteroid 20-hydroxyecdysone (**28**) in raw materials collected in Russia was 0.02–1.06% [28,56]. Plants growing in China are characterized by a higher content of **28** in the leaves (up to

1.35%) than in the roots (0.45%) [7,57]. The level of other ecdysteroids (**25**, **41**, **50**, and **53**) was characterized as trace. The concentration of the basic phenolic compounds in *R. uniflorum* flowers varied from 0.03–0.05% for **128** to 0.42–2.26% for **163** [57].

Table 3. HPLC analysis conditions used for the separation of selected *R. uniflorum* metabolites.

Compounds	Column	Elution Mode (I—Isocratic; G—Gradient), Eluents, Gradient Programm; Flow Rate (ν)	Column Temperature (T), Detector [1] (D), Analysis Duration (t)	Ref.
28, 50, 53	Ultrasphere ODS (250 × 4.6 mm, 5 µm; Hichrom Ltd., Lutterworth, UK)	I; MeOH-H_2O 40:60; ν 1.5 mL/min	T 20°C; D: UV (λ 242 nm); t 15 min	[7]
25, 28, 41	Zorbax ODS (250 × 4.6 m, 5 µm; Agilent Technologies, Santa-Clara, CA, USA)	I; MeCN-H_2O 20:80; ν 2 mL/min	T 55 °C; D: UV; t 20 min	[28]
25, 28, 41, 53	ProntoSIL 120-5 C18 AQ (60 × 1 mm, 1 µm; Knauer, Berlin, Germany)	G; A: 4.1 M $LiClO_4$-0.1 M $HClO_4$ 5:95, B: MeCN; 0–15 min 5–58% B; ν 0.15 mL/min	T 35 °C; D: UV (λ 248 nm); t 15 min	[56]
28, 109, 116, 128, 147, 163	YMC-Pack C18 (250 × 4.6 mm, 5 µm; YMC Co. Ltd., Kyoto, Japan)	G; A: 0.2% H_3PO_4, B: MeCN; 0–15 min 20–25% B, 15–50 min 25–40% B; ν 0.8 mL/min	T 35 °C; D: UV (λ 254 nm); t 50 min	[57]
28, 38, 101–107, 111, 121	GLC Mastro C18 (150 × 2.1 mm, 3 µm; Shimadzu, Kyoto, Japan)	G; A: 0.5% HCOOH in water, B: 0.5% HCOOH in MeCN; 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	T 35 °C; D: PDA (λ 254 nm), MS; t 25 min	[43]
2, 16, 57, 99, 100, 102, 106, 113, 153–155, 160, 164, 165, 170, 173, 174, 188, 193, 217	Waters Acquity UPLC HSS T3 C18 (100 × 2.1 mm, 1.8 µm)	G; A: MeCN, B:0.1% HCOOH; 0–10 min 100% B, 10–20 min 100–70% B, 10–25 min 70–60% B, 25–30 min 60–50% B, 30–40 min 50–30% B, 40–45 min 30–0% B, 45–60 min 0% B, 60–60.1 min 0–100% B, 60.1–70min 100% B; ν 0.2 mL/min	T 30 °C; D: DAD (λ 254 nm), MS; t 70 min	[9]

[1] Detectors: DAD–diode array; MS–mass spectrometric; PDA–photodiode array; UV–ultraviolet.

Table 4. Content of selected metabolites in *R. uniflorum* organs, % of dry plant weight.

Origin	Compound									
	25	**28**	**41**	**50**	**53**	**109**	**116**	**128**	**147**	**163**
					Roots					
China [7]		0.12–0.45		0.01–0.06	0.01–0.07					
Russia [28,56]	Tr.–0.02	0.09–0.85	Tr.	0.16						
					Flowes					
China [7]		0.78		0.02	Tr.					
Russia [28]		0.03								
					Leaves					
China [7,41]		0.27–1.35		Tr.–0.09	Tr.	0.08–0.24	0.19–0.60	0.03–0.05	0.66–1.26	0.42–2.26
Russia [28]	Tr.–0.06	0.02–0.85	Tr.–0.02							
					Stems					
China [7]		0.62		0.05	0.02					
Russia [28]	Tr.	0.03–0.47	Tr.							
					Herb					
Russia [56]	0.24	1.06		0.10	0.21					

Tr.—trace content.

6. Bioactivities

The known literature data on bioactivity of *R. uniflorum* are primarily related to the preparation of plant roots in the form of extracts and decoctions, as well as the bioactivity of the leaf, herb, and flower extracts (Table 5).

Table 5. Bioactivity data of *R. uniflorum*.

Extract, Compound	Assay, Model	Dose [a]	Positive Control	Result [b]	Ref.
Anti-inflammatory activity					
In vitro study					
Roots ethanol extract	LPS-stimulation of murine macrophage RAW 264.7 cells	10–100 μg/mL	Dexamethasone (10 μg/mL)	Inhibition NO, TNF-α, IL-6, IL-1β, iNOS, COX-2, HO-1, NF-κB, phospho-IκBα, IκBα, ERK1/2, p38, JNK	[58]
Roots hexane, chloroform, ethyl acetate, butanol, water extracts	LPS-stimulation of murine macrophage RAW 264.7 cells	5–100 μg/mL	N^G-monomethyl-L- arginine monoacetate (10 μM)	Inhibition NO, PGE2, IL-1β, IL-6, iNOS	[8]
Flower ethanol extract	Doxorubicin-initiated cardiotoxicity of embryonic rat cardiomyocytes H9c2	12.5–800 μg/mL	Dexrazoxane (7.5 μg/mL)	Inhibition ROS, Bax, cleaved-caspase-3, cleaved-caspase-9, cleaved-PARP, NF-κB	[16]
In vivo study					
Flower ethanol extract	Oropharyngeal aspirational LPS induced acute lung injury of male BALB/c mice	100–400 mg/kg	Dexamethasone (5 mg/kg)	Inhibition TNF-α, IL-6, NO, p-p38, p-JNK, p-ERK, TLR4, Myd88, p-IκB, p-p65, Keap1; stimulation Nrf2, HO-1, NQO1	[9]
Antitumor activity					
In vitro study					
Root ethanol extract	AGS human gastric adenocarcinoma cell	50–150 μg/mL	5-Fluorouracil (5 mg/kg)	Inhibition of tumor cells grow	[59]
Roots ethyl acetate extract	Cell carcinoma cell line SCC15	50 μg/mL	5-Fluorouracil (5 μg/mL)	Inhibition tumor grow, ETS1, Prx1	[60]
Root methylene chloride, ethyl acetate, butanol extracts	Human lung adenocarcinoma cells A549 and H1299	10–500 μg/mL	5-Fluorouracil (5 mg/kg)	Inhibition of tumor cells grow	[61]
In vivo study					
Roots ethanol extract	Mice bearing H_{22} hepatoma cells	100–400 mg/kg p.o.	5-Fluorouracil (5 mg/kg)	Anti-angiogenic and pro-apoptotic effects against H22 hepatoma cells	[62]
Roots ethyl acetate extract	Human OSCC cell line SCC15	12.5–100 μg/mL	5-Fluorouracil (5 mg/kg)	Induction of apoptosis; suppression of cell invasion and migration; inhibition Prx1, vimentin, Snail	[63]
Roots water extract	Mice bearing H_{22} hepatoma cells	100–400 mg/kg p.o.	5-Fluorouracil (5 mg/kg)	Inhibition tumor grow, TNF-α	[64]

Table 5. *Cont.*

Extract, Compound	Assay, Model	Dose [a]	Positive Control	Result [b]	Ref.
Immune-stimulating activity: in vivo study					
Roots ethanol extract	Erythrocyte immune function of rats	3–15 mg/kg; i.p.	-	Enhancement of erythrocyte immune function	[65]
Leaf ethanol extract	Cyclophosphamide-induced immunodeficiency of CBA×C57Bl/6 mice	100 mg/kg; i.p.	Echinacea extract (200 mg/kg)	Increasing of the cellular, humoral, and macrophage immunity	[66]
Nervous system effects: in vivo study					
Roots ethanol extract	Elevated plus maze test and dark/light chamber of Wistar rats	100–300 mg/kg; p.o.	*Rhaponticum carthamoides* extract (100 mg/kg)	Anti-anxiety effect	[67]
Roots ethanol extract	D-galactose-induced aging of mice	20–100 mg/kg; p.o.	-	Anti-aging effect	[68]
Roots ethanol extract	Passive avoidance test of mice	20–100 mg/kg; p.o.	-	Improving memory impairment	[69]
Leaf ethanol extract	Passive avoidance test of mice	50–200 mg/kg; p.o.	*Rhaponticum carthamoides* extract (100 mg/kg)	Anxiolytic effect	[70]
Leaf ethanol extract	Hypoxia/reoxygenation of Wistar rats	100–200 mg/kg; p.o.	*Rhaponticum carthamoides* extract (100 mg/kg)	Neuroprotective effect	[71]
Stress-protective activity: in vivo study					
Roots ethanol extract	Immobilization stress and psycho-emotional stress tests of Wistar rats	100–300 mg/kg; p.o.	*Rhaponticum carthamoides* extract (100 mg/kg)	Stress-protective effect	[67,72]
Actoprotective and anabolic activity: in vivo study					
Roots ethanol extract	Physical endurance test of Wistar rats	100–300 mg/kg; p.o.	*Rhaponticum carthamoides* extract (100 mg/kg)	Increasing of overall physical endurance, working capacity, ATP in muscles, skeletal muscle mass; decrease metabolic acidosis	[67,68]
Antihypoxic and anti-ischemic activity: in vivo study					
Roots ethanol extract	Hypercapnic, hemic, histotoxic hypoxia of Wistar rats	50–200 mg/kg; p.o.	*Rhaponticum carthamoides* extract (100 mg/kg)	Antihypoxic effect	[67]
Leaf ethanol extract	Bilateral carotid artery occlusion of Wistar rats	50–200 mg/kg; p.o.	*Rhaponticum carthamoides* extract (100 mg/kg)	Decrease mortality, neurological deficit, severity of cerebral edema	[73]

Table 5. *Cont.*

Extract, Compound	Assay, Model	Dose [a]	Positive Control	Result [b]	Ref.
Hepatoprotective activity					
In vitro study					
Root ethanol extract	H_2O_2-induced liver cells damage	12.5–400 μg/mL	-	Icreasing cell viability; reduction LDH, ALT, AST, MDA; increasing GSH	[74]
Root ethanol extract	H_2O_2-induced HepG2 cells damage	25–400 μg/mL	-	Icreasing cell viability, SOD, GSH; reduction LDH, ALT, AST, MDA, caspase-3, 8, 9, cytoplasmic cytochrome C, p-JNK, nuclear NF-κB	[75]
In vivo study					
Roots water extract	Carbon tetrachloride-induced acute liver injury of mice	50–200 mg/kg; i.p.	Bifendate (10 mg/kg)	Reduction serum ALT, AST, liver level of LOOH, MDA; increasing liver CAT, GSH-Px, SOD, Mn-SOD, Na^+-K^+-ATPase and Ca^{2+}-Mg^{2+}-ATPase; DNA damage of hepatocyte	[76]
Anti-aterosclerotic and hypolypidemic activity: in vivo study					
Root ethanol, water extract	Hypercholesterol diet of mice	100–400 mg/kg; p.o.	-	Decreasing total cholesterol, total glycerides, LDL-C; icreasing HDL-C	[77]
Root ethanol extract	Oleic acid-induced fat accumulation in HepG2 cells	10–500 μg/mL; p.o.	-	Decreasing total cholesterol, total glycerides, LDL-C; icreasing HDL-C	[78]
Inhibition of PPARγ receptors: in vitro study					
Roots ethanol extract; 7-chloroarctinone b	Cell-based transactivation assay	1.18–10 μM	-	Inhibition of rosiglitazone-induced transcriptional activity of PPARγ	[79]
Antioxidant activity: in vitro study					
Root water extract	Total antioxidant activity, hydroxyl radical scavenging, Fe2+-induced lipid peroxidation in liver mitochondria	0–100 μg/mL	Ascorbic acid	Antioxidant activity	[80]
Root butanol extract	Total antioxidant activity, hydroxyl radical scavenging, Fe^{2+}-induced lipid peroxidation in liver mitochondria	0–100 μg/mL	Ascorbic acid	Antioxidant activity	[81]

Table 5. *Cont.*

Extract, Compound	Assay, Model	Dose [a]	Positive Control	Result [b]	Ref.
Herb ethanol extract	Radical-scavenging activity against 2,2-diphenyl-1-picrylhydrazyl radicals; 2,2′-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid cation-radicals; superoxide radicals; Fe^{2+}-chelating activity	5–1000 µg/mL	Ascorbic acid	Antioxidant activity	[43]
Antibacterial activity: in vitro study					
Root water extract	Inhibition of *Gardnerella vaginalis*	0–20 mg/mL	Ampicillin	Bacterial grow inhibition	[82]
Diuretic activity: in vivo study					
Root water extract	3-Month application of extract solution by Wistar rats	100–500 mg/mL; p.o.	-	Moderarte increase of diuresis	[58]
Antidiabetic activity: in vitro study					
Seed water extract, flavonoids, lignans	Inhibition of pancreatic α-amylase	0–100 µg/mL	Acarbose	Moderarte inhibition of α-amylase	[29]

[a] p.o.–per os, oraly; i.p.–intraperitonealy. [b] ALT–alanine transaminase; AST–aspartate transaminase; Bax–Bcl-2-associated X protein; CAT–catalase; COX-2–cyclooxygenase-2; ERK–extracellular signal-regulated kinase 1/2; ETS1–protein C-ets-1; GSH–glutathione reduced; HDL–high-density lipoprotein; HO-1–heme oxygenase 1; IL-6–interleukin-6; IL-1β–interleukin-1β; iNOS–inducible nitric oxide synthase; IκBα–nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha; JNK–c-Jun N-terminal kinase; Keap1–Kelch-like ECH-associated protein 1; LDH–lactate dehydrogenase; LDL–low-density lipoprotein; LOOH–lipid hydroperoxide; MDA–malondialdehyde; Myd88–myeloid differentiation primary response 88; NF-κB–nuclear factor kappa B; NO–nitric oxide (II); NQO1–NAD(P)H dehydrogenase [quinone] 1; Nrf2–nuclear factor erythroid 2-related factor 2; PARP–poly ADP ribose polymerase; PGE2–prostaglandin E2; Prx1–peroxiredoxin-1; p38–mitogen-activated protein kinase p38; ROS–reactive oxygen species; SOD–superoxide dismutase; TNF-α–tumor necrosis factor-alpha; and TLR4–toll-like receptor 4. "-"–no data.

6.1. Anti-Inflammatory Activity

The study of the anti-inflammatory mechanisms of *R. uniflorum* roots and flowers demonstrated their effectiveness in in vitro and in vivo studies [8,9,16,19,58]. Ethanol extract of *R. uniflorum* roots significantly inhibited the secretion of nitric oxide (NO) and inflammatory cytokines in the culture of RAW 264.7 mouse macrophages and peritoneal macrophages without the manifestation of cytotoxicity [58]. The extract significantly suppressed the expression of inducible NO synthase (iNOS) and cyclooxygenase 2 while simultaneously inducing the expression of heme oxygenase 1 [58]. The inhibition of phosphorylation and degradation of the IκBα factor led to the prevention of nuclear translocation of the NF-κB transcription factor, which, in turn, controls the expression of immune response, apoptosis, and cell cycle genes. A pronounced ability of the *R. uniflorum* root extract to suppress mitogen-activated protein kinases (MAPKs), such as ERK1/2, p38, and JNK, was revealed in a culture of lipopolysaccharide (LPS)-stimulated macrophages [8]. The lipophilic components of the hexane and chloroform fractions of *R. uniflorum* had a greater inhibitory effect on NO production in a culture of LPS-stimulated macrophages and suppressed the transcription of the iNOS messenger RNA [8]. The butanol and ethyl acetate fractions reduced the synthesis of prostaglandin PGE2, while the hexane and ethyl acetate fractions led to the suppression of interleukin-1β [8]. Overall, these facts demon-

strate the effectiveness of the *R. uniflorum* root extract as an anti-inflammatory agent acting through the activation of NF-κB and MAPK signaling pathways. Investigation of the anti-inflammatory activity of the *R. uniflorum* flower extract demonstrated its facilitating potential after doxorubicin-initiated cardiotoxicity of embryonic rat cardiomyocytes H9c2 [16]. In in vivo experiments, *R. uniflorum* flower extract prevented LPS-induced pathological alterations of lung bronchoalveolar lavage fluid (BALF) [9]. Downregulation of F4/80 antigen expression in lungs and suppression of LPS-induced elevations in BALF and lung tissue levels of myeloperoxidase were observed with the simultaneous reduction of expression of proteins p-p38, p-JNK, p-ERK (mitogen-activated protein kinase signaling pathway), TLR4, Myd88, p-IκB, and p-p65 (Toll-like receptor 4 and NF-κB signaling pathway) [9]. The abovementioned results indicated that the *R. uniflorum* flower extract ameliorated LPS-induced acute lung injury by suppressing the inflammatory response and enhancing antioxidant capacity.

6.2. Antitumor Activity

The root extracts of *R. uniflorum* in in vitro studies reduced the proliferation of AGS human gastric adenocarcinoma cells [59], SCC 15 oral cancer cells [60], and human lung adenocarcinoma cells A549 and H1299 tumor cells [61]. The extracts inhibited messenger RNA (mRNA) and expressed transcription factors protein C-ets-1 (ETS1), and peroxiredoxin 1 (Prx1) resulted in the suppression the growth and proliferation of SCC 15 cells [60]. Animal experiments with H_{22} hepatoma cells demonstrated reduction of transplanted tumor grow caused by reducing DNA fragmentation and microvascular density and worsening the expression of signaling proteins, such as vascular endothelial growth factors (VEGF) and hypoxia-inducible factor 1α (HIF-1α), indicating an antiangiogenic and proapoptotic effect on H_{22} cells [62]. Root ethyl acetate extract affected the growth of SCC15 epidermoid carcinoma cells, reducing their viability and inducing their apoptosis. Treatment of cells with this fraction promoted the expression of messenger RNA and E-cadherin, while reducing the expression of peroxiredoxin 1, vimentin, and the SNAI1 protein influenced the program of the epithelial-mesenchymal transition, significantly reducing tumor growth [63]. The aqueous extract of *R. uniflorum* roots (100–400 mg/kg) slowed tumor growth by 27–38% in mice with transplanted H22 tumors, improving the immune system and antioxidant status of the organism [64].

6.3. Immune-Stimulating Activity

The immunostimulatory effect of the *R. uniflorum* root extract has been described for the experimental immune suppressions caused by azathioprine, owing to the increasing activity of the cellular, humoral, and macrophage components of the body′s immune system [65]. The extract from the leaves of *R. uniflorum* is an effective immune stimulant in cyclophosphamide-induced immunodeficiency [66].

6.4. Nervous System Effects

A study on the anti-anxiety effect of *R. uniflorum* showed that animals treated with dry root extract (200–300 mg/kg) had higher overall locomotor activity compared to control animals. Administration of the *R. uniflorum* extract had a pronounced anti-anxiety effect under conditions of unpunished behavior. An increase in exploratory activity and a decrease in the feeling of fear and anxiety in animals was explained by a decrease in their level of emotionality [67]. The administration of the extract stimulated cognitive functions, accelerated the development of conditioned reflexes, and ensured the long-term preservation of memory. The use of the *R. uniflorum* root extract in mice with galactose-induced aging contributed to the prevention of mitochondrial degeneration, increased the level of succinate dehydrogenase and superoxide dismutase in brain tissues, and decreased the level of MDA, monoamine oxidase, and lactate dehydrogenase activity [68]. Finally, it led to a decrease in the concentration of lipoperoxides and lipofuscin in brain tissues, positively affecting the learning and memory processes [69]. The leaf extract of *R. uniflorum*

(50–200 mg/kg) resulted in the adaptation of animals to unfamiliar conditions, an increase in orienting-exploratory activity, and the formation of a conditioned reflex with positive reinforcement, which has generally indicated a pronounced anti-anxiety effect [70]. After 30 min hypobaric hypoxia and 3 h reoxygenation, the use of *R. uniflorum* leaf extract (100 mg/kg) limited the formation of pyknotic neurons, sharply hypochromic neurons, and "shadow cells" in the cortex of cerebral hemispheres, indicating a neuroprotective effect during hypoxia/reoxygenation [71].

6.5. Stress-Protective Activity

In models of 18 h immobilization stress and psycho-emotional stress, it was found that extracts from the herb and roots of *R. uniflorum* (100 mg/kg) had a pronounced stress-protective effect, reducing the involution of immunocompetent organs (adrenals, thymus, spleen), delaying the development of deep destruction of the gastric mucosa, reducing the level of MDA, and increasing the concentration of reduced glutathione and the activity of catalase and superoxide dismutase [67]. After administration of *R. uniflorum* extracts, there was a decrease in blood concentration of adrenaline, norepinephrine, adrenocorticotropic hormone, corticosterone, and aldosterone [72]. The positive effect of extracts is due to the limitation of hyperactivation of sympathetic–adrenal and hypothalamic–pituitary–adrenal stress-realizing systems.

6.6. Actoprotective and Anabolic Activity

Administration of the *R. uniflorum* root extract (100 mg/kg) led to an increase in overall physical endurance in experimental animals, which affected the increase in working capacity, improved energy supply of working tissues, and increased ATP content in skeletal muscles [68]. A decrease in the severity of metabolic acidosis and the intensity of free radical processes also prolonged the possibility of performing physical work. An increase in the animal body weight, up to 16% compared with the control after application of the *R. uniflorum* root extract (100 mg/kg), occurred owing to an increase in the skeletal muscle mass [67]. An increase in the muscle protein synthesis and DNA and RNA concentrations was observed without a noticeable effect on blood glucose and somatotropic hormone levels, which indicated an anabolic effect of the *R. uniflorum* root extract.

6.7. Antihypoxic and Anti-Ischemic Activity

Dry extracts of *R. uniflorum* (50–200 mg/kg) demonstrated pronounced antihypoxic effect, while the effectiveness of root extract was higher in models of hypercapnic and hemic hypoxia, and the herb extract was more effective in histotoxic hypoxia [67]. Intragastric administration of *R. uniflorum* leaf extract (50–200 mg/kg, 14 days) before bilateral carotid artery occlusion led to a decrease in the total mortality of experimental animals, a decrease in neurological deficit, and a decrease in the severity of cerebral edema [73].

6.8. Hepatoprotective Activity

Root ethanol extract of *R. uniflorum* increased cell viability at H_2O_2-induced liver cell damage in in vitro models [74,75]. Pre-treatment of mice with an aqueous *R. uniflorum* root extract attenuated CCl_4-induced liver damage, decreased the activity of alanine aminotransferase and aspartate aminotransferase in serum, reduced the concentration of hydroperoxides and malondialdehyde in the liver, increased the level of catalase, glutathione peroxidase, and superoxide dismutase, and reduced glutathione [76]. A decrease in the activity of Na^+-K^+-ATPase and Ca^{2+}-Mg^{2+}-ATPase in liver mitochondria and a decrease in the hepatocyte DNA damage indicated a pronounced hepatoprotective effect of the extract on the function of the damaged organ.

6.9. Anti-Aterosclerotic and Hypolypidemic Activity

In a hypercholesterol diet model in birds, the *R. uniflorum* root extract was found to reduce the incidence and severity of atherosclerotic vascular lesions while protecting the

ultra-microstructural integrity of cells [77]. The ethanol *R. uniflorum* root extract reduced the levels of triglycerides and the low- and high-density lipoproteins in the blood of mice with experimental hyperlipidemia and prevented lipid accumulation in hepatocytes [78].

6.10. Other Activities

Peroxisome activator-activated receptors (PPARs) are a group of nuclear receptors that play an essential role in the regulation of metabolism. Gamma-type receptors (PPARγ) are expressed in all tissues of the body and are a therapeutic target for the treatment of obesity, diabetes, cancer, and other diseases. The *R. uniflorum* root extract, as well as its component 7-chloroarctinone b (**89**), inhibited the rosiglitazone-induced transcriptional activity of PPARγ [79]. Plasmon resonance indicated that **89** binds to PPARγ receptors, blocking the ability of PPARγ agonists to interact with the ligand-binding domains of the receptors (PPARγ-LBD). The ability of **89** to inhibit hormonal and rosiglitazone-induced adipocyte differentiation was confirmed using the Gal4/UAS model and two hybrid yeast methods, indicating its potential efficacy for the treatment of metabolic diseases.

There is also evidence that the aqueous *R. uniflorum* root extract has an antioxidant and membrane-stabilizing activity [43,80,81], an antibacterial effect against *Gardnerella vaginalis* [82], a moderate diuretic effect [58], and a pancreatic α-amylase-inhibiting potential [29].

7. Toxicity

The study of acute toxicity of *R. uniflorum* dry extracts from the herb and roots at doses of 3.5–10 g/kg demonstrated no death of animals after intragastric administration [83]. After intraperitoneal administration, the LD_{50} values were 5.8 (herb extract) and 9.5 g/kg (root extract). Long-term administration of the extracts had no negative effect on the morpho-functional parameters of the central nervous, cardiovascular, and urinary systems, organs of the gastrointestinal tract, metabolism, peripheral blood parameters, and the hemostasis system of laboratory animals [83]. Application of the extract as single injection at doses of 100 and 1000 mg/kg did not have local irritating or mutagenic effects. These results indicate that *R. uniflorum* extracts belong to the practically non-toxic group.

8. Conclusions

This review summarizes the scientific literature concerning the chemical composition, methods of analysis, and biological activity of traditional medicine *Rhaponticum uniflorum*. The presented data indicate a good degree of knowledge of the metabolites of the roots and herb of *R. uniflorum*. Of particular interest are the anti-inflammatory components of *R. uniflorum*, such as sesquiterpenes [84], ecdysteroids [85], triterpenes [86], thiophenes [87], and flavonoids [88]. Owing to the confirmed presence of these compounds in the plant, we understand its ethnopharmacological use as an anti-inflammatory agent. Despite promising information on the chemical and pharmacological composition of *R. uniflorum* and its extracts, biological studies of individual compounds are still insufficient. We note a lack of studies on metabolites (e.g., sesquiterpenes, triterpenes, and thiophenes) in aboveground organs. The composition of phenolic compounds of the whole plant has not been fully studied to date. Carbohydrates remain an unexplored class of compounds for *R. uniflorum* and the genus *Rhaponticum* in general. It is necessary to expand our knowledge about the organ-specific distribution of substances in the plant, as well as the influence of the environmental conditions of *R. uniflorum* growth on its chemical profile. Owing to the current level of scientific interest in *R. uniflorum* and its extracts, new data on the pharmacological efficacy of pure compounds in various pathologies should be expected in the near future. Therefore, we believe that this review is a starting point for future research on the health benefits of consuming products containing *R. uniflorum*, especially modern dosage forms (e.g., nanoformulations), which will contribute to a wider inclusion of this natural component in new pharmacological products.

9. Patents

Available patent information suggests that *R. uniflorum* extracts were registered as components of complex antihypoxic and adaptogenic remedy [89], cosmetic composition with a purpose of lipometabolism promoter [90], soy sauce [91], and granulated insecticide [92], as well as an independent medicine with stress-protective [93] or anxiolytic activity [94].

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References

1. Shi, Z.; Chen, Y.L.; Chen, Y.S.; Lin, Y.R.; Liu, S.W.; Ge, X.J.; Gao, T.G.; Zhu, S.X.; Liu, Y.; Yang, Q.E.; et al. Rhaponticum Ludwig. In *Flora of China*, 2nd ed.; Wu, Z.Y., Raven, P.H., Hong, D.Y., Eds.; Science Press: Beijing, China; Missouri Botanical Garden Press: St. Louis, MI, USA, 2011; Volume 20–21, pp. 177–179.
2. Kokolska, L.; Janovska, D. Chemistry and pharmacology of *Rhaponticum carthamoides*: A review. *Phytochemistry* **2009**, *70*, 842–855. [CrossRef] [PubMed]
3. Mosbah, H.; Chahdoura, H.; Kammoun, J.; Hlila, M.B.; Louati, H.; Hammami, S.; Flamini, G.; Achour, L.; Selmi, B. *Rhaponticum acaule* (L.) DC. essential oil: Chemical composition, in vitro antioxidant and enzyme inhibition properties. *BMC Complement. Altern. Med.* **2018**, *18*, 79. [CrossRef] [PubMed]
4. Dashti, A.; Shokrzade, M.; Karami, M.; Habibi, E. Phytochemical Identification, acute and subchronic oral toxicity assessments of hydroalcoholic extract of *Acroptilon repens* in BALB/c mice: A toxicological and mechanistic study. *Heliyon* **2022**, *8*, e08940. [CrossRef] [PubMed]
5. Zhang, X.-P.; Zhang, J.; Dong, M.; Zhang, M.-L.; Huo, C.-H.; Shi, Q.-W.; Gu, Y.-C. Chemical constituents of plants from the genus *Rhaponticum*. *Chem. Biodiv.* **2010**, *7*, 594–609. [CrossRef] [PubMed]
6. Malyshev, L.I. Rhaponticum Hill. (*Leuzea* DC.). In *Flora of Siberia*; Malyshev, L.I., Ed.; CRC Press: Boca Raton, FL, USA, 2007; Volume 13, pp. 322–341. [CrossRef]
7. Guo, D.A.; Lou, Z.C. Separation and quantitative determination of three phytoecdysteroids in *Rhaponticum uniflorum* by high performance liquid chromatography. *J. Chin. Pharm. Sci.* **1992**, *1*, 60–65.
8. Lee, J.-H.; Hwang, K.H.; Kim, G.H. Inhibition of wild herb *Rhaponticum uniflorum* on synthesis of inflammatory mediators in macrophage cells. *Food Sci. Biotechnol.* **2013**, *22*, 567–572. [CrossRef]
9. Zhen, D.; Liu, C.; Huang, T.; Fu, D.; Bai, X.; Ma, Q.; Jiang, M.; Gong, G. Ethanol extracts of *Rhaponticum uniflorum* (L.) DC inflorescence ameliorate LPS-mediated acute lung injury by alleviating inflammatory responses via the Nrf2/HO-1 signaling pathway. *J. Ethnopharmacol.* **2022**, *2965*, 115497. [CrossRef]
10. Gammermann, A.F.; Semichov, B.V. *Dictionary of Tibetan-Latin-Russian Names of Medicinal Plant Materials used in Tibetan Medicine*; AN SSSR: Ulan-Ude, Russia, 1963; pp. 68–70.
11. Aseeva, T.A.; Dashiev, D.B.; Dashiev, A.D.; Nikolaev, S.M.; Surkova, N.A.; Chekhirova, G.V.; Yurina, T.A. *Tibetan Medicine of Buryats*; SO RAN: Novosibirsk, Russia, 2008; pp. 218–220.
12. Batorova, S.M.; Yakovlev, G.P.; Aseeva, T.A. *Handbook of Medicinal Plants of Traditional Tibetan Medicine*; Nauka: Novosibirsk, Russia, 2013; pp. 209–292.
13. Dashiev, D.B. *Dud Rtsi: The Canon of Tibetan Medicine*; Vostochnaya Literatura: Moscow, Russia, 2001; pp. 620–622.
14. Singh, B.; Surmal, O.; Singh, B.; Mudasir, B.S.; Bhat, N.; Chowdhary, M.A.; Srinivas, S.; Shahnawaz, M. Folklore plants used in Tibetan Mountain based Sowa-Rigpa system of food and medicine: A close look on plant-people perception to herbal cure. In *Plants for Novel Drug Molecules. Ethnobotany to Ethnopharmacology*; Singh, B., Sharma, Y.P., Eds.; New India Publishing Agency: New Delhi, India, 2021; pp. 2–38.
15. Khaidav, T.; Altanchimeg, B.; Varlamova, T.C. *Medical Plants in Mongolian Medicine*; Gosizdatelstvo: Ulaan-Bator, Mongolia, 1985; pp. 232–236.
16. Hu, B.; Zhen, D.; Bai, M.; Xuan, T.; Wang, Y.; Liu, M.; Yu, L.; Bai, D.; Fu, D.; Wei, C. Ethanol extracts of *Rhaponticum uniflorum* (L.) DC flowers attenuate doxorubicin-induced cardiotoxicity via alleviating apoptosis and regulating mitochondrial dynamics in H9c2 cells. *J. Ethnopharmacol.* **2022**, *28824*, 114936. [CrossRef]

17. Wei, H.-X.; Gao, W.-Y.; Tian, Y.-J.; Guan, Y.-K.; Huang, M.-H.; Cheng, D.-L. New eudesmane sesquiterpene and thiophene derivatives from the roots of *Rhaponticum uniflorum*. *Pharmazie* **1997**, *52*, 245–247.
18. Huneck, S.; Knapp, H.D. Inhaltsstoffe weiterer Compositen aus der Mongolei. *Pharmazie* **1986**, *41*, 673–675.
19. Olennikov, D.N. Guaiane-type sesquiterpenes from *Rhaponticum uniflorum*. *Chem. Nat. Comp.* **2019**, *55*, 157–159. [CrossRef]
20. Bruno, M.; Bancheva, S.; Rosselli, S.; Maggio, A. Sesquiterpenoids in subtribe Centaureinae (Cass.) Dumort (tribe Cardueae, Asteraceae): Distribution, ^{13}C nmR spectral data and biological properties. *Phytochemistry* **2013**, *95*, 19–93. [CrossRef] [PubMed]
21. Liu, B.; Shi, R.; Yang, C. Isolation and identification of diosbulbin B in the aqueous extract of *Rhaponticum uniflorum*. *J. Beijing Univ. Trad. Chin. Med.* **2004**, *27*, 58–61.
22. Olennikov, D.N. Minor ecdysteroids from *Rhaponticum uniflorum* leaves from Eastern Siberia. *Chem Nat Comp.* **2018**, *54*, 798–800. [CrossRef]
23. Cheng, J.K.; Zhang, Y.H.; Zhang, Z.Y.; Cheng, D.L.; Zhang, G.L. Studies of ecdysterones from *Rhaponticum uniflorum*. *Chem. J. Chin. Univ.* **2002**, *11*, 2084–2088.
24. Zhang, Y.H.; Wang, H.Q. Ecdysteroids from *Rhaponticum uniflorum*. *Pharmazie* **2001**, *56*, 828–829.
25. Zhang, Y.; Cheng, J.K.; Yang, L.; Cheng, D.L. Triterpenoids from *Rhaponticum uniflorum*. *J. Chin. Chem. Soc.* **2002**, *49*, 117–124. [CrossRef]
26. Zhang, Y.H.; Li, X.P.; Lu, Z.G.; Wang, H.Q. A new ecdysteroid from *Rhaponticum uniflorum*. *Chin. Chem. Lett.* **2001**, *12*, 797–798.
27. Olennikov, D.N. Makisterone C-20,22-acetonide from *Rhaponticum uniflorum*. *Chem. Nat. Comp.* **2018**, *54*, 930–933. [CrossRef]
28. Vorob'eva, A.N.; Rybin, V.G.; Zarembo, E.V.; Boltenkov, E.V. Phytoecdysteroids from *Stemmacantha uniflora*. *Chem. Nat. Comp.* **2006**, *42*, 742–744. [CrossRef]
29. Olennikov, D.N.; Kashchenko, N.I. New inhibitors of pancreatic α-amylase from *Rhaponticum uniflorum*. *Appl. Biochem. Microbiol.* **2023**, *59*, 77–82.
30. Du, Y.; Wang, X.-Q.; Bao, B.-Q.; Hang, H. Chemical constituents from flowers of *Rhaponticum uniflorum*. *Chin. Tradit. Herb. Drugs.* **2016**, *47*, 2817–2821. [CrossRef]
31. Li, X.-Q.; Wang, J.-H.; Wang, S.-X.; Li, X. A new phytoecdysone from the roots of *Rhaponticum uniflorum*. *J. Asian Nat. Prod. Res.* **2000**, *2*, 225–229. [CrossRef]
32. Guo, D.A.; Lou, Z.C.; Gao, C.Y.; Quao, L.; Peng, J.R. Phytoecdysteroids of *Rhaponticum uniflorum* roots. *Acta Pharm. Sin.* **1991**, *26*, 442–446.
33. Olennikov, D.N.; Kashchenko, N.I. New flavonoids and turkesterone-2-*O*-cinnamate from leaves of *Rhaponticum uniflorum*. *Chem. Nat. Comp.* **2019**, *55*, 256–264. [CrossRef]
34. Cheng, J.; Huang, M.; Zhang, Z.; Cheng, D.; Zhang, G. A new ecdysterone from *Rhaponticum uniflorum*. *Acta Bot. Boreali-Occident. Sin.* **2002**, *22*, 1457–1459.
35. Tsybiktarova, L.P.; Garmaeva, L.L.; Taraskin, V.V.; Nikolaeva, I.G.; Radnaeva, L.D.; Tykheev, Z.A.; Nikolaeva, G.G. Composition of lipids from *Rhaponticum uniflorum*. *Chem. Nat. Comp.* **2017**, *53*, 939–940. [CrossRef]
36. Zhang, Y.H.; Zang, J.G.; Xie, J.M.; Cheng, G.L.; Cheng, D.L. Triterpenes from root of *Rhaponticum uniflorum*. *China J. Chin. Materia Med.* **2005**, *30*, 1833–1836.
37. Zhang, X.-P.; Yang, Y.; Wu, M.; Li, L.-G.; Zhang, M.-L.; Huo, C.-H.; Gu, Y.-C.; Shi, Q.-W. Chemical constituents of *Rhaponticum uniflorum*. *Chin. Trad. Herbal Drugs* **2010**, *41*, 859–862.
38. Zhang, Y.H.; Wu, Y.; Yang, L.; Liu, Z.L.; Cheng, D.L. Two new triterpenoid saponins from *Rhaponticum uniflorum*. *Chin. Chem. Lett.* **2009**, *20*, 690–693. [CrossRef]
39. Zhang, Y.H.; Li, X.P.; Lu, Z.G.; Wang, H.Q. A new triterpenoid saponin from *Rhaponticum uniflorum* (Compositae). *Acta Bot. Sin.* **2002**, *44*, 359–361.
40. Zhang, Y.; Wang, W.; Wang, T.; Wang, H. Triterpenes and other constituents from *Rhaponticum uniflorum*. *J. Chin. Pharm. Sci.* **2001**, *10*, 113–114.
41. Wei, H.; Gao, W.; Guan, Y.; Huang, M.; Cheng, D.; Wei, L. Studies on lipophilic chemical constituents of *Rhaponticum uniflorum*. *J. Lanzhou Univ.* **1997**, *41*, 139–142.
42. Liu, H.-L.; Guo, Y.-W. Three new thiophene acetylenes from *Rhaponticum uniflorum* (L.) DC. *Helv. Chim. Acta* **2008**, *91*, 130–135. [CrossRef]
43. Shantanova, L.N.; Olennikov, D.N.; Matkhanov, I.E.; Gulyaev, S.M.; Toropova, A.A.; Nikolaeva, I.G.; Nikolaev, S.M. *Rhaponticum uniflorum* and *Serratula centauroides* extracts attenuate emotional injury in acute and chronic emotional stress. *Pharmaceuticals* **2021**, *14*, 1186. [CrossRef]
44. Garmaeva, L.L.; Nikolaeva, I.G.; Nikolaeva, G.G. Amino acids from *Rhaponticum uniflorum*. *Chem. Nat. Comp.* **2017**, *53*, 607–608. [CrossRef]
45. Garmaeva, L.L.; Nikolaeva, I.G.; Nikolaeva, G.G.; Tsybiktarova, L.P. Vitamin B content in *Rhaponticum uniflorum*. *Chem. Nat. Comp.* **2015**, *51*, 978–979. [CrossRef]
46. Olennikov, D.N. Free carbohydrates, glucofructans, and other polysaccharides from *Rhaponticum uniflorum*. *Chem. Nat. Comp.* **2018**, *54*, 751–754. [CrossRef]
47. Kawasaki, T.; Komori, T.; Setoguchi, S. Furanoid norditerpenes from Dioscoreaceae Plants. I. Diosbulbins A, B and C from *Dioscorea bulbifera* L. forma *spontanea* Making et Nemoto. *Chem. Pharm. Bull.* **1968**, *16*, 2430–2435. [CrossRef]

48. Ma, Y.; Niu, C.; Wang, J.; Ji, L.; Wang, Z. Diosbulbin B-induced liver injury in mice and its mechanism. *Hum. Exp. Toxicol.* **2014**, *33*, 729–736. [CrossRef]
49. Russell, G.B.; Horn, D.H.S.; Middleton, E.J. New phytoecdysones from *Dacrydium intermedium*. *J. Chem. Soc.* **1971**, 71. [CrossRef]
50. Russell, G.; Fenemore, P.; Horn, D.; Middleton, E. Insect moulting hormones: The phytoecdysones of *Dacrydium intermedium*. *Austr. J. Chem.* **1972**, *25*, 1935. [CrossRef]
51. Wu, L.-H.; Annie Bligh, S.W.; Leon, C.J.; Li, X.-S.; Wang, Z.-T.; Branford-White, C.J.; Simmonds, M.S.J. Chemotaxonomically significant roburic acid from Section Cruciata of *Gentiana*. *Biochem. Syst. Ecol.* **2012**, *43*, 152–155. [CrossRef]
52. Ren, Y.L.; Yang, J.S. Hemislin B glucoside, a new lignan from *Hemistepta lyrata*. *Chin. Chem. Lett.* **2002**, *13*, 859–861.
53. Harmatha, J.; Buděšínský, M.; Vokáč, K.; Pavlík, M.; Grüner, K.; Laudová, V. Lignan glucosides and serotonin phenylpropanoids from the seeds of *Leuzea carthamoides*. *Collect. Czech. Chem. Commun.* **2007**, *72*, 334–346. [CrossRef]
54. Zhu, L.; Lu, Y.; Chen, D. Composition of essential oil from inflorescences of *Rhaponticum uniflorum* (L.) DC. *China, J. Chin. Materia Med.* **1991**, *16*, 739–740.
55. Gao, Y.; Xu, Y. Analysis of composition of the essential oil of *Rhaponticum uniflorum*. *J. Anshan Teachers College* **2013**, *2*, 38–40.
56. Nikolaeva, I.G.; Tsybiktarova, L.P.; Garmaeva, L.L.; Nikolaeva, G.G.; Olennikov, D.N.; Matkhanov, I.E. Determination of ecdysteroids in *Fornicium uniflorum* (L.) and *Serratula centauroides* (L.) raw materials by chromatography-UV spectrophotometry. *J. Anal. Chem.* **2017**, *72*, 854–861. [CrossRef]
57. Huang, H.; Wang, X.; Du, Y.; Li, C. Simultaneous determination of six components in the flowers of *Rhaponticum uniflorum* by HPLC. *Chin. J. Pharm. Anal.* **2017**, *37*, 956–961. [CrossRef]
58. Jeong, Y.H.; Oh, Y.-C.; Cho, W.-K.; Yim, N.-H.; Ma, J.Y. Anti-inflammatory effect of rhapontici radix ethanol extract via inhibition of NF-B and MAPK and induction of HO-1 in macrophages. *Mediat. Inflamm.* **2016**, *2016*, 7216912. [CrossRef]
59. Wang, Z.; Li, J.; Li, Y.; Wang, D.; Liu, Y.; Jia, Y.; Li, R. *Rhaponticum uniflorum* inhibits malignant phenotype of gastric cancer cells by down-regulating expression of oncogenic small RNA. *Chin. Arch. Trad. Chin. Med.* **2017**, *17*, 3078–3081.
60. Jin, A.-H.; Gao, F.; Xu, H.-X.; Quan, J.-S. Effects of *Rhaponticum uniflorum* on angiogenesis and apoptosis of H_{22} transplanted tumor tissue in mice. *Chin. Pharm. J.* **2016**, *51*, 280–283.
61. Chen, H.; Wang, C.X.; Zhang, M.; Tang, X.F. Effect of Radix rhapontici on the expression of transcription factor Ets-1 and Prx1 in oral cancer. *Beijing J. Stomatol.* **2016**, *24*, 83–86.
62. Chen, H.; Wang, C.; Qi, M.; Ge, L.; Tian, Z.; Li, J.; Zhang, M.; Wang, M.; Huang, L.; Tang, X. Anti-tumor effect of *Rhaponticum uniflorum* ethyl acetate extract by regulation of peroxiredoxin1 and epithelial-to-mesenchymal transition in oral cancer. *Front. Pharmacol.* **2017**, *8*, 870. [CrossRef] [PubMed]
63. Jin, A.H.; Xu, H.X.; Liu, W.J.; Quan, J.S.; Zhe, X.Y. Studies on anti-tumor effect and mechanism of *Rhaponticum uniflorum* in H_{22}-bearing mice. *Chin. J. Exp. Tradit. Med. Form.* **2011**, *5*, 165–167.
64. Zhou, T.; Wang, C.; Feng, L.; Tan, X.; Jia, X. Screening of active fractions from *Rhaponticum uniflorum* (L.) DC. for anti-lung cancer. *Chin. Trad. Patent Med.* **2016**, *39*, 2099–2105.
65. Yan, X.; Zhao, H.; Guan, Y.; Song, Y.; Meng, J. A study on the effect of ethanol extract of Radix rhapontici on erythrocyte immune function in rats. *Afr. J. Tradit. Complement. Altern. Med.* **2013**, *10*, 538–541. [CrossRef]
66. Khobrakova, V.B.; Tugarina, Y.A.; Toropova, A.A.; Olennikov, D.N.; Abidueva, L.R. Effect of the dry *Rhaponticum uniflorum* (L.) DC extract on the state of the immune and antioxidant systems of the body in experimental immunodeficiency. *Probl. Biol. Med. Pharm. Chem.* **2022**, *25*, 43–49. [CrossRef]
67. Tatarinova, N.K.; Razuvaeva, Y.G.; Shantanova, L.N. Anxiolytic effect of *Rhaponticum uniflorum* root extract. *Acta Biomed. Sci.* **2015**, *2*, 92–94.
68. Piao, L.; Zhang, X.W.; Jin, X.Z. Anti-senile effect of *Rhaponticum uniflorm* (L.) DC. extract on D-galactose induced senile in rats. *Lishizhen Med. Materia Medica Res.* **2006**, *10*, 1918–1919.
69. Zou, L.; Du, L.; Dong, A.; Li, X. Effects of the alcohol extract of *Rhaponticum uniflorum* (L.) DC. on learning and memory in the senescent mice induced by D-galactose. *J. Shenyang Pharm. Univ.* **2003**, *30*, 128–131.
70. Razuvaeva, Y.G.; Markova, K.V.; Toropova, A.A.; Olennikov, D.N. Influence of *Rhaponticum uniflorum* dry extract on the white rats in positive supported tests. *Probl. Biol. Med. Pharm. Chem.* **2020**, *23*, 28–33. [CrossRef]
71. Markova, K.V.; Razuvaeva, Y.G.; Toropova, A.A.; Olennikov, D.N. Morphological assessment of neuroprotective effects of *Rhaponticum uniflorum* and *Serratula centauroides* dry extracts in hypoxia/reoxygenation. *J. Biomed.* **2022**, *18*, 56–62. [CrossRef]
72. Shantanova, L.N.; Matkhanov, I.E.; Nikolaev, S.M.; Nikolaeva, I.G.; Khitrikheev, V.E. Stress-protective activity of *Rhaponticum uniflorum* extracts. *J. Pharm. Qual. Assur. Iss.* **2020**, *2*, 4–10. [CrossRef]
73. Markova, K.V.; Toropova, A.A.; Razuvaeva, Y.G.; Olennikov, D.N. Studying of the anti-ischemic action of *Rhaponticum uniflorum* and *Serratula centauroides* dry extracts on a model of bilateral occlusion of the carotid arteries. *Acta Biomed. Sci.* **2022**, *7*, 28–36. [CrossRef]
74. Yin, J.-F.; He, X.; Jin, H.-N.; Yin, X.-Z.; Quan, J.-S. Protective effect of *Rhaponticum uniflorum* ethanol extract on oxidative damage of chang liver cells. *Lishizhen Med. Mater. Med. Res.* **2016**, *27*, 289–291.
75. He, X.; Liu, C.-Y.; Yin, J.-F.; Jin, H.-N.; Yin, X.-Z.; Quan, J.-S. *Rhaponticum uniflorum* inhibits H_2O_2-induced apoptosis of liver cells *via* JNK and NF-κB pathways. *Chin. J. Chin. Materia Med.* **2017**, *63*, 1189–1193.
76. Song, H.; Zhao, W.-X.; Wang, Y.-J.; Quan, J.-S. Effect of *Rhaponticum uniflorum* on hepatic oxidative stress and DNA damage induced by carbon tetrachloride. *Chin. Pharm. J.* **2013**, *48*, 1915–1918.

77. Wang, Y.; Zhang, C.F.; Yang, Z.L. Experimental study of *Rhaponticum uniflorum* for antihyperlipidemia. *Acta Chin. Med. Pharmacol.* **2012**, *4*, 24–26.
78. Zhang, B.; Liu, Y.; Zhang, C.; Yang, Z. Effect of *Rhaponticum uniflorum* on oleic acid-induced fat accumulation in HepG2 cells. *Asia-Pacific Trad. Med.* **2013**, *9*, 10–12.
79. Li, Y.-T.; Li, L.; Chen, J.; Hu, T.-C.; Huang, J.; Guo, Y.-W.; Jiang, H.-L.; Shen, X. 7-Chloroarctinone-b as a new selective PPARγ antagonist potently blocks adipocyte differentiation. *Acta Pharmacol. Sin.* **2009**, *30*, 1351–1358. [CrossRef] [PubMed]
80. Liu, C.-Y.; Jin, A.-H.; Quan, J.-S. Antioxidative effect of *Rhaponticum uniflorum* water extract in vitro. *Food Res. Devel.* **2012**, *24*, 12–14.
81. Quan, J.-S.; Zhang, Z.-H.; Liu, C.-Y.; Jin, A.-H.; Yin, X.-Z. Comparative of antioxidative effect of different solvent fractuions of *Rhaponticum uniflorum*. *Food Res. Devel.* **2011**, *23*, 204–206.
82. Kim, Y.; Lee, H.-S. Antibacterial effects of oriental herb extract against *Gardnerella vaginalis*. *Korean, J. Microbiol. Biotechnol.* **2006**, *34*, 70–73.
83. Razuvaeva, Y.G.; Toropova, A.A.; Ubeeva, E.A.; Banzaraksheev, V.G.; Ausheva, V.V. Preclinical study of the safety of *Rhaponticum uniflorum* root extract. *J. Pharm. Qual. Assur.* **2021**, *32*, 34–39. [CrossRef]
84. Hall, I.H.; Lee, K.H.; Starnes, C.O.; Sumida, Y.; Wu, R.Y.; Waddell, T.G.; Cochran, J.W.; Gerhart, K.G. Anti-inflammatory activity of sesquiterpene lactones and related compounds. *J. Pharm. Sci.* **1979**, *68*, 537–542. [CrossRef]
85. Das, N.; Mishra, S.K.; Bishayee, A.; Ali, E.S.; Bishayee, A. The phytochemical, biological, and medicinal attributes of phytoecdysteroids: An updated review. *Acta Pharm. Sin. B* **2021**, *11*, 1740–1766. [CrossRef]
86. Ríos, J.L.; Recio, M.C.; Maáñez, S.; Giner, R.M. Natural triterpenoids as anti-inflammatory agents. *Stud. Nat. Prod. Chem.* **2000**, *22*, 93–143. [CrossRef]
87. da Cruz, R.M.D.; Mendonça-Junior, F.J.B.; de Mélo, N.B.; Scotti, L.; de Araújo, R.S.A.; de Almeida, R.N.; de Moura, R.O. Thiophene-based compounds with potential anti-inflammatory activity. *Pharmaceuticals* **2021**, *14*, 692. [CrossRef]
88. Maleki, S.J.; Crespo, J.F.; Cabanillas, B. Anti-inflammatory effects of flavonoids. *Food Chem.* **2019**, *299*, 125124. [CrossRef]
89. Nikolaeva, G.G.; Zanabandarova, Z.M.; Nikolaev, S.M. Antihypoxic and Adaptogenic Remedy. Patent RU2771555, 5 May 2022.
90. Kawasaki, Y.; Hori, M.; Yamamoto, Y.; Hiraki, J. Cosmetic Composition and Production Thereof. U.S. Patent 20,060,018,867, 26 January 2006.
91. Anonymous. Production Technology of *Rhaponticum uniflorum* Sauce. Patent CN104172099A, 15 July 2014.
92. He, D.; Li, R. Aqueous Dispersion Granulated Insecticide Containing *Rhaponticum uniflorum*. Patent CN100426969C, 31 December 2006.
93. Nikolaev, S.M.; Nikolaeva, I.G.; Shantanova, L.N.; Nikolaeva, G.G.; Garmaeva, L.L.; Tatarinova, N.K.; Razuvaeva, Y.G.; Matkhanov, I.E.; Li, S.; Pack, S. Stress-Protective Remedy. Patent RU2582282, 20 April 2016.
94. Nikolaev, S.M.; Shantanova, L.N.; Nikolaeva, I.G.; Razuvaeva, Y.G.; Nikolaeva, G.G.; Toropova, A.A.; Tsybiktarova, L.P.; Garmaeva, L.L.; Matkhanov, I.E. Anxiolytic Remedy. Patent RU2705582, 18 November 2019.