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Phytoecdysteroids from *Silene* plants: distribution, diversity and biological (antitumour, antibacterial and antioxidant) activities

[Fitoecdisteroides de plantas *Silene*: distribución, diversidad y actividades biológicas (antitumorales, antibacterianas y antioxidantes)]

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Abstract

Silene is a genus of the Caryophyllaceae family, contains more than 700 species, which are widely distributed in Northern Hemisphere, but also in Africa, Asia and South American. Phytochemical investigations of *Silene* species have revealed that many components from this genus are highly bioactive. More than 400 compounds has been isolated, among them major are phytoecdysteroids. The paper reviews the biological (antitumour, antibacterial and antioxidant) activities and the phytoecdysteroids of genus *Silene*. We summarized the phytoecdysteroids content referring to 171 species from the genus *Silene* and list 93 phytoecdysteroids isolated over the past few decades. There are also reports on the mentioned folk and traditional effects of *Silene* plants.

Keywords: *Silene*, phytoecdysteroids, plants, distribution, flora, traditional uses, pharmacological properties

Resumen

Silene es un género de la familia Caryophyllaceae, conteniendo más de 70 especies, ampliamente distribuidas no solo en el hemisferio norte, sino que también en África, Asia y sud América. Investigaciones fotoquímicas de las especies de *Silene* han revelado que muchos componentes de este género son altamente bioactivos. Más de 400 compuestos han sido aislados, entre ellos los mayoritarios correspondientes a fitoecdisteroides. El manuscrito revisa las actividades biológicas (antitumorales, antibacterianas y antioxidantes) y los fitoecdisteroides del género *Silene*. Resumimos el contenido de fitoecdisteroides en 171 especies del género *Silene* y listamos 93 fitoecdisteroides aislados desde hace unas pocas décadas. Hay también reportes mencionados acerca de los efectos tradicionales y folclóricos de la plantas del género *Silene*.

Palabras Clave: *Silene*; fitoecdisteroides; plantas; distribución; flora; usos tradicionales; propiedades farmacológicas.

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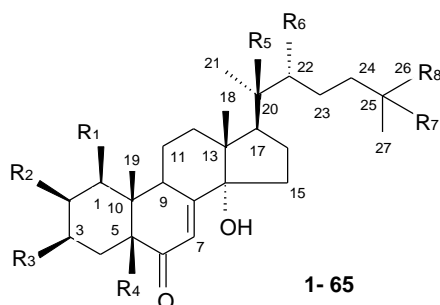
INTRODUCTION

The genus *Silene*, which belongs in the family of the Caryophyllaceae and distributed mainly in the Northern Hemisphere, but also in Africa, Asia and South America. Genus of *Silene* includes more than 700 species (which allocated to 39 sections) of annuals, biennials, and perennials with a worldwide distribution and its taxonomy appears very complex. Most of species are hermaphrodite, but a few are dioecious or gynodioecious (Grauter, 1995). Common names of *Silene* include campion (shared with the related genus *Lychnis*) and catchfly. Red campion (*S. dioica*), white campion (*S. latifolia*, *S. alba*) and bladder

campion (*S. vulgaris*) are common wildflowers throughout Europe.

In this review article, the phytoecdysteroids isolated from the genus *Silene* are listed, and the phytochemical investigation in this genus is summarized. The structures of phytoecdysteroids are shown below, i.e., their names (**Figure 1**) and the corresponding plant sources are collected in **Table 1**. The traditional and medicinal uses of *Silene* plants and biological (antitumour, antibacterial and antioxidant) activities of phytoecdysteroids isolated from these plants are also discussed.

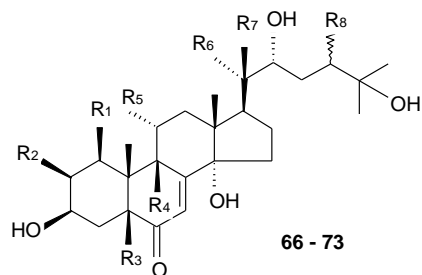
Figure 1
Chemical structures of phytoecdysteroids isolated from *Silene* plants



N	Name	Empiric formula	CAS Registry Number	Substituents in steroidal core				Substituents in side-chain			
				R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	R ₇	R ₈
1	Brahuisterone	C ₂₇ H ₄₄ O ₆	169238-28-2	H	H	OH	OH	H	OH	OH	CH ₃
2	2-Deoxy-20,26-dihydroxyecdysone	C ₂₇ H ₄₄ O ₇	397248-04-3	H	H	OH	H	OH	OH	OH	CH ₂ OH
3	22-Deoxy-20,26-dihydroxyecdysone	C ₂₇ H ₄₄ O ₇	128552-88-5	H	OH	OH	H	OH	H	OH	CH ₂ OH
4	2-Deoxyecdysone	C ₂₇ H ₄₄ O ₅	31575-91-4	H	H	OH	H	H	OH	OH	CH ₃
5	2-Deoxyecdysone-3-acetate	C ₂₉ H ₄₆ O ₆	105888-75-3	H	H	OAc	H	H	OH	OH	CH ₃
6	2-Deoxyecdysone-22-acetate	C ₂₉ H ₄₆ O ₆	76026-42-1	H	H	OH	H	H	OAc	OH	CH ₃
7	2-Deoxyecdysone-22-benzoate	C ₃₄ H ₄₈ O ₆	114317-61-2	H	H	OH	H	H	OBz	OH	CH ₃
8	2-Deoxyecdysone-22-glucoside	C ₃₃ H ₅₄ O ₁₀	627511-32-4	H	H	OH	H	H	OGlu	OH	CH ₃
9	2-Deoxy-20-hydroxyecdysone	C ₂₇ H ₄₄ O ₆	17942-08-4	H	H	OH	H	OH	OH	OH	CH ₃
10	2-Deoxy-20-hydroxyecdysone-3-acetate	C ₂₉ H ₄₆ O ₇	98149-16-7	H	H	OAc	H	OH	OH	OH	CH ₃
11	5 α -2-Deoxy-20-hydroxyecdysone-3-acetate	C ₂₉ H ₄₆ O ₇	188247-16-7	H	H	OAc	H (α)	OH	OH	OH	CH ₃
12	2-Deoxy-20-hydroxyecdysone-22-acetate	C ₂₉ H ₄₆ O ₇	117048-09-6	H	H	OH	H	OH	OAc	OH	CH ₃
13	2-Deoxy-20-hydroxyecdysone-25-acetate	C ₂₉ H ₄₆ O ₇	478809-55-1	H	H	OH	H	OH	OH	OAc	CH ₃
14	2-Deoxy-20-	C ₃₄ H ₄₈ O ₇	345958-46-5	H	H	OBz	H	OH	OH	OH	CH ₃

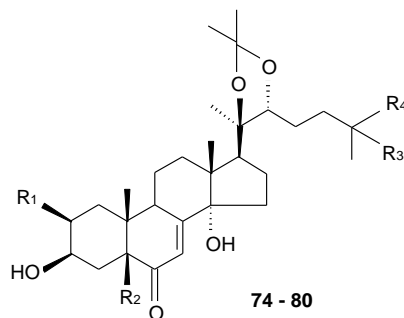
	hydroxyecdysone-3-benzoate											
15	2-Deoxy-20-hydroxyecdysone-22-benzoate	C ₃₄ H ₄₈ O ₇	128529-85-1	H	H	OH	H	OH	OBz	OH	CH ₃	
16	2-Deoxy-20-hydroxyecdysone-3-crotonate	C ₃₁ H ₄₈ O ₇	200867-02-3	H	H	OCOC ₂ H ₂ CH ₃	H	OH	OH	OH	CH ₃	
17	2-Deoxy-20-hydroxyecdysone-3,22-diacetate	C ₃₁ H ₄₈ O ₈	102942-11-0	H	H	OAc	H	OH	OAc	OH	CH ₃	
18	2-Deoxy-20-hydroxyecdysone-22-glucoside	C ₃₃ H ₅₄ O ₁₁	478062-03-2	H	H	OH	H	OH	O-β-D-Glu	OH	CH ₃	
19	2-Deoxy-20-hydroxyecdysone-25-glucoside	C ₃₃ H ₅₄ O ₁₁		H	H	OH	H	OH	OH	O-β-D-Glu	CH ₃	
20	2-Deoxyintegristerone A	C ₂₇ H ₄₄ O ₇	117048-08-5	OH	OH	OH	H	OH	OH	OH	CH ₃	
21	5α-2-Deoxyintegristerone A	C ₂₇ H ₄₄ O ₇	482662-85-1	OH	OH	OH	H (α)	OH	OH	OH	CH ₃	
22	22-Deoxyintegristerone A	C ₂₇ H ₄₄ O ₇	128529-87-3	OH	OH	OH	H	OH	H	OH	CH ₃	
23	5α-22-Deoxyintegristerone A	C ₂₇ H ₄₄ O ₇	128529-88-4	OH	OH	OH	H (α)	OH	H	OH	CH ₃	
24	2-Deoxypolypodine B-3-glucoside	C ₃₃ H ₅₄ O ₁₂	397248-06-5	H	H	O-β-D-Glu	OH	OH	OH	OH	CH ₃	
25	2-Deoxy-5,20,26-trihydroxyecdysone	C ₂₇ H ₄₄ O ₈	1039035-94-3	H	H	OH	OH	OH	OH	OH	CH ₂ OH	
26	20,26-Dihydroxyecdysone (Podecdysone C)	C ₂₇ H ₄₄ O ₈	19458-46-9	H	OH	OH	H	OH	OH	OH	CH ₂ OH	
27	20,26-Dihydroxyecdysone-2,22-diacetate	C ₃₁ H ₄₈ O ₁₀	809239-25-6	H	OAc	OH	H	OH	OAc	OH	CH ₂ OH	
28	20,26-Dihydroxyecdysone-3,22-diacetate	C ₃₁ H ₄₈ O ₁₀	50907-59-0	H	OH	OAc	H	OH	OAc	OH	CH ₂ OH	
29	Ecdysone	C ₂₇ H ₄₄ O ₆	3604-87-3	H	OH	OH	H	H	OH	OH	CH ₃	
30	Ecdysone-22-sulfate	C ₂₇ H ₄₄ O ₉ S	93552-65-9	H	OH	OH	H	H	OSO ₃ H	OH	CH ₃	
31	Ecdysteroside	C ₃₉ H ₆₄ O ₁₇	209850-88-4	H	OH	O-α-D-Gal (1→6) α-D-Gal	H	OH	OH	OH	CH ₃	
32	5α-20-Hydroxyecdysone	C ₂₇ H ₄₄ O ₇	35241-82-8	H	OH	OH	H (α)	OH	OH	OH	CH ₃	
33	5α-20-Hydroxyecdysone-22-benzoate	C ₃₄ H ₄₈ O ₈	113814-96-3	H	OH	OH	H (α)	OH	OBz	OH	CH ₃	
34	20-Hydroxyecdysone	C ₂₇ H ₄₄ O ₇	5289-74-7	H	OH	OH	H	OH	OH	OH	CH ₃	
35	20-Hydroxyecdysone-2-acetate	C ₂₉ H ₄₆ O ₈	19536-25-5	H	OAc	OH	H	OH	OH	OH	CH ₃	
36	20-Hydroxyecdysone-3-acetate	C ₂₉ H ₄₆ O ₈	22961-68-8	H	OH	OAc	H	OH	OH	OH	CH ₃	
37	20-Hydroxyecdysone-22-acetate	C ₂₉ H ₄₆ O ₈	22799-02-6	H	OH	OH	H	OH	OAc	OH	CH ₃	
38	20-Hydroxyecdysone-20-benzoate	C ₃₄ H ₄₈ O ₈	114317-60-1	H	OH	OH	H	OBz	OH	OH	CH ₃	
39	20-Hydroxyecdysone-22-benzoate	C ₃₄ H ₄₈ O ₈	103654-38-2	H	OH	OH	H	OH	OBz	OH	CH ₃	
40	20-Hydroxyecdysone-22-benzoate-25-glucoside	C ₄₀ H ₅₈ O ₁₃	128552-87-4	H	OH	OH	H	OH	OBz	O-β-D-Glu	CH ₃	
41	20-Hydroxyecdysone -2,3-diacetate-22-benzoate	C ₃₈ H ₅₂ O ₁₀		H	OAc	OAc	H	OH	OBz	OH	CH ₃	
42	20-Hydroxyecdysone-22,25-dibenzoate	C ₄₁ H ₅₂ O ₉	148031-28-1	H	OH	OH	H	OH	OBz	OBz	CH ₃	
43	20-Hydroxyecdysone-3-	C ₃₃ H ₅₄ O ₁₂	128365-93-5	H	OH	O-β-D-	H	OH	OH	OH	CH ₃	

	glucoside					Glu					
44	20-Hydroxyecdysone-25-glucoside	C ₃₃ H ₅₄ O ₁₂	116424-80-7	H	OH	OH	H	OH	OH	O-β-D-Glu	CH ₃
45	26-Hydroxyintegristerone A	C ₂₇ H ₄₄ O ₉		OH	OH	OH	H	OH	OH	OH	CH ₂ OH
46	26-Hydroxypolypodine B	C ₂₇ H ₄₄ O ₉	121043-41-2	H	OH	OH	OH	OH	OH	OH	CH ₂ OH
47	Inokosterone	C ₂₇ H ₄₄ O ₇	15130-85-5	H	OH	OH	H	OH	OH	H	CH ₂ OH
48	Integristerone A	C ₂₇ H ₄₄ O ₈	66450-91-7	OH	OH	OH	H	OH	OH	OH	CH ₃
49	Integristerone A-25-acetate	C ₂₉ H ₄₆ O ₉	269739-15-3	OH	OH	OH	H	OH	OH	OAc	CH ₃
50	Polypodine B	C ₂₇ H ₄₄ O ₈	18069-14-2	H	OH	OH	OH	OH	OH	OH	CH ₃
51	Ponasterone A	C ₂₇ H ₄₄ O ₆	13408-56-5	H	OH	OH	H	OH	OH	H	CH ₃
52	Sileneoside A	C ₃₃ H ₅₄ O ₁₂	81655-86-9	H	OH	OH	H	OH	O-α-D-Gal	OH	CH ₃
53	Sileneoside B	C ₃₉ H ₆₄ O ₁₇	84699-93-4	H	OH	O-β-D-Gal	H	OH	O-β-D-Gal	OH	CH ₃
54	Sileneoside C	C ₃₃ H ₅₄ O ₁₃	83207-65-2	OH	OH	OH	H	OH	O-α-D-Gal	OH	CH ₃
55	Sileneoside D	C ₃₃ H ₅₄ O ₁₂	93552-68-2	H	OH	O-β-D-Gal	H	OH	OH	OH	CH ₃
56	Silenoside E (Blechnoside A)	C ₃₃ H ₅₄ O ₁₀	104406-79-3	H	H	O-β-D-Glu	H	H	OH	OH	CH ₃
57	5α-Silenoside E	C ₃₃ H ₅₄ O ₁₀	176166-62-4	H	H	O-β-D-Glu	H (α)	H	OH	OH	CH ₃
58	Sileneoside F	C ₃₃ H ₅₄ O ₁₁	170663-52-2	H	H	O-β-D-Glu	OH	H	OH	OH	CH ₃
59	Sileneoside G	C ₃₉ H ₆₄ O ₁₇	241478-02-4	H	OH	O-α-D-Glu	H	OH	O-α-D-Gal	OH	CH ₃
60	Sileneoside H	C ₃₅ H ₅₆ O ₁₄	289622-72-6	OH	OH	OH	H	OH	O-α-D-Gal	OAc	CH ₃
61	Taxisterone	C ₂₇ H ₄₄ O ₆	19536-24-4	H	OH	OH	H	OH	H	OH	CH ₃
62	Tomentesterone A	C ₃₆ H ₅₀ O ₇	178405-18-0	H	H	OH	H (α)	H	OAc	OBz	CH ₃
63	Tomentesterone B	C ₃₄ H ₄₈ O ₆	181939-54-8	H	H	OH	H (α)	H	OH	OBz	CH ₃
64	Viticosterone E	C ₂₉ H ₄₆ O ₈	22033-96-1	H	OH	OH	H	OH	OH	OAc	CH ₃
65	Viticosterone E-22-benzoate	C ₃₆ H ₅₀ O ₉	118201-53-9	H	OH	OH	H	OH	OAc	OAc	CH ₃



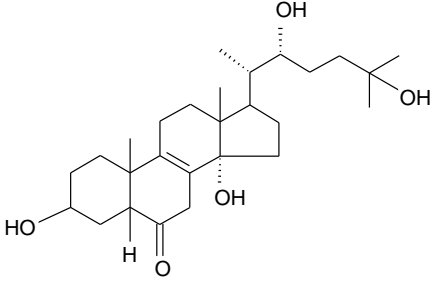
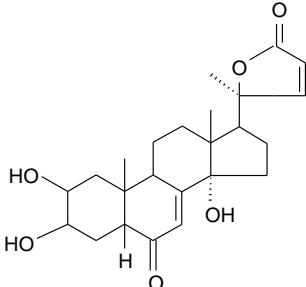
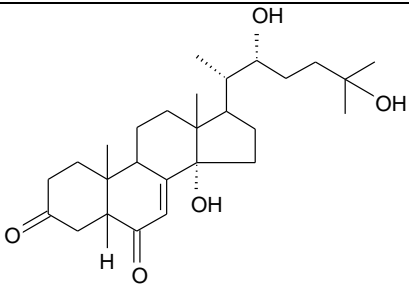
N	Name	Empiric formula	CAS Registry Number	Substituents in steroidal core					Substituents in side-chain		
				R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	R ₇	R ₈
66	24(28)-Dehydromakisterone A	C ₂₈ H ₄₄ O ₇	68556-61-6	H	OH	H	H	H	CH ₃	OH	CH ₂
67	2-Deoxy-21-hydroxyecdysone	C ₂₇ H ₄₄ O ₆	232280-38-5	H	H	H	H	H	CH ₂ OH	H	H
68	5α-2-Deoxy-21-hydroxyecdysone	C ₂₇ H ₄₄ O ₆	232280-39-6	H	H	H (α)	H	H	CH ₂ OH	H	H
69	9α,20-Dihydroxyecdysone	C ₂₇ H ₄₄ O ₈	157977-59-8	H	OH	H	OH (α)	H	CH ₃	OH	H
70	9β,20-Dihydroxyecdysone	C ₂₇ H ₄₄ O ₈	790701-24-5	H	OH	H	OH	H	CH ₃	OH	H
71	Makisterone A	C ₂₈ H ₄₆ O ₇	20137-14-8	H	OH	H	H	H	CH ₃	OH	CH ₃

72	Nusilsterone	C ₂₇ H ₄₄ O ₉	102099-20-7	OH	OH	H	H	H	CH ₃	OH	OH
73	Turkesterone	C ₂₇ H ₄₄ O ₈	41451-87-0	H	OH	H	H	OH	CH ₃	OH	H



N	Name	Empiric formula	CAS Registry Number	Substituents in steroidal core		Substituents in side-chain	
				R ₁	R ₂	R ₃	R ₄
74	2-Deoxy-20-hydroxyecdysone-20,22-acetonide	C ₃₀ H ₄₈ O ₆	142735-52-2	H	H	OH	CH ₃
75	5 α -2-Deoxy-20-hydroxyecdysone-20,22-acetonide	C ₃₀ H ₄₈ O ₆	188246-96-0	H	H (α)	OH	CH ₃
76	2-Deoxy-5,20,26-trihydroxyecdysone-20,22-acetonide	C ₃₀ H ₄₈ O ₈	1039036-00-4	H	OH	OH	CH ₂ OH
77	20,26-Dihydroxyecdysone-20,22-acetonide	C ₃₀ H ₄₈ O ₈	245323-26-6	OH	H	OH	CH ₂ OH
78	20-Hydroxyecdysone-20,22-acetonide	C ₃₀ H ₄₈ O ₇	22798-96-5	OH	H	OH	CH ₃
79	20-Hydroxyecdysone 20,22-acetonide-25-acetate	C ₃₂ H ₅₀ O ₈		OH	H	OAc	CH ₃
80	5,20,26-Trihydroxyecdysone-20,22-acetonide	C ₃₀ H ₄₈ O ₉	1039035-97-6	OH	OH	OH	CH ₂ OH
81	20-Hydroxyecdysone-2,3-acetonide	C ₃₀ H ₄₈ O ₇	113866-76-5	R ₁ = OH	<p style="text-align: center;">81, 82</p>		
82	20-Hydroxyecdysone-2,3-acetonide-22-benzoate	C ₃₇ H ₅₂ O ₈	103654-40-6	R ₁ = OBz			
83	5 α -Dihydroxypurosterone	C ₁₉ H ₂₈ O ₅	232280-44-3	R ₁ = H (α)	<p style="text-align: center;">83, 84</p>		
84	5 β -Dihydroxypurosterone	C ₁₉ H ₂₈ O ₅	232280-43-2	R ₁ = H			

85	20, 22-Acetal isovaleric aldehyde-5 β -cholest-7-en-2 β ,3 β ,14 α ,20R,22R,25-hexahydroxy-6-on	C ₃₂ H ₅₂ O ₇	404589-60-2	R ₁ = H (α)	
86	20,22-Acetal epiisovaleric aldehyde-5 β -cholest-7-en-2 β ,3 β ,14 α ,20R,22R,25-hexahydroxy-6-on	C ₃₂ H ₅₂ O ₇	404589-62-4	R ₁ = H	
87	Dihydropoststerone	C ₂₁ H ₃₂ O ₅	128574-64-1		
88	Poststerone	C ₂₁ H ₃₀ O ₅	10162-99-9		
89	Rubrosterone	C ₁₉ H ₂₆ O ₅	19466-41-2		
90	Makisterone C-2,3;20,22-diacetonide	C ₃₅ H ₅₆ O ₇	1146696-54-9		

91	Praemixisterone	$C_{27}H_{44}O_5$	74396-17-1	
92	Sidisterone	$C_{24}H_{32}O_6$	176391-32-5	
93	Silenosterone	$C_{27}H_{42}O_5$	74396-16-0	

RESULTS AND DISCUSSION

Chemical constituents

Chemical investigations of the genus *Silene* have led to the isolation of phytoecdysteroids, triterpene glycosides (Gaidi *et al.*, 2002), terpenoids, benzenoids, flavonoids (Darmograi, 1977), anthocyanins, N-containing compounds (Dotterl *et al.*, 2005), fatty acids (Kucukboyaci *et al.* 2010; Mamadalieva *et al.*, 2010a; Mamadalieva *et al.*, 2010b), amino acids (Terrab *et al.*, 2007), polysaccharides (Ovodova *et al.*, 2000), sugars (Mogosanu *et al.*, 2011), sterols, vitamins, organic acids and microelements (Eshmirzayeva *et al.*, 2005; Arnetoli *et al.*, 2008).

Phytoecdysteroids

Phytoecdysteroids are contentedly widespread in the plant world. They are isolated from the main types of higher plants - ferns, gymnosperms and angiosperms, but their function in plants are yet studied insufficiently. One can conclude that the role of ecdysteroids in various plants and plant families may

differ: when the ecdysteroid content is low, these exert a determinative effect on the plant growth and development; when it is high (several percent), these may be involved in the biochemical processes of storage, transportation, and metabolism of sterols. In this case, such metabolic products are not excluded that can defend the plant against the harmful factors of the environment (Baltaev, 2000). High concentrations of phytoecdysteroids have found in the reproductive organs, the anthers, apical leaves, and roots. Up to date, phytoecdysteroids isolated from more than 400 species of the plants and fungus belonging to 52 families (Mamadalieva, 2012a). As can be seen, phytoecdysteroids is the predominant constituents within the genus *Silene* (Table 1). Given the complexity of ecdysteroid cocktails existing in many *Silene* species, it has been proposed that ecdysteroids have a chemotaxonomic value in this genus (Zibareva *et al.*, 2009). *Silene* plants accumulate high levels of phytoecdysteroids and have therefore been exploited as an industrial source for the

production of phytoecdysteroids. The qualitative and quantitative composition of phytoecdysteroid cocktails depends considerably on the plant species, but possibly also on soil climatic conditions and on the developmental stage of the plant.

More than 170 *Silene* species have been analyzed for their phytoecdysteroid content, and 140 of them were found to be positive and 93 different ecdysteroids (ca. 25% of the known phytoecdysteroids) have been detected from these plants (Table 1). Some of them contain a high concentration of 20-hydroxyecdysone, such as *Silene otites* (almost 1%) and *Silene multiflora* (1.9%) (Bathori *et al.*, 1987). In the Table 1 we can see, that some species of *Silene* genus characterized by the absence of phytoecdysteroids. Zibareva *et al.*, (2009) explained that by the assumption that some sections of *Silene* (for example, Siphonomorpha, Chloranthae, Coronatae, Graminiformes, Otites, *Silene*, Dipterosperma, Lasiocalycinae, Holopetalae) consist

of only ecdysteroid-containing species, whereas other sections (Behen, Atocion, Psammophilae, Odontopetalae, etc.) contain only ecdysteroid-negative species. In these sections, it is possible, with high probability, to predict ecdysteroid presence or absence in as yet uninvestigated species.

The major phytoecdysteroids identified in *Silene* plants include: 20-hydroxyecdysone, polypodine B, 2-deoxy-20-hydroxyecdysone, 2-deoxyecdysone, inokosterone, integristerone A and ecdysone. Natural derivatives of phytoecdysteroids are also considered as phytoecdysteroids in the definite sense. *Silene* spp. plants are characterized by the highest diversity of ecdysteroid derivatives, such as acetates, acetonides, benzoates, cinnamates, coumarates, crotonates, glycosil-ferulates, glucosides, galactosides, ramosides, xylosides, sulfates, etc. The presence of furan, epoxy and lactone ring contains derivatives of phytoecdysteroids is typical for this genus (Lafont *et al.*, 2002).

Table 1
Distribution of phytoecdysteroids in the genus of *Silene*

Plant species	Isolated phytoecdysteroids	Reference
<i>Silene acaulis</i> (L) Jacq.	34	Zibareva, 1995; Zibareva, 2000; Zibareva <i>et al.</i> , 2003a
<i>S. alba</i> (Miller) E.H.L. Krause	-	Zibareva, 2000; Zibareva <i>et al.</i> , 2003a
<i>S. alpestris</i> Jacq.	-	Zibareva, 2000; Zibareva <i>et al.</i> , 2003a
<i>S. altaica</i> Pers.	34, 50	Bathori <i>et al.</i> , 1995; Zibareva, 1999; Zibareva, 2000
<i>S. ambigua</i> Turcz.	34	Zibareva, 2009
<i>S. antirrhina</i> L.	9, 34, 50, 51	Mamadalieva <i>et al.</i> , 2004b; Meng <i>et al.</i> , 2001; Zibareva <i>et al.</i> , 2003a; Zibareva, 2009
<i>S. apetala</i> Willd.	34	Zibareva <i>et al.</i> , 2003a; Zibareva <i>et al.</i> , 2003b
<i>S. aprica</i> Turel	34	Munkhzhargal <i>et al.</i> , 2010
<i>S. armeria</i> L.	34	Bathori <i>et al.</i> , 1995; Zibareva, 1997; Zibareva, 2000; Zibareva <i>et al.</i> , 2003a; Zibareva <i>et al.</i> , 2003b
<i>S. asterias</i> Griseb.	-	Zibareva, 2000; Zibareva <i>et al.</i> , 2003a
<i>S. bashkirorum</i> Janish	34	Zibareva, 2000
<i>S. bellidifolia</i> Juss. ex Jacq.	34	Zibareva, 2000; Zibareva and Yeryomina, 2002; Zibareva <i>et al.</i> , 2003a
<i>S. bellidioides</i>	-	Zibareva <i>et al.</i> , 2003a
<i>S. bergiana</i> Lindm	34	Zibareva <i>et al.</i> , 2003b
<i>S. boryi</i> Boiss.	-	Zibareva, 2000
<i>S. borystenica</i>	34	Zibareva <i>et al.</i> , 2003b
<i>S. bourgeaui</i> H. Christ.	34	Zibareva, 2009
<i>S. brachypoda</i> Rouy	34, 50	Zibareva, 2000
<i>S. brahuica</i> Boiss.	1, 6, 4, 9, 70, 30, 34, 48-60,	Abubakirov, 1982; Abubakirov, 1984; Bathori <i>et al.</i> ,

	64	1995; Dzhukharova <i>et al.</i> , 1991; Dzhukharova <i>et al.</i> , 1993; Dzhukharova <i>et al.</i> , 1994; Dzhukharova <i>et al.</i> , 1995; Sadikov & Saatov, 1998; Sadikov & Saatov, 1999; Saatov <i>et al.</i> , 1981; Saatov <i>et al.</i> , 1982a; Saatov <i>et al.</i> , 1982b; Saatov <i>et al.</i> , 1984a; Saatov <i>et al.</i> , 1984b; Saatov <i>et al.</i> , 1986b; Saatov <i>et al.</i> , 1993; Saatov <i>et al.</i> , 1999
<i>S. bupleroides</i> L.	-	Zibareva, 2000
<i>S. burchelli</i> Otth.	34	Zibareva <i>et al.</i> , 1998; Zibareva <i>et al.</i> , 2003a
<i>S. campanula</i> Pers.		Zibareva, 2000
<i>S. campanulata</i> S. Watson	34, 50	Zibareva, 1999; Zibareva <i>et al.</i> , 1998
<i>S. caramanica</i> Boiss.	34, 50	Zibareva, 1999; Zibareva <i>et al.</i> , 1998
<i>S. caroliniana</i>	-	Zibareva <i>et al.</i> , 2003a
<i>S. catholica</i> (L) Aiton fil.	34, 50	Bathori <i>et al.</i> , 1995; Zibareva, 1999; Zibareva, 2000; Zibareva, 2003b
<i>S. caucasica</i> Boiss.	34, 50	Zibareva, 1998; Zibareva, 1999; Zibareva <i>et al.</i> , 1998
<i>S. chamarensis</i> Turcz.	34	Munkhzhargal <i>et al.</i> , 2010; Revina <i>et al.</i> , 1988; Saatov <i>et al.</i> , 1993
<i>S. chlorantha</i> Willd.	34	Bathori <i>et al.</i> , 1995; Sviridova <i>et al.</i> , 1995; Zibareva, 1995; Zibareva, 1999; Zibareva, 2000
<i>S. chlorifolia</i> Smith.	9, 34, 50, 51	Bathori <i>et al.</i> , 1995; Zibareva, 1995; Zibareva, 1999; Zibareva, 2000; Zibareva, 2003b; Mamadalieva <i>et al.</i> , 2004b; Meng <i>et al.</i> , 2001; Zibareva, 2009
<i>S. chlorifolia cordifolia</i> All.	-	Pongracz <i>et al.</i> , 2003b
<i>S. ciliata</i> Pourret	34, 50	Bathori <i>et al.</i> , 1995; Zibareva, 1995; Zibareva, 1999; Zibareva, 2000
<i>S. ciliate</i> var <i>graefteri</i> (P).	34	Zibareva, 2000
<i>S. clandestina</i>	+	Zibareva <i>et al.</i> , 2003a
<i>S. claviformis</i>	4, 9, 34, 48, 85, 86	Sadikov <i>et al.</i> , 2001
<i>S. coeli-rosa</i> (L.) Godron in Gren.	34	Bathori <i>et al.</i> , 1995; Zibareva, 2000; Zibareva, 2009; Zibareva <i>et al.</i> , 2003a
<i>S. colorata</i> Poiret.	34	Pongracz <i>et al.</i> , 2003b; Zibareva, 1995; Zibareva, 1999; Zibareva, 2000; Zibareva <i>et al.</i> , 2003a; Zibareva & Yeryomina, 1996
<i>S. colorata</i> ssp. <i>trichocalysina</i>	34	Zibareva, 1995; Zibareva, 1999; Zibareva, 2000
<i>S. compacta</i> Fisher.	-	Pongracz <i>et al.</i> , 2003b; Zibareva, 2000
<i>S. conica</i> L.	-	Pongracz <i>et al.</i> , 2003b; Zibareva, 1997; Zibareva, 2000; Zibareva <i>et al.</i> , 2003a
<i>S. conoidea</i> L.	-	Zibareva, 2000
<i>S. coronaria</i> (L.) Clairv	34	Zibareva, 1995; Zibareva, 1999; Zibareva <i>et al.</i> , 2003a
<i>S. cretica</i> L.	9, 29, 34, 50	Mamadalieva <i>et al.</i> , 2004b; Meng <i>et al.</i> , 2001; Zibareva, 1997; Zibareva, 2009; Zibareva <i>et al.</i> , 1997a; Zibareva <i>et al.</i> , 2003a; Zibareva <i>et al.</i> , 2003b; Zibareva & Yeryomina, 1996
<i>S. cucubalus</i> Wibel.	+	Pongracz <i>et al.</i> , 2003b

<i>S. damboldtiana</i> Greuter et Melzh.	34, 50	Zibareva, 1999; Zibareva <i>et al.</i> , 1998
<i>S. densiflora</i> (L.) Wib. Drurv.	34	Sviridova <i>et al.</i> , 1995; Zibareva, 1999; Zibareva, 2000; Zibareva <i>et al.</i> , 1998
<i>S. dichotoma</i> Ehrh.	-	Zibareva, 2000
<i>S. dinarica</i> Sprengel.	-	Zibareva, 2000
<i>S. dioica</i> (L.) Clairv.	34, 92	Girault <i>et al.</i> , 1996; Lafont and Horn, 1989; Saatov <i>et al.</i> , 1993; Zibareva, 1997; Zibareva, 2000; Zibareva <i>et al.</i> , 2003a
<i>S. disticha</i> Willd.	9, 29, 34, 47, 50, 51	Lafont and Horn, 1989; Mamadalieva <i>et al.</i> , 2004b; Meng <i>et al.</i> , 2001; Zibareva, 1995; Zibareva, 1997; Zibareva, 2009; Zibareva <i>et al.</i> , 2003a; Zibareva <i>et al.</i> , 2003b; Zibareva & Yeryomina, 1996.
<i>S. divaricata</i> Clemente	-	Zibareva, 2000
<i>S. echinata</i> Otth.	29, 34, 50, 51	Mamadalieva <i>et al.</i> , 2004b; Meng <i>et al.</i> , 2001; Zibareva. 2000; Zibareva, 2009; Zibareva <i>et al.</i> , 2003a; Zibareva <i>et al.</i> , 2003b
<i>S. elegans</i> L.	34	Zibareva, 2009
<i>S. fabaria</i> (L.) Sm.	-	Zibareva, 2000
<i>S. fabariodes</i> Husskn.	+	Pongracz <i>et al.</i> , 2003b; Zibareva, 2000
<i>S. fetissoyii</i> Lazkov	34	Zibareva <i>et al.</i> , 2003b
<i>S. firma</i> Siebold et Zucc.	34	Zibareva, 1999; Zibareva & Yeryomina, 1996
<i>S. flavescens</i> Waldst et Kit	34	Bathori <i>et al.</i> , 1995; Zibareva, 1999
<i>S. foliosa</i> Maxim.	34	Novozhilova <i>et al.</i> , 2007; Zibareva <i>et al.</i> , 2003b
<i>S. fortunei</i>	+	Gaidi <i>et al.</i> , 2002
<i>S. fridvaldszkyana</i> Hampe	4, 9, 26, 34, 45, 46, 48, 50, 66	Louden <i>et al.</i> , 2002; Mamadalieva <i>et al.</i> , 2004b; Sviridova <i>et al.</i> , 1995; Zibareva, 1996; Zibareva, 1997; Zibareva <i>et al.</i> , 1997a; Zibareva <i>et al.</i> , 2003a; Zibareva <i>et al.</i> , 2003b; Zibareva <i>et al.</i> , 2009
<i>S. fruticosa</i> L.	34	Zibareva, 2000; Zibareva <i>et al.</i> , 1997a
<i>S. fruticososa</i> L.	-	Pongracz <i>et al.</i> , 2003b
<i>S. fuscata</i> Link in Brot.	-	Zibareva, 2000
<i>S. gallica</i> L.	34	Bathori <i>et al.</i> , 1995; Bergamasco & Horn, 1983; Zibareva, 2000; Zibareva <i>et al.</i> , 2003a
<i>S. gallica</i> var. <i>quiquivulnera</i> (L) Koch.	34	Zibareva, 1999; Zibareva, 2000; Zibareva <i>et al.</i> , 2003
<i>S. gebleriana</i> Schrenk.	34	Zibareva <i>et al.</i> , 2003b
<i>S. gigantea</i> L.	4, 9, 19, 34, 48	Zibareva, 1999; Zibareva, 2000; Zibareva <i>et al.</i> , 2009;
<i>S. goulimyi</i> Turrill.	34	Zibareva, 2000
<i>S. graefferi</i> Guss.	34	Zibareva <i>et al.</i> , 2003b
<i>S. graminifolia</i> Otth.	4, 34	Munkhzhargal <i>et al.</i> , 2010; Revina <i>et al.</i> , 1988; Saatov <i>et al.</i> , 1993; Zibareva, 1997; Zibareva <i>et al.</i> , 2009; Zibareva and Yeryomina, 1996
<i>S. guntensis</i> B. Fredtsch	9, 34, 41	Mamadalieva <i>et al.</i> , 2011

<i>S. hifacensis</i> Rouy ex willk.	34	Zibareva, 2000
<i>S. holopetala</i> Lebed.	34	Zibareva <i>et al.</i> , 2003b
<i>S. ichebogda</i> Glub.	34	Munkhzhargal <i>et al.</i> , 2010
<i>S. inaperta</i> L.	-	Zibareva, 2000
<i>S. incurvifolia</i> Kar et Kir.	34	Zibareva <i>et al.</i> , 2003b
<i>S. inflata</i> Sm.	+	Pongracz <i>et al.</i> , 2003b
<i>S. italica</i> (L.) Pers.	9, 29, 34, 50, 51	Mamadalieva <i>et al.</i> , 2004b; Meng <i>et al.</i> , 2001; Sviridova <i>et al.</i> , 1995; Zibareva, 1996; Zibareva, 1997; Zibareva, 2009; Zibareva <i>et al.</i> , 2003a
<i>S. italica</i> ssp. <i>nemoralis</i>	9, 18, 20-22, 29, 32, 34, 48, 50, 61, 66, 69, 70	Bathori <i>et al.</i> , 2000a; Bathori <i>et al.</i> , 2002a; Bathori <i>et al.</i> , 2002b; Pongracz <i>et al.</i> , 2003; Simon <i>et al.</i> , 2004; Zibareva, 1996; Zibareva, 1997; Zibareva, 2000; Zibareva <i>et al.</i> , 2003b
<i>S. jensseensis</i> Willd.	34	Munkhzhargal <i>et al.</i> , 2010; Revina <i>et al.</i> , 1988; Saatov <i>et al.</i> , 1993; Zibareva, 1997; Zibareva <i>et al.</i> , 1997a
<i>S. jundzillii</i>	+	Zibareva, 2009
<i>S. keiskei</i>	+	Zibareva <i>et al.</i> , 2003a
<i>S. kungessana</i> B. Fedtsch	34	Zibareva <i>et al.</i> , 2003b
<i>S. laeta</i> (Aiton) Godron in Gren.	-	Zibareva, 2000
<i>S. laciniata</i>	+	Zibareva <i>et al.</i> , 2003a
<i>S. latifolia</i> (Gilib) Aschers	4, 9, 34	Abubakirov, 1982; Abubakirov, 1984; Bathori <i>et al.</i> , 1995; Saatov <i>et al.</i> , 1982a; Saatov <i>et al.</i> , 1982b; Saatov <i>et al.</i> , 1993; Zibareva <i>et al.</i> , 2003a
<i>S. linicola</i> C.C.Gmelin.	9, 29, 34, 48, 50, 64, 73	Mamadalieva <i>et al.</i> , 2002b; Mamadalieva <i>et al.</i> , 2004b; Zibareva, 1997; Zibareva <i>et al.</i> , 1997a; Zibareva <i>et al.</i> , 2003a; Zibareva & Yeryomina, 1996
<i>S. longicalycina</i> Kom.	34	Abubakirov, 1982; Abubakirov, 1984; Bathori <i>et al.</i> , 1995; Saatov <i>et al.</i> , 1982a; Saatov <i>et al.</i> , 1982b; Saatov <i>et al.</i> , 1993
<i>S. longicilia</i> (Brot.) Otth. in DC	34	Zibareva, 2009
<i>S. longiflora</i> Ehrh.	+	Pongracz <i>et al.</i> , 2003b
<i>S. maritima</i>	-	Zibareva <i>et al.</i> , 2003a
<i>S. maritime</i> (With.) A. & Love	+	Pongracz <i>et al.</i> , 2003b
<i>S. mellifera</i> Boiss. et Reuter	34, 50	Zibareva, 1996; Zibareva, 1999; Zibareva, 2000; Zibareva <i>et al.</i> , 1997a; Zibareva <i>et al.</i> , 2003; Zibareva <i>et al.</i> , 2009
<i>S. melzheimeri</i> Greuter	34	Zibareva, 2009
<i>S. micropetala</i> Lag.	34	Bathori <i>et al.</i> , 1995; Saatov <i>et al.</i> , 1993; Zibareva, 1997; Zibareva & Yeryomina, 1996
<i>S. mollissima</i> (L.) Pers.	34	Zibareva <i>et al.</i> , 2003b
<i>S. mongolica</i> Maxim	34	Munkhzhargal <i>et al.</i> , 2010
<i>S. multicaulis</i> Guss.	34	Bathori <i>et al.</i> , 1995; Zibareva, 2000

<i>S. multiflora</i> (Waldst. et Kit) Pers	34	Bathori, 1998; Revina <i>et al.</i> , 1988; Zibareva <i>et al.</i> , 2003°
<i>S. nemoralis</i> Waldst. et Kit.	34	Sviridova <i>et al.</i> , 1995; Zibareva, 1999
<i>S. noctiflora</i> L.	-	Pongracz <i>et al.</i> , 2003b; Zibareva, 2000; Zibareva <i>et al.</i> , 2003°
<i>S. nutans</i> L.	3, 15, 22, 23, 26, 34, 46, 48, 50, 52, 61, 72	Baltaev <i>et al.</i> , 1984; Baltaev <i>et al.</i> , 1985a; Baltaev <i>et al.</i> , 1985b; Bathori, 1998; Bathori <i>et al.</i> , 1986a; Bathori <i>et al.</i> , 1986c; Bathori <i>et al.</i> , 1987; Bathori <i>et al.</i> , 1995; Buckman <i>et al.</i> , 1986; Davis <i>et al.</i> , 1993; Girault <i>et al.</i> , 1990; Lafont <i>et al.</i> , 1993; Louden <i>et al.</i> , 2002; Ramazanov <i>et al.</i> , 1997; Ramazanov <i>et al.</i> , 2007; Raynor <i>et al.</i> , 1989; Read <i>et al.</i> , 1990; Revina <i>et al.</i> , 1988; Saatov <i>et al.</i> , 1993; Sviridova <i>et al.</i> , 1995; Wilson & Morden, 1999; Zibareva, 1997; Zibareva, 2000; Zibareva, 2009; Zibareva <i>et al.</i> , 1997a; Zibareva <i>et al.</i> , 2003a
<i>S. obovata</i> Schischk.	34	Zibareva <i>et al.</i> , 2003b
<i>S. odoratissima</i> Bunge	34	Zibareva <i>et al.</i> , 2003b
<i>S. olgae</i> (Maxim.) Rohrb.	-	Novozhilova <i>et al.</i> , 2007
<i>S. oligantha</i> Boiss.	34	Zibareva <i>et al.</i> , 2003b
<i>S. orphanidis</i> Boiss.	-	Zibareva, 2000
<i>S. otites</i> (L.) Wibel.	4, 6, 9-12, 15-17, 20, 26, 29, 34-37, 39, 40, 43, 44, 48, 64, 66-68, 71, 83, 84, 87-89, 92	Bathori, 1986; Bathori, 1998; Bathori <i>et al.</i> , 1986a; 1 Bathori <i>et al.</i> , 1986b; Bathori <i>et al.</i> , 1988; Bathori <i>et al.</i> , 1995; Bathori <i>et al.</i> , 1997; Bathori <i>et al.</i> , 1999; Bathori <i>et al.</i> , 2000a; Bathori <i>et al.</i> , 2001b; Bathori <i>et al.</i> , 2003; Bathori & Kalasz, 2001; Davis <i>et al.</i> , 1993; Girault <i>et al.</i> , 1990; Girault <i>et al.</i> , 1996; Large <i>et al.</i> , 1992; Louden <i>et al.</i> , 2002; Raynor <i>et al.</i> , 1989; Saatov <i>et al.</i> , 1993; Wilson, 2000; Wilson <i>et al.</i> , 1990; Wilson <i>et al.</i> , 1998; Wilson <i>et al.</i> , 1999; Wilson & Morden, 1999; Zibareva, 2000; Zibareva, 2009; Zibareva <i>et al.</i> , 1997a; Zibareva <i>et al.</i> , 1998
<i>S. otites</i> ssp. <i>hungarica</i>	+	Bathori <i>et al.</i> , 1987; Zibareva <i>et al.</i> , 2003a
<i>S. otites</i> var. <i>parviflorus</i>	34	Zibareva, 1995; Zibareva, 1999; Zibareva, 2000
<i>S. paradoxa</i> L.	34, 50	Zibareva, 1995; Zibareva, 1999; Zibareva, 2000; Zibareva <i>et al.</i> , 1998
<i>S. parnassica</i> Boiss.	34, 50	Zibareva, 1995; Zibareva, 1997; Zibareva, 1999; Zibareva, 2000; Zibareva <i>et al.</i> , 1997b
<i>S. patula</i> Desf.	34	Zibareva, 1995; Zibareva, 1999; Zibareva, 2000; Zibareva <i>et al.</i> , 1997b
<i>S. paucifolia</i>	+	Volodin <i>et al.</i> , 2002; Zibareva, 2009
<i>S. pendula</i> L.	+	Pongracz <i>et al.</i> , 2003b; Zibareva <i>et al.</i> , 2003a
<i>S. polaris</i>	-	Zibareva, 1997
<i>S. portensis</i> L.	9, 29, 34, 50, 51	Mamadalieva <i>et al.</i> , 2004b; Meng <i>et al.</i> , 2001; Zibareva, 1995; Zibareva, 1999; Zibareva, 2000; Zibareva, 2009; Zibareva <i>et al.</i> , 1997b; Zibareva <i>et al.</i> , 2003a; Zibareva <i>et al.</i> , 2003b

<i>S. praemixta</i> M. Pop	4, 9, 10, 29, 34, 64, 91, 93	Abubakirov, 1980; Abubakirov, 1982; Abubakirov, 1984; Saatov <i>et al.</i> , 1979a; Saatov <i>et al.</i> , 1979b; Saatov <i>et al.</i> , 1982a; Saatov <i>et al.</i> , 1982b; Saatov <i>et al.</i> , 1985; Saatov <i>et al.</i> , 1993
<i>S. procumbens</i> Murr.	-	Zibareva, 2000
<i>S. pseudotites</i> Bess. ex Reichenb	2, 4, 8, 9, 20, 21, 24, 29, 34, 47, 50, 51, 67, 92	Mamadalieva <i>et al.</i> , 2004b; Meng <i>et al.</i> , 2001; Zibareva, 1999; Zibareva, 2000; Zibareva, 2009; Zibareva <i>et al.</i> , 2003b
<i>S. psevdovelutina</i> Rothm	34	Zibareva, 1999; Zibareva, 2000
<i>S. pusilla</i> Waldst.	+	Dinan <i>et al.</i> , 2001; Zibareva <i>et al.</i> , 2003a
<i>S. pygmaea</i> Adams	34	Bathori <i>et al.</i> , 1995; Zibareva, 1999
<i>S. quinquevulnera</i> L.	34	Zibareva <i>et al.</i> , 2003b
<i>S. radicata</i> Bois et Heldr	29, 34, 50, 51	Mamadalieva <i>et al.</i> , 2004b; Meng <i>et al.</i> , 2001; Zibareva, 2000; Zibareva, 2009; Zibareva <i>et al.</i> , 1998
<i>S. regia</i>	34, 47, 50, 51	Zibareva, 2009
<i>S. reichenbachii</i> Vis.	34	Zibareva, 2000; Zibareva <i>et al.</i> , 2003b
<i>S. repens</i> Patrín.	4, 9, 34, 48, 50	Munkhzhargal <i>et al.</i> , 2010; Novozhilova <i>et al.</i> , 2007; Revina <i>et al.</i> , 1988; Saatov <i>et al.</i> , 1993; Zibareva, 2000; Zibareva <i>et al.</i> , 2009
<i>S. requienii</i> Otth.	-	Pongracz <i>et al.</i> , 2003b; Zibareva, 2000
<i>S. roemerii</i> Friv.	4, 9, 34, 50, 66	Meng <i>et al.</i> , 2001; Zibareva, 2000; Zibareva <i>et al.</i> , 1998; Zibareva <i>et al.</i> , 2003a; Zibareva <i>et al.</i> , 2003b
<i>S. rubella</i> L.	34	Zibareva, 2000; Zibareva <i>et al.</i> , 1998
<i>S. rupestris</i> L.	+	Pongracz <i>et al.</i> , 2003b; Zibareva <i>et al.</i> , 2003a
<i>S. saxatilis</i> Sims.	34	Zibareva, 2009
<i>S. saxifraga</i> L.	34	Zibareva <i>et al.</i> , 2003a; Zibareva <i>et al.</i> , 2003b
<i>S. scabriflora</i> Brot.	34	Zibareva, 2009
<i>S. scabrifolia</i> Kom.	4, 5, 9, 33, 34, 39, 42, 48, 52, 55, 78, 81, 82	Saatov <i>et al.</i> , 1986a; Saatov <i>et al.</i> , 1986c; Saatov <i>et al.</i> , 1987a; Saatov <i>et al.</i> , 1987b; Saatov <i>et al.</i> , 1990; Saatov <i>et al.</i> , 1993; Saatov <i>et al.</i> , 1999; Zibareva, 2009; Zibareva <i>et al.</i> , 2003a
<i>S. schafta</i> S.G.Gmel. ex Hohen	34	Saatov <i>et al.</i> , 1993; Zibareva <i>et al.</i> , 2003a; Zibareva <i>et al.</i> , 2003b
<i>S. schischkinii</i> (M.Pop) Vved.	34	Zibareva <i>et al.</i> , 2003b
<i>S. schmuckeri</i> Wettst.	34, 50	Bathori <i>et al.</i> , 1995; Zibareva, 1999; Zibareva, 2000; Zibareva <i>et al.</i> , 2009
<i>S. schumacheri</i>	34	Bathori <i>et al.</i> , 1995
<i>S. schwarzenbergeri</i> Pers.	-	Zibareva, 2000
<i>S. secundiflora</i> Otth.	34	Zibareva, 1997; Zibareva & Yeryomina, 1996
<i>S. sendtneri</i> Boiss.	34, 50	Bathori <i>et al.</i> , 1995; Zibareva, 1995; Zibareva, 1999; Zibareva, 2000; Zibareva <i>et al.</i> , 2003a
<i>S. sericea</i> All.	34	Zibareva <i>et al.</i> , 2003b
<i>S. sieberi</i> Fenzl.	34	Zibareva, 2000
<i>S. sobolevskajae</i> Czer.	34	Ramazanov <i>et al.</i> , 1997c; Revina <i>et al.</i> , 1988; Saatov <i>et al.</i> , 1993; Zibareva, 1999
<i>S. supina</i> Bieb.	15, 34, 48, 50, 52, 55	Ramazanov <i>et al.</i> , 1997; Revina <i>et al.</i> , 1988; Zibareva, 1999; Zibareva, 2009

<i>S. spergulifolia</i> (Willd) Bieb.	34	Zibareva <i>et al.</i> , 2003b
<i>S. squamigera</i> Boiss	34	Zibareva & Yeryomina, 2002; Zibareva <i>et al.</i> , 2003a; Zibareva <i>et al.</i> , 2003b
<i>S. stenophylla</i> Ledeb.	34	Zibareva <i>et al.</i> , 2003b
<i>S. stylosa</i> Bunge	34	Zibareva <i>et al.</i> , 2003b
<i>S. succulenta</i> Forskal.	-	Zibareva, 2000
<i>S. sussamyrica</i> Lazkov	34	Zibareva, 2009; Zibareva <i>et al.</i> , 2003b
<i>S. tatarica</i> (L.) Wild.	15, 31, 34, 38, 48, 50, 52, 55	Baltaev, 1998; Baltaev <i>et al.</i> , 1987; Bathori <i>et al.</i> , 1995; Bathori & Mathe, 1996; Girault <i>et al.</i> , 1990; Ramazanov <i>et al.</i> , 2007; Saatov <i>et al.</i> , 1993; Zibareva, 1997; Zibareva, 1999; Zibareva, 2009; Zibareva & Yeryomina, 1996; Zibareva <i>et al.</i> , 2003a
<i>S. thessalonica</i> Boiss et Heldr.	34	Zibareva <i>et al.</i> , 1997a; Zibareva <i>et al.</i> , 2003a
<i>S. tomentella</i> Schischk.	4, 34, 48, 50, 62-64	Ramazanov <i>et al.</i> , 1995; Ramazanov <i>et al.</i> , 1996; Ramazanov <i>et al.</i> , 2007
<i>S. turchaninova</i> Lazkov	34	Zibareva, 2009; Zibareva <i>et al.</i> , 2003b
<i>S. turgida</i> L.	34	Munkhzhargal <i>et al.</i> , 2010; Revina <i>et al.</i> , 1988
<i>S. undulata</i>	+	Zibareva <i>et al.</i> , 2003a
<i>S. uniflora</i>	-	Zibareva <i>et al.</i> , 2003a
<i>S. uralensis</i> (Rupr.) Bocquet	34	Zibareva, 2009
<i>S. vallesia</i> L.	+	Zibareva, 2000; Zibareva <i>et al.</i> , 2003a
<i>S. virginica</i>	+	Zibareva <i>et al.</i> , 2003a
<i>S. viridiflora</i> L.	9, 20, 24-28, 34, 46, 48, 50, 52, 55, 61, 74-77, 79, 80, 90	Mamadalieva, 2007; Mamadalieva <i>et al.</i> , 2003; Mamadalieva <i>et al.</i> , 2004a; Mamadalieva <i>et al.</i> , 2004b; Mamadalieva <i>et al.</i> , 2009; Mamadalieva <i>et al.</i> , 2010a; Ramazanov <i>et al.</i> , 1997c; Toth <i>et al.</i> , 2008; Zibareva, 1995; Zibareva, 1997; Zibareva <i>et al.</i> , 1997a; Zibareva <i>et al.</i> , 2003a
<i>S. viscosa</i> (L.) Pers.	34	Munkhzhargal <i>et al.</i> , 2010; Volodin <i>et al.</i> , 2002; Zibareva, 2009
<i>S. vulgaris</i> (Moench.) Garcke	-	Zibareva, 1997; Zibareva, 2000; Zibareva <i>et al.</i> , 2003a
<i>S. waldsteinii</i> Griseb.	-	Zibareva, 2000
<i>S. wallichiana</i> Klotsch	4, 7, 9, 13, 14, 34, 39, 48, 64, 65	Abubakirov, 1982; Abubakirov, 1984; Bathori <i>et al.</i> , 1995; Mamadalieva <i>et al.</i> , 2000; Mamadalieva <i>et al.</i> , 2002a; Saatov <i>et al.</i> , 1987c; Saatov <i>et al.</i> , 1988; Saatov <i>et al.</i> , 1990; Saatov <i>et al.</i> , 1993; Saatov <i>et al.</i> , 1999
<i>S. wolgensis</i>	34	Zibareva <i>et al.</i> , 2003b
<i>S. zawadskii</i> Herbich.	34	Bathori <i>et al.</i> , 1995; Zibareva, 2000; Zibareva, 2009; Zibareva <i>et al.</i> , 2003a

(-) - denotes no phytoecdysteroid content; (+) - phytoecdysteroids were detected but not identified.

Traditional uses of *Silene* plants

Some plants of this genus such as *S. acaulis*, *S. multifida* and *S. regia* as ornamental plants and have beautiful flowers and have been cultured as garden

plants in many countries (Erturk *et al.*, 2006). The root of *S. latifolia* is used as a soap substitute for washing clothes etc. The soap is obtained by simmering the root in hot water (Uphof, 1968; Usher, 1974). Also *S.*

acaulis and *S. conoidea*, used as fodder as well as substitute for soap (Ahmad *et al.*, 1998; Nasir and Ali 1986).

The use of edible wild species *S. acaulis*, *S. cucubalis* and *S. vulgaris* has been reported by several authors (Fernald *et al.*, 1996; Hadjichambis *et al.*, 2007; Guarrera, 2003; Alarcon *et al.*, 2006). Several ethnobotanical studies reveal that especially young shoots and the leaves of *S. vulgaris* is very much appreciable in the traditional gastronomy of Turkey, Italy, Austria, Germany and Spain (Hadjichambis *et al.*, 2007).

Traditional medicinal uses of *Silene* plants

The plant of *S. acaulis* has been used in the treatment of children with colic (Moerman, 1998). Some of members of this genus are used in folk medicine, mainly as an emollient and used as fumigant (Ali, 1998). Juice of *S. cucubalis* L. is prescribed in ophthalmia (Chadha, 1972). The flowers of *S. nigrescens* used in Tibetan medicine in the treatment for hearing loss, blocking otic canal and volvulus (Tsarong Tsewang, 1994). The seeds of *S. dioica* have also been used to cure snakebites [<http://en.wikipedia.org>]. *S. szechuensis* Williams has been used in Chinese medicine as antipyretic, analgesic, diuretic (Zhang *et al.*, 1997). *S. vulgaris* also widely used in medicine as antianemic (Conforti *et al.*, 2011), sedative, anti-inflammatory and antitoxic agent (Ballero and Fresu, 1993, Golovko and Bushneva, 2007). The plant *S. undulata* Aiton is used as a medicine in treating many diseases particularly fevers and delirium (Sobiecki, 2008). Root barks of *S. undulata* (syn. *S. capensis*) is used by the Zulu and Xhosa of Africa people as an onerogenic agent (Hirst, 1997; Hirst, 2005; Sobiecki, 2008). Other *Silene* species such as *S. bellidioides* Sond and *S. pilosellifolia* Cham. & Schltdl. used by the Zulus and taken as a love charm emetic, treatment of scrofula, to combat sleepiness, in tonic baths after severe illness, to produce dreams relating to the ancestral spirits in South Africa (Sobiecki, 2008).

Biological activities of phytoecdysteroids

Biological investigations on phytoecdysteroids have indicated their anabolic (Syrov, 2000), adaptogenic, tonic (Syrov and Kurmukov, 1977), cardiogenic (Kurmukov and Yermishina, 1991), hypoglycemic, hypolipidemic, hepatoprotective (Kurtepova *et al.*, 2001; Syrov *et al.*, 1983) and other activities. Drugs derived from phytoecdysteroids can regulate mineral, carbohydrate, lipid and protein metabolism (Dinan and

Lafont, 2006). Also these compounds appear in many plants mostly as a protection agent (toxins or antifeedants) against herbivore insects (Kubo and Klocke, 1983). Several reviews dealing with mentioned pharmacological effects of phytoecdysteroids have been reviewed recently (Slama and Lafont, 1995; Bathori, 2002; Lafont and Dinan, 2003; Bathori and Pongracz, 2005; Dinan and Lafont, 2006) and we will describe in this paper only antitumour, antibacterial and antioxidant effects of phytoecdysteroids.

Antitumour activity

There are some data on the inhibition effect of sarcoma and other types of cancer cells growth by phytoecdysteroids. Burdette and Richards (1961) observed proliferation-inhibitory effects on sarcoma cells *in vitro*, which they used extract from silkworm pupae containing ecdysteroids. But later investigations with individual phytoecdysteroids showed no effects (Burdette, 1974). Also, El-Mofti (1987, 1994) reported that ecdysone was able to induce neoplastic lesions in toads and mice; other researchers reported that ecdysteroid-containing extract of *Silene viridiflora* exerted antitumour activity *in vivo* (Zibareva, 2003). Some phytoecdysteroids isolated from *Ajuga* species showed antitumour activities in a mouse-skin model *in vivo* in a two-stage carcinogenesis trial, using 7,12-dimethylbenz[a]anthracene as initiator and 12-O-tetradecanoylphorbol-13-acetate (TPA) as the promoter (Takasaki *et al.*, 1999). However, Lagova and Valueva (1981) reported that 20-hydroxyecdysone was mainly ineffective in preventing tumour growth in mice, but it stimulated the growth of mammary gland carcinomas. Also in the our *in vitro* experiments phytoecdysteroid 2,3-diacetate-22-benzoate-20-hydroxyecdysone showed a moderate inhibition against HeLa and HepG-2 cells [IC₅₀ values (127.97 ± 11.34) and (106.76 ± 7.81) μM, respectively], while 2-deoxy-20-hydroxyecdysone was most active against MCF-7 cells [IC₅₀ (126.54 ± 12.09) μM]. As compared to doxorubicin (IC₅₀ between 0.28 to 1.07 μg/mL) the phytoecdysteroids showed moderate cytotoxicity (Mamadalieva *et al.*, 2011).

Compare the results from others and our experiments are difficult, because of used different tumor models, phytoecdysteroids and assay methods. Most likely, since phytoecdysteroids structurally resemble sex hormones, they may bind to steroid hormone receptors in mammals and stimulate the growth of hormone-dependent tumours.

Antibacterial activity

We studied the antimicrobial activity of different extracts and phytoecdysteroids from *Silene* plants towards the pathogenic microorganisms. The plant extracts obtained from *S. wallichiana* were tested at various concentrations ranging from 0.6 – 5 mg/ml and the evaluated MIC values (Mamadalieva *et al.*, 2012b). The *Acinetobacter* sp, *Enterococcus faecalis*, *Klebsiella oxytoca*, *Pantoea agglomerans*, *Proteus rettgeri*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* strains were inhibited by the methanol extract of *S. wallichiana* at MIC = 2.5 mg/ml, while *Escherichia coli* and *Klebsiella pneumoniae* was inhibited at MIC = 1.25 mg/ml. The butanol extract of *S. wallichiana* showed activity against the pathogenic bacterium *Acinetobacter* sp., *E. coli*, *K. pneumoniae*, *P. agglomerans*, *P. aeruginosa* (MIC = 2.5 mg/ml), and *P. rettgeri* (MIC = 1.25 mg/ml), although with weaker action respect to the methanol extract. The chloroform extract had minimum activity against all bacterial strains and only inhibited *Citrobacter freundii*, *E. coli* (MIC = 2.5 mg/ml) and *P. aeruginosa* (MIC = 1.25 mg/ml). The *S. wallichiana* aqueous extract also showed low antimicrobial activity against two strains only, *E. coli* and *P. aeruginosa* (MIC = 2.5 and 1.25 mg/ml, respectively). But pure phytoecdysteroids (viticosterone E, 20-hydroxyecdysone-22-benzoate, 2-deoxy-20-hydroxyecdysone, 2-deoxyecdysone, 20-hydroxyecdysone and integristerone A) isolated from *S. wallichiana* exhibited very low activity against the bacteria (Mamadalieva *et al.*, 2012b).

The CHCl₃ extract of *S. brachiuca* inhibited growth of three Gram-negative (*Enterococcus faecalis*, *Proteus rettgeri*, and *Pseudomonas aeruginosa*) and one Gram-positive (*Micrococcus luteus*) bacterial strain. The CHCl₃ extract of *S. viridiflora* was active against *M. luteus*, *P. rettgeri*, *Klebsiella pneumoniae*, and *P. aeruginosa*, whereas the extract of *S. wallichiana* exhibited activity against only pathogenic bacteria *M. luteus* and *P. aeruginosa* (Mamadalieva *et al.*, 2010b). Also preliminary screening of the CHCl₃ extract from the aerial part of *S. guntensis* found that it exhibited antibacterial effects against *Escherichia coli*, *P. aeruginosa*, and *Acinetobacter* sp. (Mamadalieva *et al.*, 2010c).

In another our experiments the phytoecdysteroids of *A. turkestanica* had weak antimicrobial activity against Gram-positive bacteria, *Candida glabrata*, except *S. pyogenes*. Only cyasterone showed activity (MIC > 0.5 mM and MMC

> 0.5 mM) against *C. glabrata* (Mamadalieva *et al.*, 2012c).

From above mentioned results, we can conclude that antibacterial activity is more consistent in total extracts respect to the single tested phytoecdysteroids. In addition, this finding was consistent with the previous results of Ahmad *et al.*, (1996), Volodin *et al.*, (1999) and Shirshova *et al.*, (2006), who claimed that most likely such compounds are not the major molecules responsible for the antibacterial activity of the plant extracts. Ahmad *et al.*, (1996) and Shirshova *et al.*, (2006) reported that some natural phytoecdysteroids, including 20-hydroxyecdysone, inokosterone, and ecdysone, did not exhibit antimicrobial activity with respect to most standard test microbe cultures. However, introduction of the acetyl group into the 20-hydroxyecdysone molecule significantly increased the antibacterial activity with respect to microbes inducing inflammatory and purulent processes (Shirshova *et al.*, 2006). In our case, besides phytoecdysteroids, extracts exhibiting antibacterial activity were related to the chemical nature of the solvents which play a key role in the extraction of different chemical compounds from the plant material.

Antioxidant activity

Drugs derived from phytoecdysteroids exhibit antioxidant properties and have a similar effect with vitamin D₃ (Kuzmenko *et al.*, 1997). Miliauskas and coworkers (2005) reported mild radical scavenging activity for 20-hydroxyecdysone. These observations are contradictory to what was found in other studies (Osynskaya *et al.*, 1992).

The radical scavenging ability of the extracts and phytoecdysteroids of *S. guntensis* were evaluated by us using the reaction with the stable DPPH radical (Mamadalieva *et al.*, 2011). In our experiments phytoecdysteroids were ineffective for DPPH radical scavenging activity (IC₅₀ value > 100 µg/mL) compared to that for quercetin (3.37 µg/mL). Maximum scavenging activity of DPPH was observed with the water extract (IC₅₀ 68.90 µg/mL) of *S. guntensis*, followed by the activity of the n-butanol, methanol, and chloroform extracts with IC₅₀ values of 69.12, 122.48, and 148.28 µg/mL, respectively. The activity of 20-hydroxyecdysone, 2-deoxy-20-hydroxyecdysone, and 2,3-diacetate-22-benzoate-20-hydroxyecdysone were 144.75, 157.29, and 291.38 µg/mL, respectively.

However, we assume that the antioxidant effect of these extracts might be attributed to some co-

eluting phenolic compounds other than phytoecdysteroids. It is known that the presence of the ortho arrangement of two hydroxyl groups on the aromatic ring and 2,3-double bond in conjugation with 4-oxo function is essential for the antiradical activity of flavonoids. More effective is the ortho-arrangement of hydroxyl groups on the aromatic ring B (quercetin). Ecdysteroids are polyhydroxylated steroids, contain 7,8-double bond and 6-oxo function. The latter explanation seems to be more convincing, since the structure of ecdysteroid molecules is unlikely to exert an antioxidant effect, as compared to the common antioxidative flavonoids (Lu and Yeap, 2001).

CONCLUSION

This review summarizes and characterizes the diversity and distribution of phytoecdysteroids found from a wide range of *Silene* species. The plants of the genus *Silene* are well known as rich sources of phytoecdysteroids. Almost quarter of the known phytoecdysteroids have been detected from *Silene* plants. The studies on chemical constituents in recent years have disclosed many different activities for phytoecdysteroids, such as anabolic, adaptogenic, tonic and other activities. Plants of this genus may serve as a potential source for dietary supplements for humans as food supplements for sportsmen or for use as additives in medicine and cosmetics. From the above is obvious, that phytoecdysteroids could serve as new lead molecules having great expectations in the development of new classes of pharmaceuticals and dietary supplements.

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