The genus *Seseli* L.: A comprehensive review on traditional uses, phytochemistry, and pharmacological properties

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ABSTRACT

Introduction

The present article is the first comprehensive review of *Seseli* L. species. *Seseli* is one of the largest genera of the Apiaceae, and some species have been used in traditional medicine and foods besides their medicinal importance. This review aims to provide a comprehensive and critical appraisal of the past and present medicinal uses of *Seseli* species with their relevant bioactivity. This review also brings a new perspective in all aspects and emphasizes the importance of these species.

Methodology

Mainly electronic databases were used as the primary sources for screening related articles and applying related search terms.

Results

To date, the *Seseli* species have no or little attention and few phytochemical and pharmacological studies. Previous phytochemical investigations have confirmed that some species have mainly essential oils and coumarins. This review has also been established by reporting on the pharmacological activities of *Seseli* species. The genus *Seseli* has been reported as a good source of coumarins (especially anomalin, and osthol), which may be considered a chemotaxonomic marker.

Conclusion

The literature available to date on the genus *Seseli* partially confirms the basis for some of the traditional uses of this genus and its remarkable pharmacological effects. The *Seseli* species has proven to be a good source of coumarins, especially pyranocoumarins, like anomalin. However, the uses of *Seseli* species to treat various diseases need different pharmacological studies before applying or starting clinical trials.

Keywords: Apiaceae; *Seseli*; Coumarins; Pyranocoumarins; Phytochemicals; Uses

Abbreviations

A549	Adenocarcinomic human alveolar basal epithelial cells
ABTS	2,2-azinobis-(3-ethylbenzothiazoline-6-sulphonic acid)
AChE	Acetylcholine Esterase
ATCC	American Type Culture Collection
CC	Column Chromatography
CCC	Counter-Current Chromatography
CCL2/MCP-1	Chemokine (C-C motif) ligand 2/monocyte chemoattractant protein-1
CH_2Cl_2	Dichloromethane
$CHCl_3$	Chloroform
COX-2	Cyclooxygenase-2
CUPRAC	Cupric Reducing Antioxidant Capacity
DCFC	Dry-Column Flash Chromatography
DNA	Deoxyribonucleic acid
DPPH	1,1-diphenyl-2-picrylhydrazyl)
Et_2O	Diethylether
EtOAc	Ethyl acetate
EtOH	Ethanol
Fe	Ferrum
FRAP	Ferric Reducing Antioxidant Power Assay
GC-MS	Gas Chromatography-Mass Spectrometry
HaCaT	Immortalized human keratinocytes cells
HD	Hydrodistillation
HEMWat	*n*-Hexane : EtOAc : MeOH : Water
HPLC	High Performance Liquid Chromatography
HS/GC-MS	Head Space/Gas Chromatography-Mass Spectrometry
HS-SPME	Headspace Solid-Phase Micro-Extraction
IAM	Institute of Applied Microbiology (Culture Collection-University of Tokyo)
IC_{50}	Half maximal inhibitory concentration
IL-1β	Interleukin-1β
IL-6	Interleukin-6
IL-8	Interleukin-8
iNOS	Inducible Nitric Oxide Synthase
IUCN	International Union for Conservation of Nature
IκBα	Nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha
KB	A subline of the ubiquitous keratin-forming tumor cell line HeLa
L-1210	Murine leukemia cells
LC_{50}	Half maximal lethal concentration
LPO	Lipid Peroxidation
LPS	Lipopolysaccharides
MAPK	Mitogen Activated Protein Kinase
MBC	Minimum Bactericide Concentration
MeOH	Methanol
MFC	Minimum Fungucide Concentration
MIC	Minimum Inhibitory Concentration
MLC	Minimal Lethal Concentration
MPNS	Medicinal Plant Name Services
MTT	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide
NF-κB	Nucleer Factor κB
NO	Nitric Oxide
ODS-HPLC	Octadecyl-High Performance Liquid Chromatography
P-388	Murine leukemia cells
PGE2	Prostaglandin E2

Abbreviations (Continuous)

qRT-PCR	Quantitative Real-Time Polymerase Chain Reaction
R	Rectus, right
S	Sinister, left
SC_{50}	Half-maximal inhibitory sample concentration
SD	Steam Distillation
SFE	Solid Phase Microextraction
TNF-α	Tumor Necrosis Factor-*α*
TUBIVES	Türkiye's Plants Data Service

1. Introduction

Natural products, including plants and phytochemicals, have long been used to treat many diseases (Dias et al., 2012). Phytochemicals have granted many drug candidates with a wide range of biological activities, either directly or through various modifications (Kinghorn et al., 2011; Kingston, 2011; Newman and Cragg, 2012). Medicinal and aromatic plants have been the sources of raw materials used in medicines, cosmetics, perfumery, food, and many other critical industrial materials (Canter et al., 2005; Cragg and Newman, 2013).

The Apiaceae family (previously Umbelliferae), rich in medicinal and aromatic plants, is considered one of the oldest families in the plant kingdom. Most of the members are native to the Mediterranean region and Southwest Asia. The major secondary metabolites are generally coumarins, essential oils, terpenoids, and polyacetylenes (Crowden et al., 1969; Williams and Harborne, 1972). The species of the Apiaceae family are indispensable for foodstuff, nutrition, spices, beverages, pharmaceutical, and cosmetic-fragrances industries, with significant economic importance (Hedge and Lamond, 1972; Hunault et al., 1989; Downie et al., 1998; Rajamanickam et al., 2013; Sayed-Ahmad et al., 2017). The plants of this family are cultivated and used as vegetables, for culinary and medicinal purposes, with some famous examples, such as *Anethum*, *Anthriscus*, *Apium* species, etc. (Amiri and Joharchi, 2016).

Seseli L. from the Apiaceae family, with a wide variety of species, is distributed in many European, Asian, African countries, North America, and Australia (Pimenov and Leonov, 1993; Pimenov and Leonov, 2004; Doğan Güner et al., 2011; Doğan Güner and Duman, 2013; Çetin et al., 2015). Also, *Seseli* is an ancient Greek name that has been used since Hippocrates' time for some members with delicately divided leaves of the Apiaceae species (Hamlyn, 1969). The bioactive metabolites, including coumarins, essential oils, terpenes, and polyacetylenes, have been obtained from different *Seseli* species. Coumarins and essential oils are the dominant groups of secondary metabolites in almost all *Seseli* species and may be responsible for the biological activities and pharmacological effects (Tosun and Özkal, 2003).

Surprisingly, according to the literature search, there are no comprehensive reviews on the *Seseli* species, which points out the originality of this review. This review article presents a complete overview with the latest updated information summarizing the botanical characteristics, traditional importance, phytochemistry, and pharmacological activities, including ethnopharmacological studies of the genus *Seseli*. This review also highlights the importance of coumarins from the *Seseli* species for preventing and treating many diseases. All this information warranted further research on *Seseli* species to find the mode of action of the pharmacological effects, new therapeutic applications, and active molecules.

2. Research methodology

The present review comprises a detailed bibliographic search to prepare a comprehensive report on the genus *Seseli*, incorporating the literature published before 2022. All the current information on the *Seseli* species was collected via an electronic search using PubMed, Science Direct, Web of Science, Google Scholar, and Scopus databases. Many articles about the *Seseli* species have been selected carefully from peer-reviewed journals dealing with the valuable properties of the *Seseli* species systematically reviewed. Several published books and pharmacopeias were also consulted. Also, the scientific names of the species mentioned in the text were carefully checked using World Flora Online, Medicinal Plant Names Services (MPNS), and both were given in Table 1, and the text. The species that cannot be found in these services are given based on the mentioned publication. The species names that have been changed or modified after revision over the years are presented with their current names. In some cases, the version mentioned in the publication is also indicated in parentheses.

Table 1
The scientific names, status, and locations of *Seseli* species in this article (Based on Data from World Flora Online 2021 and Medicinal Plants Names Services, including references)

No	*Seseli* L. Species	Endemism	Location	Status	References
1	*S. ammoides* L. [*Syn: Ammoides pusilla* (Brot.) Breistr.]	-		-	World Flora Online MPNS
2	*S. andronakii* Woronow ex Schischk.	Endemic	Türkiye	Ambiguous	World Flora Online Tosun et al., 2006a Lyskov et al., 2018
3	*S. annuum* L.	-	Serbia	Accepted name	World Flora Online Milosavljević et al., 2007 Vučković et al., 2010
4	*S. bocconei* Guss.	Endemic	Italy	Accepted name	World Flora Online Bellino et al., 1986
5	*S. bocconei* Guss. subsp. *praecox* Gamisans [*Syn: S. praecox* (Gamisans) Gamisans]	-	Sardinia/Italy	-	World Flora Online Marongiu et al., 2006
6	*S. buchtormense* (Fisch.) W.D.J. Koch [*Syn: Libanotis buchtormensis* (Fisch.) DC.]	-	Siberia	Accepted Name	World Flora Online Tkachev et al., 2006
7	*S. campestre* Besser (*Syn: S. rubellum* Post)	-	Türkiye, Ukraine	Accepted name	World Flora Online Baser et al., 2000 Kaya et al., 2010 Lyskov et al., 2018
8	*S. carvifolia* L. [*Syn: Selinum carvifolia* (L.) L.]	-	-	-	World Flora Online
9	*S. coronatum* Ledeb.	-	Kazakhstan	Accepted name	World Flora Online Dukhovlinova et al., 1974
10	*S. corymbosum* Boiss. & Heldr. [*Syn*: *S. gummiferum* subsp. *corymbosum]*	Endemic	Türkiye	Ambiguous	World Flora Online Tosun et al., 2005a,b Chun et al., 2016 Tosun et al., 2016 Lyskov et al., 2018
11	*S. corymbosum* Boiss. & Heldr. ex Boiss. subsp. *phrygium* (Pimenov & Kljuykov) E.Doğan & H.Duman*	Endemic	Türkiye	Ambiguous	Doğan Güner and Duman, 2013
12	*S. devenyense* Simonk. [*Syn*: *S. elatum* subsp. *osseum* (Crantz) P.W.Ball; *S. osseum* Crantz]	-	Europe	Accepted name	World Flora Online Widelski et al., 2005
13	*S. elatum* subsp. *gouanii* (W.D.J.Koch) P.W.Ball	-	-	Accepted name	World Flora Online
14	*S. elatum* subsp. *austriacum* (Beck) P.W.Ball	-	-	Accepted name	World Flora Online

15	*S. elatum* L. [*Syn: S. longifolium* L.]	-	-	Accepted name	World Flora Online
16	*S. farrenyi* Molero & J.Pujadas	Endemic	Spain	Ambiguous	World Flora Online Muckensturm et al., 1997 López-Pujol et al., 2002
17	*S. glaucum* L. [*Syn: S. montanum* L.]	-	-	-	World Flora Online
18	*S. glaucum* M. Bieb. [*Syn: S. tortuosum* L.]	-	-	-	MPNS
19	*S. globiferum* Vis.	-	Montenegro	Accepted name	World Flora Online Janaćković et al., 2011
20	*S. gouani* W.D.J. Koch [*S. elatum* subsp. *gouanii* (W.D.J.Koch) P.W.Ball]	-	-	-	World Flora Online
21	*S. gracile* Waldst. & Kit.	Endemic	Serbia, Romania	Accepted name	World Flora Online Marčetić et al., 2017a
22	*S. grandivittatum* Schischk.	-	Nakhichevan	Ambiguous	World Flora Online Abyshev et al., 1978 Lyskov et al., 2018
23	*S. gummiferum* Pall. ex Sm.	Endemic	Türkiye	Accepted name	World Flora Online Nielsen et al., 1971 Lyskov et al., 2018
24	*S. gummiferum* subsp. *gummiferum* Pall. ex Sm.*	Endemic	Türkiye, Crimea	-	Nielsen et al., 1970 Nielsen et al., 1971 Tosun et al., 2016 Lyskov et al., 2018
25	*S. gummiferum* Pall. ex Sm. subsp. *ilgazense* A. Duran, O. Cetin & M. Ozturk*	Endemic	Türkiye	Accepted Name	World Flora Online Çetin et al., 2015 Lyskov et al., 2018 Kurkcuoglu et al., 2018
26	*S. hartvigiii* Parolly & Nordt [*Syn: S. ramosissimum* (Port. ex Spreng.) Ces.]	Endemic	Türkiye	Accepted Name	World Flora Online Parolly and Nordt, 2001 Tosun, 2006 Lyskov et al., 2018
27	*S. indicum* Wight & Arn. [*Syn: S. diffusum* (Roxb. ex Sm.) Santapau & Wagh]	-	Pakistan, India, SE Asia	Accepted name	World Flora Online, MPNS Murayama et al., 2009 Singh et al., 2012 Gupta and Gupta, 2012 Abbashan et al., 2012

					Kabir et al., 2013
28	*S. laxifragum* L.*	-	-	-	Linnaeus, 1753 Doğan Güner and Duman, 2013
29	*S. leucospermum* Waldst. & Kit.	-	-	Accepted name	World Flora Online
30	*S. libanotis* (L.) W.D.J.Koch	-	Austria, Italy, Türkiye	Accepted name	MPNS, World Flora Online Ozturk and Ercisli, 2006 Skalicka–Woźniak et al., 2010 Chizzola, 2019
31	*S. libanotis* (L.) W.D. Koch var. *armeniacum* Bordz.	-	Iran	-	Masoudi et al., 2006
32	*S. libanotis* (L.) Koch subsp. *eu-libanotis* Thellung*	-	Denmark (Funen Island), Serbia	-	Lemmich et al., 1966 Matejić et al., 2012
33	*S. libanotis* subsp. *intermedium* (Rupr.) P.W.Ball	-	Serbia	Accepted name	World Flora Online Matejić et al., 2012
34	*S. longifolium* L.	-	-	Accepted name	World Flora Online
35	*S. mairei* H.Wolff	-	-	Accepted name	World Flora Online, MPNS
36	*S. marashicum* E. Doğan & H. Duman* [*Syn: S. gummiferum* subsp. *ilgazense* A.Duran, O.Çetin & M.Öztürk]	Endemic	Türkiye	Accepted name	Doğan Güner and Duman, 2013 Lyskov et al., 2018
37	*S. montanum* L.	-	-	Accepted name	World Flora Online
38	*S. montanum* subsp. *peixotoanum* (Samp.) M. Laínz*	-	Portugal		Council of Europe, 1997 Gonçalves et al., 2012
39	*S. montanum* subsp. *tommasinii* (Rchb.f.) Arcang.	-		Accepted name	World Flora Online
40	*S. mucronatum* (Schrenk) Pimenov & Sdobnina	-	Kyrgyzstan	Accepted name	World Flora Online Dukhovlinova et al., 1979
41	*S. pallasii* Besser [*Syn: S. varium* Trevir.]	-	Czech Republic, Serbia	Accepted name	World Flora Online Pavela, 2009 Matejić et al., 2012 Suručić et al., 2017
42	*S. paphlagonicum* Pimenov & Kljuykov [*Syn*: *S. gummiferum* Pall. ex Sm.	Endemic	Türkiye	Ambiguous	World Flora Online; Pimenov and Kljuykov, 2010 Lyskov et al., 2018
43	*S. parnassicum* Boiss. & Heldr.	Endemic	Greece	-	Kokkoris et al., 2014
44	*S. petraeum* M. Bieb. [*Syn: S. floribundum* Sommier & Levier]	-	Türkiye	Accepted name	World Flora Online Tosun et al., 2006a Lyskov et al., 2018 Önder et al., 2021 Onder et al., 2022

45	*S. peucedanoides* (M.Bieb.) Koso-Pol.	-	Nakhichevan	Accepted name	World Flora Online Bagirov and Belyi, 1981 Bulatović et al., 2006
46	*S. phrygium* Pimenov & Kljuykov [*Syn: S. corymbosum* subsp. *phrygium* (Pimenov & Kljuykov) E. Doğan & H. Duman]	Endemic	Türkiye, Russia	-	Pimenov and Kljuykov, 2010 Lyskov et al., 2018
47	*S. pimpinelloides* Spreng.	-	-	Ambiguous	World Flora Online
48	*S. praecox* (Gamisans) Gamisans	Endemic	Sardinia/Italy	Ambiguous	World Flora Online Leonti et al., 2010
49	*S. pyrenaeum* L. [*Syn: Selinum pyrenaeum* (L.) Gouan]	-	-	-	World Flora Online
50	*S. ramosissimum* Hartvig & Strid.	Endemic	Türkiye	Ambiguous	World Flora Online Lyskov et al., 2018
51	*S. resinosum* Freyn & Sint.	Endemic	Türkiye	Ambiguous	World Flora Online Tosun et al., 2006b Tosun et al., 2007a Shehzad et al., 2013 Khan et al., 2015 Lyskov et al., 2018
52	*S. rigidum* Waldst. & Kit.	Endemic	Serbia, Balkan peninsula, Bulgaria	Accepted name	World Flora Online Šavikin-Fodulović et al., 2006 Stojković et al., 2009 Todorova et al., 2013 Marčetić et al., 2013 Jakovljević et al., 2015 Stankov-Jovanović et al., 2015 Ilić et al., 2015 Marčetić et al., 2017b
53	*S. serpentinum* B.L.Burtt ex H.Duman & E.Doğan* [*Syn: S. rubellum* auct. Southam, non Post]	Endemic	Türkiye	Accepted name	Doğan Güner and Duman, 2013 Lyskov et al., 2018
54	*S. sessiliflorum* Schrenk	-	Kyrgyzstan	Accepted name	World Flora Online Savina et al., 1970 Aminov and Nikonov, 1974
55	*S. sibiricum* (L.) Garcke	-	-	Accepted name	World Flora Online
56	*S. tenuisectum* Regel & Schmalh.	-	Tajikistan, Russia	Accepted name	World Flora Online Aminov and Nikonov, 1970
57	*S. tschuense* Nikitina [*Syn: S. sessiliflorum* Schrenk]	-	Kyrgyzstan	-	World Flora Online Aminov and Nikonov, 1974

58	*S. tortuosum* L. [*Syn: S. littoraee* Willk. (1851)] [*S. massiliense* Bubani (1899)?] [*S. pauciradiatum* Schischk., *S. proliferum* Spreng., *S. puberulum* DC., *S. rigidum* Waldst., *S. tauricum* Link ex Spreng., *S. tenderiense* Kotov, *S. tortuosum* var. *paucirdiatum* Tamamsch.] -*S. tortuosum* subsp. *maritimum* (Guss.) C.Brullo, Brullo, Giusso & Sciandr	-	Türkiye, Italy, Portugal, Spain, France, Croatia, Slovenia, Tunisia, Algeria, Lybia	Accepted name	World Flora Online, MPNS Uysal et al., 2017 Bader et al., 2003 Costa et al., 2018 Gonçalves et al., 2012 Lyskov et al., 2018
59	*S. tortuosum* L.B.S.Eur.	-	Italy, Spain	-	Gonzales et al., 1979 Ceccherelli et al., 1990
60	*S. tortuosum* L. subsp. *kiabii* Akhani	-	Iran	-	Habibi et al., 2003
61	*S. transcaucasicum* Pimenov & Sdobnina	-	Türkiye	Accepted name	World Flora Online Shahabipour et al., 2013 Zengin et al., 2021
62	*S. vayredanum* Font Quer [*Syn: Athamanta vayredana* (Font Quer) C. Pardo]	-	-	Accepted name	World Flora Online

*Species have not been found on World Flora Online-Plant List and Medicinal Plant Names Services (MPNS), but references are given that report them

3. Taxonomical and botanical information

The Apiaceae Lindl. (Umbelliferae Juss.) or "Carrot Family" (Downie et al., 2000), attracted people's attention throughout the 15th century with its fragrance and flavor but occasional toxicity. However, the influence of this family in history goes back to ancient times, in old Chinese in "Materia Medica" and the Sanskrit language. Theophrastus called the Apiaceae "*Narthekodes,*" and Dioscorides has also cited about 50 Apiaceae species in "Greek Herbal" in the title of "Herbs." It is one of the most prominent families of flowering plants comprising 3800 species in 466 genera, distributed worldwide (Reduron, 2021), generally in mild northern climates, high altitudes, and tropical regions. The plants are used as food and spice, beneficial in pharmaceutical and cosmetic fields (Davis, 1972; Berenbaum, 1990; Christensen and Brandt, 2006; Özhatay et al., 2009; Pimenov and Kljuykov, 2010; Sayed-Ahmad et al., 2017). Also, they have been used in folk medicine for centuries (Dioscorides, 2002). The Apiaceae species have the common principles as aromatic herbs due to schizocarp fruits with oil ducts (Davis, 1972; Berenbaum, 1990; Downie et al., 1998; Christensen and Brandt, 2006), providing unique odor and flavor (Acimovic et al., 2015). All 40 plants of Codex Neapolitanus Graecus, specified in the Apiaceae, provided a mostly documented definition. The genus *Seseli* L. possesses common properties of Apiaceae, also identified by Dioscorides by post-Linnaean scholars (Evergetis and Haroutounian, 2014) as one of the Apiaceae family members. Moreover, in Reduron’s chapter (2021), the *Seseli* (about 140 species) is among the third largest genera after *Ferula* and *Pimpinella* in the Old World (Reduron, 2021).

The genus *Seseli* L. has been listed taxonomically in the IUCN (International Union for Conservation of Nature) and TUBIVES (Türkiye's Plants Data Service). In the taxonomic order, the *Seseli* genus belongs to the Spermatophyta division, Dicotyledones class, and Apiales order (Ekim et al., 2000; Gagnidz et al., 2014). *Seseli* L. (*Syn.*: *Libanotis* Hall.) is represented by intraspecific and interspecific diversity, 80 of which are grown within Asia (Pimenov and

Leonov, 1993; Pimenov and Leonov, 2004; Doğan Güner et al., 2011; Akalın Uruşak and Kızılaslan, 2013; Aytaç and Duman, 2013; Doğan Güner and Duman, 2013; Çetin et al., 2015) as mentioned in Davis's Flora in Irano-Turanian, Euro-Siberian and East Mediterranean phytogeographic regions (Hedge and Lamond, 1972; Davis et al., 1988). However, the *Seseli* species have been listed in "The Plant List" with 388 species, some of which have been accepted, but others have not yet been resolved (http://www.theplantlist.org/). On the other hand, 34 species have been recorded in the Flora Europaea (Tutin et al., 1968), while 7 *Seseli* species are listed in the Austrian flora (Fischer et al., 2008).

The *Seseli* inherently exhibits the Apiaceae family characteristics. The species are perennial or biennial herbaceous plants and have a fibrous collar consisting of the stems of dead leaves at the base that emerges from the root and surrounds the body. In some species, the branches of withered leaves are permanent but do not form a fibrous structure, even though, sometimes found in both fibrous structure and the stalk of the stem. The fibrous collar is almost unique for the *Seseli* species to distinguish it from the other Apiaceae species. In *Seseli* species (Fig. 1, 2), leaves are 1-4 pinnate, with or without braces, while bracteoles may be united or separated at the base. Sepals are small or absent; petals are usually yellow or purple; the fruit is oblong-ovoid, glabrous, or pubescent; the fruit is stylopodium conical in shape, and the styluses are permanent (Hedge and Lamond, 1972). Most species are restricted endemics, growing preferentially in dry climate conditions, in calcareous rocks, and on rocky slopes, such as limestone, cliffs, and cracks of rocks in high altitudes (ca. 3000 m). The flowering period of *Seseli* taxa is between June and November (Hedge and Lamond, 1972; Davis et al., 1988; Duman, 2000; Pimenov and Kljuykov, 2010; Lyskov et al., 2018), thus yielding late fruit. However, most species are unknown (Hedge and Lamond, 1972). According to the authors' observations, *Seseli* species have a pungent, resinous, exotic, and unusual odor, especially in the stems and roots. Even resins that emerge to the surface are encountered in these parts of the plants.

The discovery of new species continues and contributes to the biological diversity of *Seseli* species (Parolly and Nordt, 2001; Çetin et al., 2015). It is known that the first leading revision of *Seseli* species in Türkiye was performed by Hedge and Lamond (1972) who identified 10 taxa (Hedge and Lamond, 1972). Later, *Seseli gummiferum* Pall. ex Sm. (but as the name *S. gummiferum* subsp. *gummiferum*) was recorded as a new species from Türkiye about two decades ago (Duman, 2000). After a revision by Parolly and Nordt, *S. ramosissimum* Hartvig & Strid. growing in Türkiye was accepted as *S. hartvigii* Parolly & Nordt (Parolly and Nordt, 2001). It should be admitted that *Seseli* species have some taxonomic problems in species distinction. Nonetheless, two new species from the Turkish Flora, *S. marashica* E. Doğan & H. Duman and *S. serpentina* B.L. Burtt ex H. Duman & E. Doğan, have been described well. The *S. paphlagonicum* Pimenov & Kljuykov became synonymous with the species known as *S. gummiferum* Pall. ex Sm., and *S. corymbosum* Boiss. & Heldr. was accepted as *S. corymbosum* Boiss. & Heldr. ex Boiss. subsp. *phrygium* (Pimenov & Kljuykov) E. Doğan & H. Duman. In this context, Turkish *Seseli* species have been revised by Doğan Güner and Duman (2013), and 13 taxa were reported (Doğan Güner and Duman, 2013). The patterns of various *Seseli* species have also been investigated with the help of molecular approaches to phylogenetic and genetic diversity (López-Pujol et al., 2002; Kokkoris et al., 2014). Since the botanical definitions of the *Seseli* species are confusing and complicated, professionals should carefully examine the species distinction. Identifying *Seseli* species is difficult but requires careful determination to perform the proper phytochemical studies on these plants.

In "Species Plantarum," *Seseli* is reported with nine species (*S. pimpinelloides* L., *S. montanum* L., *S. glaucum* L., *S. annuum* L., *S. ammoides* L., *S. tortuosum* L., *S. carviflora* L., *S. pyreneacum* L., and *S. laxifragum* L.) (Linnaeus, 1753; Doğan Güner and Duman, 2013). *Seseli tortuosum* has been defined as "the type of the taxon" and has been identified as "the lectotype of *Seseli*" (Linnaeus, 1754; Doğan Güner and Duman, 2013). According to Lyskov et al. (2018), the properties of the *Seseli* species closely related to *S. tortuosum* L. have not been indicated up to date (Lyskov et al., 2018).

It was represented that the synonyms of the *Seseli* L. genus have been assigned as "*Athamantha* L., Sp. Pl. 1: 244 (1753); = *Bubon* Linnaeus, Sp. Pl. 253 (1753); = *Libanotis* Haller ex Zinn, Cat. Pl. Hort. Gott. 226 (1757); = *Hippomarathrum* P.G. Gaertner, B. Meyer et J. Scherbius, Oekon.-Techn. Fl. Wetterau 1: 249, 413 (1799); = *Hippaton* Rafinesque, Good Book 51 (1840)" (Doğan Güner and Duman, 2013).

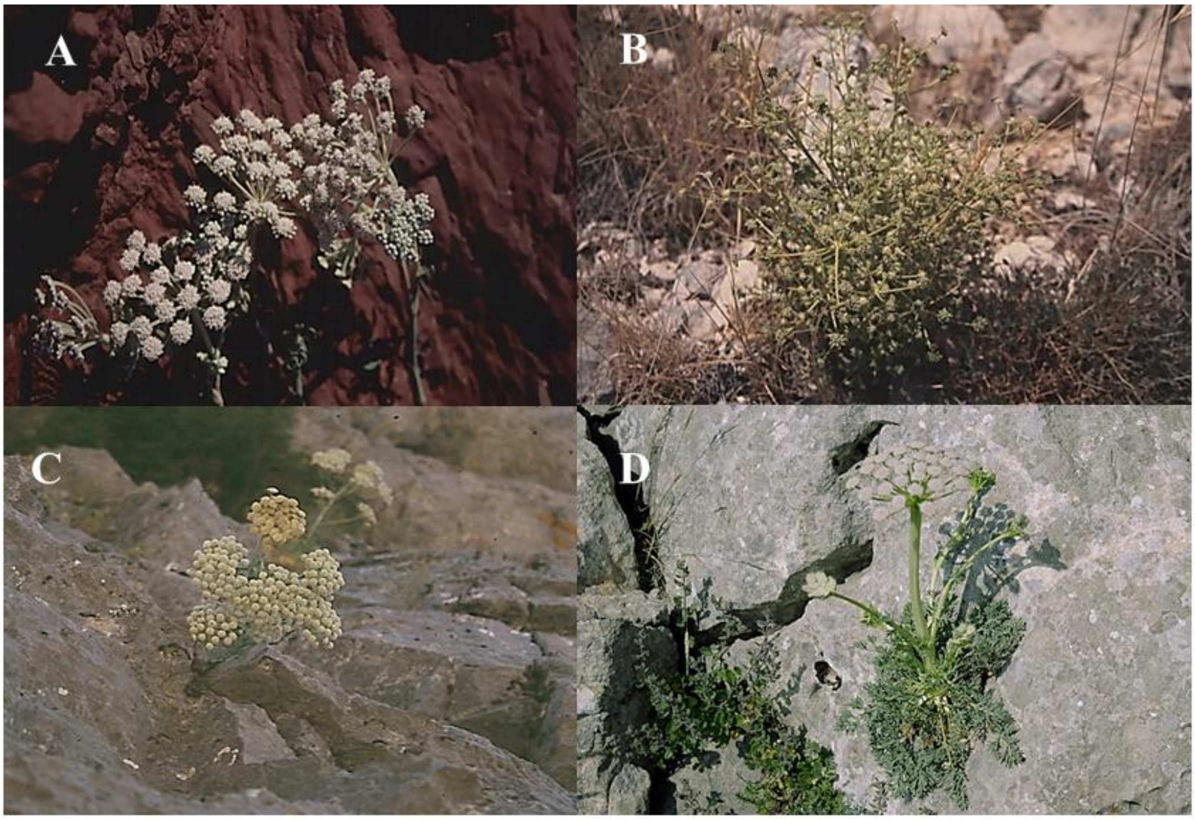


Fig. 1. Some endemic *Seseli* L. species from the Turkish Flora: A: *Seseli resinosum* Freyn & Sint.; B: *Seseli hartvigii* Parolly & Nordt; C: *Seseli corymbosum* Boiss. & Heldr.; D: *Seseli gummiferum* Pall. ex. Sm. (*Photo by Alev ÖNDER*)

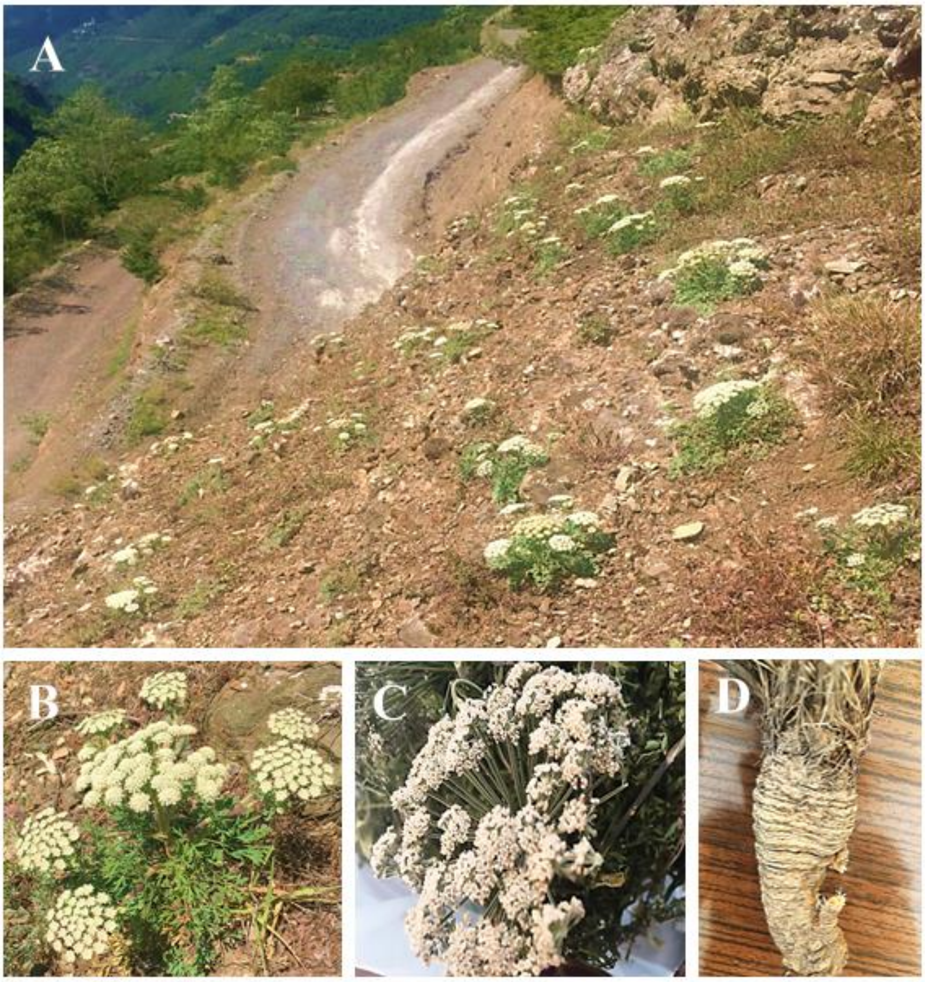


Fig. 2. Morphological representation of various parts of *Seseli petraeum* M. Bieb. from Trabzon-Gümüşhane (Türkiye) growing in a limited area; A: The habitat of the species in nature; B: The whole plant-herbal parts; C. The flowers of the species; D: The roots of the species (*Photo by Ahsen Sevde ÇINAR*)

4. Traditional uses

Medicinal plants and phyto-components have made significant progress in the scientific field and ethnopharmacological studies (Karunamoorthi et al., 2013; Yuan et al., 2016). The popular plants from the Apiaceae family are often used as home-based remedies to treat various ailments (Acimovic et al., 2015). Many aromatic plants that also grow wild in the Apiaceae family are an important and valuable source of phytochemicals and need investigation on bioactivity.

Seseli is an old Greek name used by Hippocrates for some members of the Apiaceae family, which have beautiful appearances (Hamlyn, 1969). If we venture back to ancient times, *Seseli* was used by Hippocrates and Dioscorides in traditional medicine and originated from the words "Seseli, seselis, or sesili" (Dioscorides, 2002; Stojković et al., 2009). The genus also has economic importance throughout the world. The dried leaves located in the basement are used in animal nutrition. The plants from this genus are used to decorate gardens and parks in Europe (Syed et al., 1989; Hu et al., 1990; Doğan Güner et al., 2011). The *Seseli* species have been broadly used in traditional medicine (Table 2), especially in European folk medicine, indicated for antibacterial, antifungal, insect repellent, emmenagogue, anti-flatulence, anti-inflammatory, antinociceptive, antitumor, antirheumatic effects and protective effects on human lymphocytes (Ilić et al., 2015). In Serbian traditional medicine, different *Seseli* species under the common name "Devesilje" have been used as a tonic, diuretic, emmenagogue, and digestive remedies (Suručić et al., 2017). However, the reputation of these species is also well-known in Eastern countries. For example, the roots of *S. mairei* H. Wolff, a plant from Chinese medicine, are known as “Zhu Ye Fang Feng” and are used for human inflammation, edema, rheumatism, pain, and common cold (Hu et al., 1990). On the other hand, the fruits (seeds) of *S. indicum* Wight & Arn., are traditionally used in India, with anthelmintic, carminative, stomachic, and stimulant properties (Tandan et al., 1990). In Ayurvedic medicine, a herbal mixture known as "Bhuutakeshi," including *S. sibiricum* (L.) Garcke, together with the *Selinum* species, is used as a sedative in mental disorders (Jamwal et al., 1963; Suručić et al., 2017). An Indian species, *S. diffusum* (Roxb. ex Sm.) Santapau & Wagh (Indian celery) is used in Pakistan to treat amenorrhea, urinary discharges, rheumatism, chest pains, inflammations, and fever accompanied by cough. The fruits (seeds) of *S. diffusum* have also been prescribed for their antispasmodic effect to remedy bronchitis, asthma, hepatic obstructions, bowel flow, and splenic disorders in traditional medicine (Usmanghani et al., 1997; Abbaskhan et al., 2012). In Turkish folk medicine, the fruits of *S. tortuosum* L. (Horozgözü in Turkish) have been reported for digestive disorders and as an emmenagogue (Baytop, 1999). For hundreds of years, many species of *Seseli* genus have been used to protect and provide the flavour in cheese. For example, the *S. libanotis* (L.) W.D.J. Koch (Kelemkeşir or kelemenkeşir in Turkish) leaves are utilized as a vegetable in Eastern Türkiye (Baytop, 1994) and used as a conservator in cheese and flavoring (Öztürk et al., 2000; Öztürk and Ercişli, 2006). A juice prepared from the aromatic roots of *S. libanotis* was recommended for joint pains by Matthiolus and Tabernaemontanus in the 16th and 17th centuries (Adams et al., 2009; Chizzola, 2019). Traditional, ethnopharmacological, and medicinal uses of the species of *Seseli* from different origins with local names are summarized in Table 2.

Table 2
Traditional uses of some *Seseli* species

Species	**Location**	**Local name**	**Plant Part Used**	**Traditional Uses**	**References**
S. diffusum	Pakistan	Indian celery	-	Amenorrhea, urinary discharges, fever with cough, rheumatism, chest pains, inflammation	Usmanghani et al., 1997
			Fruits (seeds)	Antispasmodic, remedy for bronchitis, asthma, hepatic obstructions, bowel flow, splenic disorders	Abbaskhan et al., 2012
S. indicum (*Syn: S. diffusum*)	India	Indian celery	Fruits (seeds)	Anthelmintic, carminative, stomachic, stimulant	Tandan et al., 1990
S. libanotis	Türkiye	Kelemkeşir, Kelemenkeşir	Leaves	Salad, vegetable Cheese conservative, as an aroma	Baytop, 1994 Öztürk et al., 2000 Öztürk and Ercişli, 2006
	Europe	Moon carrot/mountain stone-parsley	Roots	Aromatics, joint pain	Adams et al., 2009 Chizzola, 2019
S. mairei	China	Zhu Ye Fang Feng	Roots	Human inflammation, swelling, rheumatism, pain, common cold	Hu et al., 1990
S. sibiricum	India	Bhuutakeshi (Herbal mixture with *Selinum* species)	Herbs	Sedative in mental disorders	Jamwal et al., 1963 Suručić et al., 2017
S. tortuosum	Türkiye	Horozgözü	Fruits	Digestive disorders, emmenagogue	Baytop, 1999
Seseli sp.	Europe	-	-	Antibacterial, antifungal, insect repellent, emmenagogue, anti-flatulence, anti-inflammatory, antinociceptive, anti-tumor, anti-rheumatic activities, protective effect on human lymphocytes DNA	Ilić et al., 2015

5. Phytochemical profiles

The phytochemical diversity and importance of the Apiaceae family arise from the fact that it comprises a large number of spices, vegetables, and plants used as condiments globally. Almost all family members are aromatic plants due to their essential oils and resins. In addition, the Apiaceae appears to be unrivaled in terms of the structural richness of coumarins (Berenbaum, 1990). Moreover, some polyacetylenes with potent bioactivity were also found in this family (Crowden et al., 1969; Christensen and Brandt, 2006).

Earlier phytochemical investigations on the *Seseli* species (Fig. 3) have mainly revealed coumarins, essential oils, cinnamic acid derivatives, sesquiterpene lactones, and phenylpropanoids (Barrero et al., 1990; Tosun and Özkal, 2003). The current review aims to provide in-depth knowledge of all aspects, along with chemical compositions of the essential oils from different wild-growing *Seseli* species several places worldwide. In addition, the phytochemistry of the species is available with all valuable prior publications. In particular, beneficial information on essential oils obtained from endemic species and all data on phytochemical compositions are compiled here.

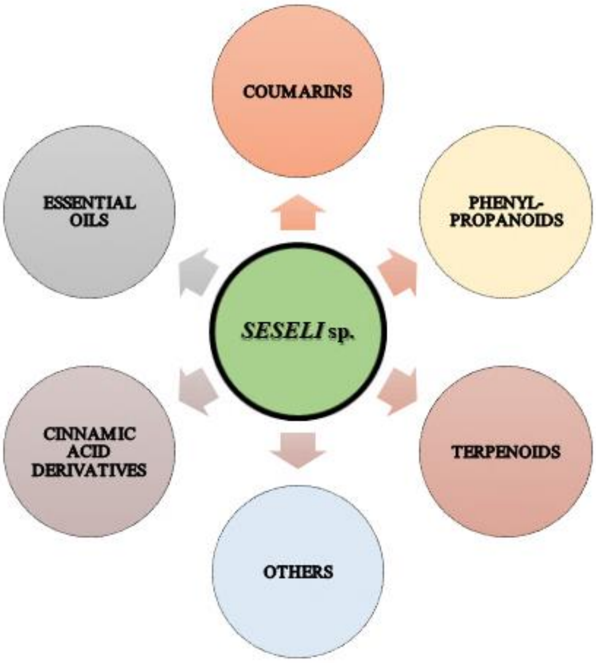


Fig. 3. The highlights in the phytochemical distribution of *Seseli* species

5.1. Chemical profile of the volatiles

Essential oils are natural complex mixtures obtained from aromatic plants by distillation method and produced from the unique elements of the plants. It has a vital use in cosmetics, aromatherapy, and therapeutic settings. In addition, it is a sought-after group in industrial areas. Many Apiaceae species are known as important essential oil sources with their aromatic plants; *Seseli* species, which are among the aromatic plants, are also frequently mentioned with their essential oils. The main components in the essential oil chemical profiles of the *Seseli* species are listed in Table 3.

The essential oils from many of the *Seseli* L. species listed in the Flora Europea have been studied (Tutin et al., 1968). Previous studies showed that α-pinene, sabinene (monoterpenes), and carotol (a sesquiterpene) are the main components in the essential oil of the *Seseli* species (Chizzola, 2010).

The leaves of *Seseli bocconi* Guss. subsp. *praecox* Gamisans collected from different localities in Sardinia were applied to supercritical fluid (CO_2) extraction (SFE) and hydrodistillation. Each sample showed significant differences (Table 3), which were obtained by different methods (Marongiu et al., 2006). The differences probably arise from the diversity in the geographical region. The composition of the essential oils of *S. elatum* L. from northeast Italy, collected from three different populations, showed quantitatively and qualitatively differences in leaves, stems, inflorescences, and fruits. The study was important in finding a chemotaxonomic similarity (Coassini Lokar et al., 1986). The essential oil from whole fresh flowering tops of *S. buchtormense* (Fisch.) W.D.J. Koch, an endangered species from the rocky and sunny regions in Altai-Siberia, was evaluated for the volatile components varied according to the altitude of the plant samples collected (Tkachev et al., 2006). After the comparison of the aerial parts and fruits of *S. campestre* Besser (collected from Kahramanmaraş-Doğankonak village of Türkiye); in the fruit oil, *α*-pinene (26.2%) and (*E*)-sesquilavandulol (11.8%); in the aerial parts oil, *α*-pinene (35.8%) and (*E*)-sesquilavandulol (3.2%) have been determined as the main constituents (Baser et al., 2000). The occurrence of (*E*)-sesquilavandulol and its acetate in the essential oil of *S. campestre* were unusual because these compounds were found in another Apiaceae plant (Kubeczka et al., 1986; Baser et al., 2000). Moreover, the aerial parts of *S. campestre*, collected from the different localities (from Istanbul province) during flowering time, were subjected to hydrodistillation using a Clevenger-type apparatus to obtain the essential oil. (*E*)-sesquilavandulol (10.3±0.8%) was also found as the main component (Kaya et al., 2010). The essential oil from aerial parts, unripe and ripe fruits of *S. globiferum* Vis. had common main components: sabinene (38.0%, 53.1%, and 65.3%), *α*-pinene (21.2%, 7.2%, and 4.4%), and *β*-phellandrene (13.5%, 5.0%, and 4.9%), respectively (Stojković et al., 2008; Janaćković et al., 2011). Germacrene D (14.01%) and bicyclogermarene (11.92%) in *S. corymbosum* Boiss. & Heldr. and spatulenol (19.91%) in *S. gummiferum* Pall. ex Sm. were found from the aerial parts of two endemic subspecies (Tosun et al., 2005b). The main constituents were germacrene D (54.1%) and sabinene (22.4%) in *S. gummiferum* fruits and *β*-phellandrene (29.2%) and *α*-phellandrene (8.2%) in *S. corymbosum* fruits by GC/FID and GC/MS analysis (Tosun et al., 2016). As a new species from the Turkish flora, *S. gummiferum* Pall. ex Sm. subsp. *ilgazense* A. Duran, O. Cetin & M. Ozturk (Çetin et al., 2015), has also been studied for the essential oil composition. The essential oil from the aerial parts obtained by hydrodistillation has sabinene (28.8%), germacrene D (9.5%), and *α*-pinene (7.2%) as significant components (Kurkcuoglu et al., 2018). It is clearly understood that three interrelated endemic species have similar chemical components. In a different work, significant differences can not be found in the composition of the essential oils between the natural and cultivated *S. gracile* Waldst. & Kit. forms. In the essential oil of aerial parts obtained by hydrodistillation according to the European Pharmacopoeia, terpinolene (6.1–57.5 %), *γ*-terpinene (3.3–24.2 %), and *p*-cymene (1.3–25.2 %) have been found as dominant. In the fruit essential oil, *γ*-terpinene (24.2 %), *α*-pinene (9.6 %), *β*-pinene (7.6 %), and *δ*-cadinene (5.9 %) were the major ones (Marčetić et al., 2017a). In addition, the essential oil from the aerial parts of *S. gracile* was obtained by hydrodistillation, according to the European Pharmacopoeia. The major constituents of the essential oil were determined as terpinolene (40.55%), *γ*-terpinene (23.34%), and *p*-cymene (9.62%) (Surućić et al., 2021). *S. devenyense* Simonkai and *S. libanotis* have been studied for essential oil components. The major components have been found as *β*-sesquiphellanderene (17.79%), spathulenol (5.70%), and *β*-caryophyllene (3.30%) in *S. devenyense* essential oil and *β*-caryophyllene (28.70%), sabinene (18.37%), *β*-phellanderene (13.16%) and spathulenol (12.80%) in *S. libanotis* essential oil (Widelski et al., 2021a). *S. libanotis* (L.) W.D.J.Koch, which is called “moon carrot or mountain stone-parsley,” is a perennial plant diversified in Central and Eastern Europe and Asia Minor (List and Hörhammer, 1979). The essential oil composition from the aerial parts of *S. libanotis* from

Türkiye (Öztürk and Ercişli, 2006), and fruits essential oil from Poland were found to be completely different (Skalicka-Woźniak et al., 2010). The essential oil from the aerial parts of *S. libanotis* has a complex variability, including common terpenoids such as *α*-pinene, sabinene, myrcene, and germacrene D. In contrast, carotol or acorenone B has been observed in flower and fruit essential oils. The *α*-pinene was dominant in the root essential oil (Chizzola, 2019).

The essential oils from mature umbels, together with fruits of *Seseli montanum* subsp. *peixotoanum* (Samp.) M. Laínz and *S. tortuosum* L. (Council of Europe, 1997), growing in the north of Portugal, were compared. In the essential oils of *S. tortuosum, α*-pinene (24.8–24.9%), *β*-pinene (23.5–23.9%), and *Z-β*-ocimene (13.3–16.0%) are the main constituents and in the oils of *S. montanum* subsp. *peixotoanum, α*-pinene (36.0–37.1%), *β*-pinene (22.5–23.6%), limonene (7.7–8.8%) and *β*-elemene (5.2–5.8%) were found as the major components (Gonçalves et al., 2012). In this study, these two essential oils differ in the presence of *β*-elemene, but *α*-pinene was detected in the highest amount in both species. In another work, the essential oil from *S. montanum* subsp. *tommasinii* (Rchb.f.) Arcang., has *β*-pinene (30.2%), germacrene D (10.1%), sabinene (8.0%), *α*-pinene (7.2%), and limonene (6.6%) as the dominant components (Šiljegović et al., 2011). The essential oil composition from air-dried parts from *S. pallasii* Besser (Syn. *S. varium* Trevir.) in Serbia was compared, and the flowering and fruiting phases have been found almost the same profile (Suručić et al., 2017). In addition, *S. pallasii* have *α*-pinene 27.3 % in stems and 84.7 % in fruit essential oil as a major component, besides *n*-nonane (45.2 %), Z-*β*-ocimene *(*34.5 %) and *n*-undecane (13.3 %) in root essential oil (Stankov-Jovanović et al., 2016). The fruit parts of *S. petraeum* M. Bieb. and *S. andronakii* Woronow ex Schischk. from the northern side of Türkiye have carotol (20.7%), *γ*-terpinene (11.3%), sabinene (9.5%), germacrene D (7.8%) for *S. petraeum,* and carotol (52.7%) and germacrene D (8.7%) for *S. andronakii* (Tosun et al., 2006a). In addition, the fruits essential oil of *S. petraeum* was also studied recently, and carotol (17.25%), γ-terpinene (10.73%), *β*-farnesene (8.50%), *p*-cymene (7.93%), germacrene-D (7.65%) and sabinene (7.31%) were reported as the major components (Önder et al., 2021). The germacrene D (29.8%) was also the main one in the essential oil of *S. annuum* L. aerial parts, a native species in Serbia (Milosavljević et al., 2007). The essential oil from the aerial parts of the *S. peucedanoides* (M.Bieb.) Koso-Pol. revealed the presence of *α*-pinene (69.4%), *β*-pinene (4.9%), and limonene (4.6%) as the major constituents (Bulatović et al., 2006). Petrović et al. also investigated the essential oils obtained by the static headspace method from the flowers and leaves of the *S. peucedanoides.* In both oils, the major components were (*E*)-caryophyllene and germacrene D. In addition, the main components of the headspace samples were *α*-pinene, (*E*)-*β*-ocimene, (*E*)-caryophyllene and (*Z*)-3-hexen-1-ol (Petrović et al., 2019).

The most investigated species among the other *Seseli* plants in terms of essential oil is *S. rigidum* Waldst. & Kit.. *S. rigidum,* as an endemic plant, mainly grows in some Balkan countries. Ilić et al. (2015) showed that the chemical composition of the fruits' essential oil from *S. rigidum* exhibited diversity according to geographical conditions. Moreover, Marčetić et al. (2013) stated that climate could affect the chemical composition of *S. rigidum* root oil more than soil. The composition of the *S. rigidum* fruit essential oils from different origins (post-fire and control areas after two years from a forest fire) was not considerably different. In the essential oil, *α*-pinene and sabinene were the main components. Still, there were significant differences in the existence and distribution of other components and substantial differences compared to different geographical origins (Ilić et al., 2015). In the essential oil obtained from aerial parts of *S. rigidum* from Western Serbia, *α*-pinene was reported as the main compound (57.4%), then limonene, camphene and sabinene. In the fruit essential oil, the main ones were *α*-pinene (23.3%), *β*-phellandrene and sabinene. However, the root essential oil comprises interestingly almost all falcarinol (88.8%) (Marčetić et al., 2012; Marčetić et al., 2013). In another study, *S. rigidum* was collected from South-eastern Serbia in July (flowering time) and in September (fruiting time), then fresh flowers, leaves, fruit, and roots were applied to hydro-distillation. The samples were analyzed and evaluated by GC/MS and HS/GC-MS (Stankov-Jovanović et al., 2015). When the flower essential oil of *S. rigidum* (yielded 0.6% v/w) was analyzed, the highest one was found as α-pinene (48.5%) (Stojković et al., 2009). *S. rigidum* from Bulgaria was also evaluated for the essential oil composition. The essential oil of the species parts (flowers, leaves, stems, and roots) was obtained by micro-steam distillation (SD)-extraction in a modified Lickens–Nickerson apparatus using diethyl ether (Et_2O) as a solvent and analyzed by GC/MS. In the essential oil, β-phellandrene (47.5 and 19.8%) and sabinene (63.1 and 6.5%) were the major components in flower and stem essential oils. Sabinene (39.8%) was also the main one in the essential leaf oil. The major components of root essential oil are *Z*-falcarinol (48.7%), sabinene (12.4%), and elemol (8.7%) (Todorova et al., 2013). The essential oils from roots, aerial parts, and fruits of plants from 7 populations of *S. rigidum* were analyzed to identify the different chemotypes. The essential oils obtained from the roots of *S. rigidum* displayed a falcarinol chemotype; oils from aerial parts -an α-pinene or α-pinene/sabinene chemotype and the fruit essential oils -a complex as sabinene/α-pinene/β-phellandrene/falcarinol/germacrene B chemotype (Marčetić, 2017b). The essential oil composition of *S. rigidum* aerial parts from Serbia was characterized (Table 3), representing 99.2% of the oil (Šavikin-Fodulović et al., 2006).

On the other hand, an endemic species *S. resinosum* Freyn & Sint. and a common species *S. tortuosum* L. from Turkish flora were compared in a study for their essential oil components, where α-pinene (13.7% and 13.5%, respectively) were almost in the same concentrations in the essential oils (Dogan et al., 2006). The essential oil composition of the *S. tortuosum* collected from different geographical origins was also studied. The essential oil of *S. tortuosum* from Italy, distributed towards Ligurian coasts and Sicily and Sardinia islands, obtained from leaves, stems, and flowers afforded mainly myrcene (29.2%), *α*-pinene (18.6%), *β*-pinene (13.2%) and limonene (10.6%) and a sesquiterpene known as acorenone (6.3%) (Bader et al., 2003). Acorenone is a rare sesquiterpene found in essential oil compositions (Vrkoč et al., 1961; Pigulevskii and Kovaleva, 1966). It was also determined in the fruits essential oil of *Libanotis transcaucasica* Schischk. (Syn: *Seseli transcaucasicum* Pimenov & Sdobnina from World Flora Online) (Pigulevskii and Bakina, 1968; Shahabipour et al., 2013). The essential oil of the aerial parts of the *S. tortuosum* L. subsp. *Kiabii* Akhani (Habibi et al., 2003) contains *α*-pinene (21.2%), sabinene (13.4%), *β*-pinene (14.2%) and *β*-phellandrene (14.9%). The main constituents are characterized in the water-distilled essential oil from the aerial parts of *S. tortuosum* as *α*-pinene (35.9%), sabinene (8.8%), (*E*)-sesquilavandulol (8.4%) and *β*-pinene (7.0%) (Kaya et al., 2003). The *α*-pinene, sabinene, and *β*-pinene were the common components, (*E*)-sesquilavandulol and *β*-phellandrene were found differently in this study. In another work, the aerial parts of *S. tortuosum* collected from Beira Litoral, Portugal, implemented a Clevenger-type apparatus using hydro-distillation depending on the method in the European Pharmacopoeia. The *α*-pinene, *β*-pinene, and sabinene were the common compounds of the essential oils, like in the other *S. tortuosum* essential oils (Costa et al., 2018).

Table 3

The major components of the essential oils obtained from *Seseli* species

Species	**Origin**	**Method (*)**	**Plant part**	**Major constituents (%)**	**Reference**
S. andronakii	Türkiye	HD	Fruit	Carotol (52.7%), germacrene D (8.7%)	Tosun et al., 2006a
S. annuum	Serbia	HD	Aerial part	Germacrene D (29.8%), sabinene (10.3%), *β*-ocimene *Z* (9.8%), limonene (8.6%)	Milosavljević et al., 2007
S. bocconi subsp. *praecox*	Italy (Sardinia)	SFE	Leaf	Himachalol (16.4%), sabinene (14.8%), *β*-phellandrene (8.1%), *cis*-sabinene hydrate (4.5%) from Buggerru sample	Marongiu et al., 2006
				β-Phellandrene (29.2%), undecane (9.6%), *α*-pinene (6.1%), *β*-guaiene (5.7%) from Carloforte sample	
				α-Humulene (17.7%), *β*-himachalene (9.3%), *γ*-phellandrene (8.0), bicyclogermacrene (7.7%) from the Ogliastra inland	
		HD	Leaf	Sabinene (20.1%), *β*-phellandrene (812.5%), *cis*-sabinene hydrate (0.5%) from Buggerru sample	
				α-Pinene (16.7%) myrcene (5.6%), *β*-phellandrene (37.9%), undecane (8.7%) from the Carloforte sample	
				α-Humulene (20.1%), *γ*-phellandrene (10.4%), bicyclogermacrene (8.3%) from the Ogliastra sample	
S. buchtormense	Siberia	SD	Flowering tops	Sabinene 25.1%, *α*-pinene 14.6%, *β*-phelandrene 7.0% at 700 m	Tkachev et al., 2006
				(*E*)-Nerolidole (11.6%), *β*-myrcene (6.6%), limonene (4.5%) at 400 m	
				δ-Cadinene (6.0%), epi-*α*-cadinol (2.5%), *α*-cadinol (3.0%) at 300 m	
				Fenchone (7.0%), germacrene D-4-ol (4.6%), 6-α-dehyroxy-germacra-1 (10),4-diene (4.3%), *α*-bisabolol (7.7%) at 2030 m	

S. campestre	Türkiye (Kahramanmaraş)	HD	Fruit	*α*-Pinene (26.2%), (E)-sesquilavandulol (11.8%)	Baser et al., 2000
			Aerial part	*α*-Pinene 35.8%, (*E*)-sesquilavandulol (3.2%)	
	Türkiye (Istanbul)		Aerial part in flowering time	*α*-Pinene (38.6±0.5%), *β*-pinene (17.5±0.1%), (*E*)-sesquilavandulol (10.3±0.8%)	Kaya et al., 2010
S. corymbosum	Türkiye	HD	Aerial part	Germacrene B (14.01%), bicyclogermarene (11.92%)	Tosun et al., 2005b
			Fruit	*β*-Phellandrene (29.2%), *α*-phellandrene (8.2%), germacrene D (2.5%)	Tosun et al., 2016
S. devenyense	Poland (Lublin)	HD	Aerial part with fruits	*β*-Sesquiphellanderene (17.79%), spathulenol (5.70%), *β*-caryophyllene (3.30%)	Widelski et al., 2021a
S. elatum	Italy	-	Leaf, stem, inflorescence, fruit	-	Coassini Lokar et al., 1986
S. globiferum	Serbia	HD	Aerial part	Sabinene (38.0%), *α*-pinene (21.2%), *β*-phellandrene (13.5%)	Janaćković et al., 2011
			Unripe fruit	Sabinene (53.1%), *γ*-terpinene (7.7%), *α*-pinene (7.2%), *β*-phellandrene (5.0%)	Stojković et al., 2008
			Ripe fruit	Sabinene (65.3%), *γ*-terpinene (6.6%), *α*-pinene (4.4%), *β*-phellandrene (4.9%)	
S. gracile	Serbia	HD	Aerial part	Terpinolene (6.1–57.5%), *γ*-terpinene (3.3–24.2%), *p*-cymene (1.3–25.2%)	Marčetić et al., 2017a
			Aerial part	Terpinolene (40.55%), *γ*-terpinene (23.34%), *p*-cymene (9.62%)	Suručić et al., 2021
			Fruit	*γ*-Terpinene (24.2%), *α*-pinene (9.6%), *β*-pinene (7.6%), *δ*-cadinene (5.9%)	Marčetić et al., 2017a
S. gummiferum	Türkiye	HD	Aerial part	Spatulenol (19.91%)	Tosun et al., 2005b
			Fruit	Germacrene D (54.1%), sabinene (22.4%)	Tosun et al., 2016
S. gummiferum subsp. *ilgazense*	Türkiye	HD	Aerial part	Sabinene (28.8%), germacrene D (9.5%), *α*-pinene (7.2%)	Kurkcuoglu et al., 2018
S. libanotis	Türkiye	HD	Aerial part	*trans*-Caryophyllene (20.39%), spathulenol (11.89%), (-)-caryophyllene oxide (11.47%), euasarone (10.66%), *δ*-cadinene (9.16%)	Öztürk and Ercişli, 2006
S. libanotis	Poland (Lublin)	HD	Aerial part with fruits	*β*-Caryophyllene (28.70%), sabinene (18.37%), *β*-phellanderene (13.16%), spathulenol (12.80%)	Widelski et al., 2021a

S. libanotis subsp. libanotis	Poland	HD	Fruit	Sabinene (37.4%), *β*-phellandrene (19.0%)	Skalicka–Woźniak et al., 2010
		HS-SPME		Sabinene (46.2%), *β*-phellandrene (23.5%)	
S. montanum subsp. *peixotoanum*	Portugal	HD	Ripe umbel with mature seed	*α*-Pinene (36.0–37.1%), *β*-pinene (22.5–23.6%), limonene (7.7–8.8%), *β*-elemene (5.2–5.8%)	Gonçalves et al., 2012
S. montanum subsp. *tommasinii*	Montenegro	HD	Aerial part	*β*-Pinene (30.2%), germacrene D (10.1%), sabinene (8.0%), *α*-pinene (7.2%), limonene (6.6%)	Šiljegović et al., 2011
S. pallasii (*Syn*: *S. varium*)	Serbia	HD	Flowering phase	*α*-Pinene (48.2%), caryophyllene oxide (4.4%), germacrene D (4.1%), limonene (3.3%), spathulenol (3.1%), *β*-pinene (2.9%)	Suručić et al., 2017
			Fruiting phase	*α*-Pinene (42.7%), *β*-pinene (4.6%), caryophyllene oxide (4.3%), limonene (3.8%), germacrene D (2.9%)	
S. pallasii (*Syn: S. varium*)	Serbia	HD	Fruit	*α*-Pinene (84.7%)	Stankov-Jovanović et al., 2016
			Root	*n*-Nonane (45.2%), (*Z*)-*β*-ocimene (34.5%), *n*-undecane (13.3%)	
			Stem	*α*-Pinene (27.3%)	
S. petraeum	Türkiye	HD	Fruit	Carotol (20.7%), *γ*-terpinene (11.3%), sabinene (9.5%), germacrene D (7.8%)	Tosun et al., 2006a
S. peucedanoides	Serbia	HD	Aerial part	*α*-Pinene (69.4%), *β*-pinene (4.9%), limonene (4.6%)	Bulatović et al., 2006
		HD	Flower	*α*-Pinene, (*E*)-*β*-ocimene, (*E*)-caryophyllene, (*Z*)-3-hexen-1-ol	Petrović et al., 2019
		Static headspace	Leaf		
S. resinosum	Türkiye	HD	Aerial part	*β*-Pinene (37.5%), 4-*α*-hydroxygermacra-1(10)-5-diene (21.7%), *α*-pinene (13.7%)	Dogan et al., 2006
S. rigidum	Serbia	HD	Fruit	*α*-Pinene (23.3%), *β*-phellandrene, sabinene	Ilić et al., 2015
			Root	Falcarinol (88.8%)	Marčetić et al., 2012 Marčetić et al., 2013
			Aerial part	*α*-Pinene (57.4%), limonene, camphene, sabinene	Marčetić et al., 2012 Marčetić et al., 2013
	Bulgaria		Flowers	*α*-Pinene (33%), germacrene D (10.1%), sabinene (7.9%), limonene (7.1%)	Marčetić et al., 2017b
			Leaf	*α*-Pinene (26.3%), sabinene (7.8%), limonene (5.4%), *trans*-verbenol (5%)	

			Fruit	*α*-Pinene 33.2%, sabinene (18.5%), limonene (8.7%), *γ*-terpinene (5.5%)	
			Flower	*α*-Pinene (57.2%), sabinene (7.8%), camphene, limonene (6.5%)	Stankov-Jovanović et al., 2015
		HS-SPME	Leaf	*α*-Pinene (76.7%), camphene (7.5%), limonene (6.6%)	
S. rigidum var rigidum			Fruit	*α*-Pinene (35%), sabinene (28.7%), limonene (12%), *o*-cymene (5.3%)	
			Root	(*Z*)-Falcarinol (14.3%), *n*-octanal (7.7%), terpinen-4-ol (3.9%), cadin-1(10)-en-5,11-oxide (3.6%)	
			Flower	*α*-Pinene (48.5%), camphene (4.6%), *β*-pinene (4.2%), limonene (4.1%)	Stojković et al., 2009
		SD by Lickens–Nickerson apparatus	Flower	*β*-Phellandrene and sabinene (47.5 and 19.8%)	Todorova et al., 2013
			Stem	*β*-Phellandrene and sabinene (63.1 and 6.5%)	
			Leaf	Sabinene (39.8%)	
			Root	*Z*-Falcarinol (48.7%), besides sabinene (12.4%), elemol (8.7%)	
	Serbia	HD	Aerial part	*α*-Pinene (53.31%), limonene (10.04%), germacrene D (9.32%)	Šavikin-Fodulović et al., 2006
S. tortuosum	Türkiye	HD	Aerial part	(*E*)-Sesquilavandulol (37.0%), sabinene (19.7%), *α*-pinene (13.5%), *β*-phellandrene (7.8%)	Dogan et al., 2006
	Italy	HD	Aerial part with leaf, flower, fruit	Myrcene (29.2%), *α*-pinene (18.6%), *β*-pinene (13.2%), limonene (10.6%), acorenone (6.3%)	Bader et al., 2003
	Iran	HD	Aerial part	*α*-Pinene (21.2%), sabinene (13.4%), *β*-pinene (14.2%), *β*-phellandrene (14.9%)	Habibi et al., 2003
	Türkiye	HD	Aerial part	*α*-Pinene (35.9%), sabinene (8.8%), (*E*)-sesquilavandulol (8.4%), *β*-pinene (7.0%)	Kaya et al., 2003
	Portugal	HD	Aerial part	*α*-Pinene (27.4%), *β*-pinene (16.0%), limonene (10.0%), *γ*-terpinene (9.3%), *Z*-*β*-ocimene (8.0%), *β*-myrcene (3.0%), camphene (2.1%), sabinene (2.0%)	Costa et al., 2018
	Portugal	HD	Ripe umbel with mature seed	*α*-Pinene (24.8–24.9%), *β*-pinene (23.5–23.9%), *Z*-*β*-ocimene (13.3–16.0%)	Gonçalves et al., 2012

(*) HD: Hydrodistillation, SD: Steam distillation, SFE: Supercritical Fluid Extraction, HS-SPME: Head Space-Solid Phase Micro Extraction

5.2. Coumarin derivatives

Coumarins are well-known bioactive compounds, and the occurrence of these compounds is widespread, mainly in the Apiaceae family (Murray et al., 1982; Jain and Joshi, 2012; Matos et al., 2015; Sarker and Nahar, 2017). The coumarins can be classified into basic classes, such as simple coumarins, furanocoumarins, pyranocumarins, and pyrone-substituted coumarins (Önder, 2020). Based on the literature search and our experience, the *Seseli* L. species are significant sources of diverse coumarin structures, especially a complex mixture of coumarins studied long ago (Table 4). In particular, khellactone esters (pyranocoumarins) are distinctive for the *Seseli* species and widely distributed in this genus, but other coumarins were also found in many parts of the species (Fig. 4). In the literature survey, the papers debated regarding coumarins of *Seseli* species. However, a compilation of these species' coumarins has not yet been written comprehensively. Several phytochemicals have been recently reported from *Seseli* species, but the coumarins seem dominant. Furthermore, all relevant papers have mentioned pyranocoumarins of the *Seseli* species as an excellent bioactive group.

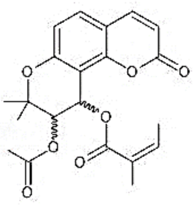
5.2.1. Pyranocoumarin derivatives

If we go back to the 1960s, Lemmich et al. 1966 investigated pyranocoumarins from the roots of *Seseli libanotis* (L.) W.D.J. Koch. Pteryxin (3'-acetoxy-4'-angeloyloxy-3',4'-dihydroseselin) (**1**), (formerly isolated from the roots of *Pteryxia terebinthina* var. *terebinthina*), 3'(*S*),4'(*S*)-3',4'-disenecioyloxy-3',4'-dihydroseselin (**2**), 3'(*S*),4'(*S*)-3'-acetoxy,4'-senecioyloxy-3',4'-dihydroseselin (**3**), (-)-3'-hydroxy-3',4'-dihydroxanthyletin (**4**) and its angeloyl ester were separated from the ether extract of *S. libanotis*. In addition, (±)-3'-hydroxy, 3',4'-dihydroxanthyletin (**5**) and (±)-4'-hydroxy,3',4'-dihydroxanthyletin (**6**) (the xanthyletin series is the linear type pyranocoumarins) have been synthesized from the natural xanthyletin (**7**). Regarding the determination of the isomerism of the khellactones; the relative *cis*-

configuration was assigned based on the coupling constant $J_{3',4'}$, which was between 2.4 and 3.0 Hz for *trans* compounds and between 4.1 and 5.0 Hz for the *cis* compounds. The *geminal*-dimethyl signals generally appear as a separate doublet in *trans* isomers and an almost broad singlet or two close singlets in *cis* isomers (Lemmich et al., 1966). The coumarins called (3′*R*)-lomatin-3′-sulphate (**8**) and (3′*R*,4′*R*)-khellactone-3′-sulphate (**9**), which are known as sulfate ester salts derived from coumarin alcohols were reported from roots of *S. libanotis* (L.) Koch subsp. *eu-libanotis* (Lemmich and Shabana, 1984). Afterward, floroselin [3′-angeloyloxy-2′,2′-dimethyl-4′-(*trans*-3-methylthioacryloyloxy)-3′,4′-dihydropyrano-5′,6′: 8, 7-coumarin] (**10**) was described from the methanol (MeOH) extracts of the roots of *S. sessiliflorum* Schrenk, which was the other proposed coumarin (Savina et al., 1970b). In addition, 3'(*R*)-(+)-3'-hexanoyloxy-3',4'-dihydroseselin (**11**), 3'(*R*)-(+)-3'-octanoyloxy-3',4'-dihydroseselin (**12**) and 3'(*R*)-(+)-3'-*cis*-4-octenoyloxy-3',4'-dihydroseselin (**13**) were obtained from the ether extract of the stems of *S. gummiferum* Pall. subsp. *gummiferum*. The saponification of 3'-*cis*-4-octenoyloxy-3',4'-dihydroseselin gave lomatin (**14**) [3'(*R*)-3'-hydroxy-3',4'-dihydroseselin]. The absolute configuration of lomatin (**14**) indicated the "*R*" enantiomer (Nielsen et al., 1970). In further investigation, 3'(*R*)-4'(*R*)-3'-isovaleryloxy-4'-angeloyloxy-3',4'-dihydroseselin (**15**), 3'(*R*)-4'(*R*)-3'-senecioyloxy-4'-angeloyloxy-3',4'-dihydroseselin (**16**), 3'(*R*)-4'(*R*)-3'-acetoxy-4'-senecioyloxy-3',4'-dihydroseselin (**17**), (+)-*cis*-khellactone (**18**) and *cis*-khellactone mixtures had been obtained from the stems of *S. gummiferum* Pall. subsp. *gummiferum* (Nielsen et al., 1971). The roots and herbal parts of *S. tenuisectum* Regel & Schmalh. were also investigated regarding the coumarins. As a result of this, anomalin (**19**), along with (+)-*cis*-methylkhellactone (**20**), 3'-angeloyloxy-4'-hydroxy-3',4'-dihydroseselin (**21**), 3'-hydroxy-4'-angeloyloxy-3',4'-dihydroseselin (**22**) and pteryxin (**1**), were obtained from the MeOH and ether extracts of the plant parts (roots and aerial) (Aminov and Nikonov, 1972). The sulfur-containing coumarins were not often inside coumarin-containing plants, but in ongoing studies, a sulfur-containing coumarin called sechulin (**23**), based on a 2,3-dimethyl-dihydropyranocoumarin nucleus, was discovered in the *S. tschuense* Nikitina (*Syn: S. sessiliflorum* Schrenk from World Flora Online) roots (Aminov and Nikonov, 1974). In addition, (-)-3'*R*-decursinol (**24**), its angelate, grandivittin (3'-senecioyloxy-3',4'-dihydro-3'R-xanthyletin) (**25**) and grandivittinol [7-hydroxy-6-(3'-hydroxy-2'-senecioyloxyisopentyl) coumarin (**26**), have been found from the $CHCl_3$ extract subjected to alumina column eluting petroleum ether: $CHCl_3$: MeOH gradually from the roots of the *S. grandivittatum* Schischk. (Abyshev et al., 1977). Isofloroselin (**27**) from the acetone extracts of the roots of *S. coronatum* Ledeb. (Savina et al., 1970b; Dukhovlinova et al., 1974), anomalin (**19**) and pteryxin (**1**) as two common pyranocoumarins were also isolated from the roots of *S. mucronatum* (Schrenk) Pimenov & Sdobnina with increasing gradient of the ethyl acetate (EtOAc) in petroleum ether: EtOAc system (Dukhovlinova et al., 1979). Gonzáles et al. (1979) investigated pyranocoumarin derivatives in the Spanish *S. tortuosum* and *trans*-khellactone (**28**), *cis*-khellactone (**18**), 3'-senecioyl-*cis*-khellactone (**29**), 3'-senecioyl-4'-acetyl-*cis*-khellactone (**30**), 4'-senecioyl-*cis*-khellactone (**31**), 3'-acetyl-4'-senecioyl-*cis*-khellactone (**32**), 3',4'-di-isovaleryl-*cis*-khellactone (**33**), 3',4'-disenecioyl-*cis*-khellactone (**34**), 3'-angeloyl-4'-isovaleryl-*cis*-khellactone (**35**) and 3'-isovaleryl-4'-angeloyl-*cis*-khellactone (**36**), were determined from the ether extracts of the aerial parts of this plant (Gonzáles et al., 1979). In continuing studies, (–)-2'-senecioyloxy-1',2'-dihydroxanthyletin (**37**), and (–)-2'-isovaleryloxy-1'-2'-dihydroxanthyletin (**38**) have been reported from the acetone extract of *S. tortuosum* L.B.S. Eur. (Ceccherelli et al., 1990; Bader et al., 2003). However, seseloside (3'-O-*β*-D-glucopyranosyloxy-8-hydroxy-2',2'-dimethyl-3',4'-dihydropyrano-5',6':6,7-coumarin) (**39**), a linear-type pyranocoumarin monoglycoside, was determined from the roots of *S. peucedanoides* (Bagirov and Belyi, 1981). Other khellactone esters called 3',4'-diangeloyl-(–)-*cis*-khellactone (anomalin) (**19**), 3'(*R*)-4'(*R)*-3'-angeloyl-4'-acetyl-(–)-*cis*-khellactone (isopteryxin) (**40**), 3'(*R*)-4'(*R)*-3'-angeloyl-(–)-*cis*-khellactone (**41**) and 3'-isobutyl-4'-acetyl-(+)-*cis*-khellactone (bocconin) (**42**), were obtained from *S. bocconi* Guss subsp. *bocconi* growing in Sicily (Italy). The coumarins were extracted with Et_2O to obtain an oily crude extract, then dissolved in 90% MeOH defatted the lipids, and eluted on silica gel with increasing polarity petroleum ether: Et_2O: EtOAc: MeOH. In addition, these two compounds (**41, 42)** were also isolated from the other subspecies, *S. bocconi* Guss subsp. *praecox* Gamisans, growing in Corsica. Concerning the stereochemistry of these compounds, the optical rotations of anomalin $[\alpha]_D^{20}$ ─50.2, isopreryxin -48.4, and -89.8 indicated the configuration 3'*R*, *4'R* (Bellino et al., 1986). Seselin (**43**), a basic pyranocoumarin structure, was also obtained from *S. elatum* subsp. *gouanii* (W.D.J. Koch) P.W. Ball, *S. elatum* subsp. *austriacum* (Beck) P.W.Ball (Coassini Lokar and Delben, 1988) and from the seeds of *S. diffusum* (Roxb. ex Sm.) Santapau & Wagh, known as Indian celery (Abbaskhan et al., 2012). The pyranocoumarins were also reported as the (+)-lomatin decanoic and dodecanoic esters (**44, 45**). The decanoates of (+)-*cis*-khellactone at positions 3' and 4' (**46, 47**) from the mature fruits of *S. devenyense* Simonk. were obtained on a silica column following a preparative reverse-phase high-performance liquid chromatography (RP-HPLC) (Widelski et al., 2005). Widelski et al. (2021) also isolated several pyranocoumarins from mature fruits of *S. devenyense*, called *cis*-khellactone (**18**), d-laserpitin (**48**), isolaserpitin (**49**) and octanoyllomatin (**50**) by countercurrent chromatography (CCC) at 320 nm (Widelski et al., 2021b). A new angular-type pyranocoumarin called corymbocoumarin [(−)-(*3′S,4′S*)-3′-acetoxy-4′-isovaleryloxy-3′,4′-dihydroseselin] (**51**), besides the (−)-(*3′S,4′S*)-3′-acetoxy-4′-angeloyloxy-3′,4′-dihydroseselin (**52**), (+)-(*3′S,4′S*)-3′-hydroxy-4′-angeloyloxy-3′,4′-dihydroseselin (d-laserpitin) (**48**), (−)-(*3′S,4′S*)-3′-angeloyloxy-4′-hydroxy-3′,4′-dihydroseselin (**53**) and 3′-acetoxy-4′-isobutyloxy-3′,4′-dihydroseselin (**54**) were purified from the hexane extract of the aerial parts of *S. gummiferum* Pall. ex Sm. subsp. *corymbosum* (Boiss. & Heldr.) P.H. Davis (Syn: *S.*

corymbosum Boiss. & Heldr.) which is an endemic species collected from the Taurus (Toros) Mountains in Southern Anatolia of Türkiye. The absolute configurations of the structures were determined by the spectral methods and comparison of the chemical correlations with similar known compounds (Tosun et al., 2005a). In the other work, *cis*-(3'*R*,4'*R*)-3'-angeloyloxy-4'-acetoxy-3',4'-dihydroseselin (isopteryxin) (**40**) was determined from the *n*-hexane extract of the aerial parts of *S. hartvigii* (Tosun, 2006). In addition, (+)-samidin [(3'*S*,4'*S*)-3'-senecioyloxy-4'-acetoxy-3',4'-dihydroseselin] (**55**), (–)-anomalin [(3'*R*,4'*R*)-3',4'-diangeloyloxy-3',4'-dihydroseselin] (**19**) and calipteryxin (3'*R*,4'*R*)-3'-angeloyloxy-4'-senecioyloxy-3',4-dihydroseselin (**56**) were identified from the dried roots of *S. resinosum* Freyn & Sint. in *n*-hexane extract (Tosun et al., 2006b). A different separation method, called semi-preparative CCC (Countercurrent Chromatography), known as a high purity, economical, productive and time-saving process, using biphasic solvent systems such as *n*-hexane: EtOAc: MeOH: Water (HEMWat) for the fast isolation in a single run and a one-step separation, has been applied to separate the coumarins such as (3'*S*,4'*S*)-3'-acetoxy-4'-angeloyloxy-3',4'-dihydroseselin (**52**), d-laserpitin (**48**), (3'*S*,4'*S*)-3'-angeloyloxy-4'-hydroxy-3',4'-dihydroseselin (**53**), (+)-samidin (**55**), calipteryxin (**56**), (3'*S*,4'*S*)-3',4'-disenecioyloxy-3',4'-dihydroseselin (**2**) and (-)-anomalin (**19**) from the roots of *S. resinosum* (Shehzad et al., 2013). In a recent study, a new pyranocoumarin called 3'-isovaleryl-4'-oxo-lomatin (petracoumarin) (**57**), together with other known coumarins, such as *cis*-khellactone (**18**), anomalin (**19**), 3'-senecioyl-*cis*-khellactone (**29**), 4'-senecioyl-*cis*-khellactone (**31**), 3'-angeloyl-4'-isovaleryl-*cis*-khellactone (**35**), 3'-isovaleryl-4'-angeloyl-*cis*-khellactone (**36**), octanoyllomatin (**50**), samidin (**55**), calipteryxin (**56**), selinidin (**58**) and 3'-isobutryl-lomatin (**59**), were isolated from the aerial parts from *Seseli petraeum* M. Bieb. (Onder et al., 2022).

The angular or linear pyranocoumarins obtained from the *Seseli* species have been given in Fig. 4.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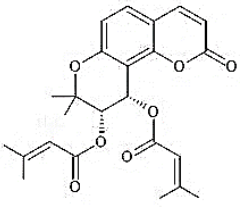
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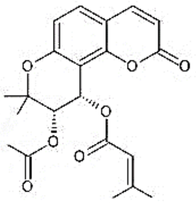
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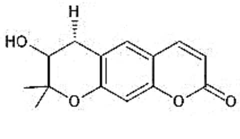
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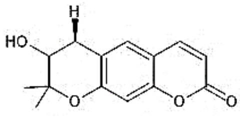
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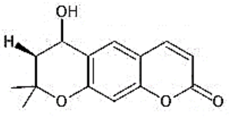
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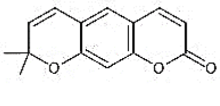
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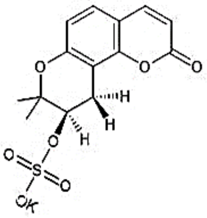
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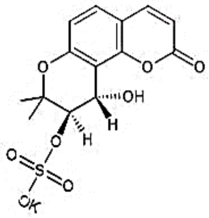
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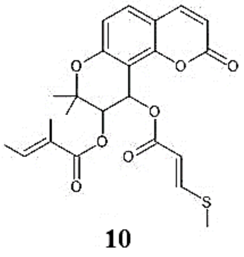
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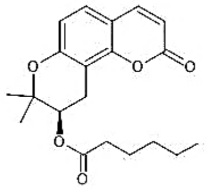
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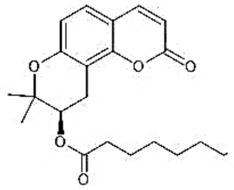
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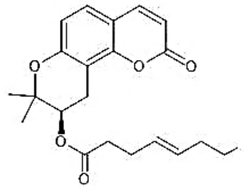
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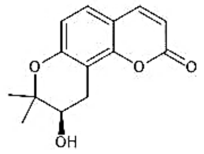
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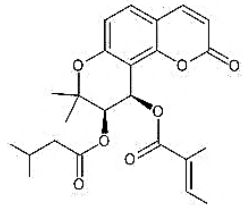
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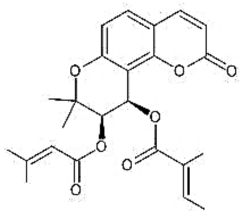
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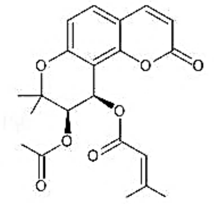
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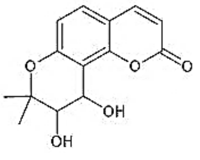
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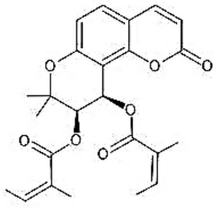
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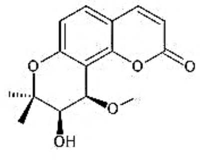
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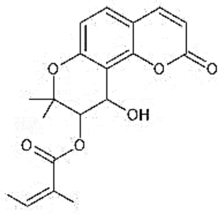

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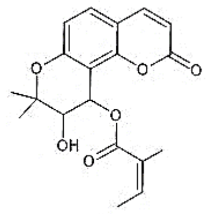

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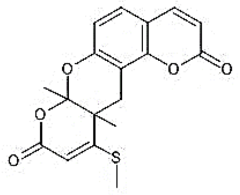

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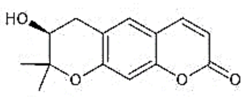

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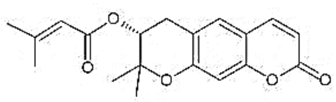

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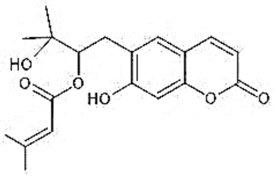

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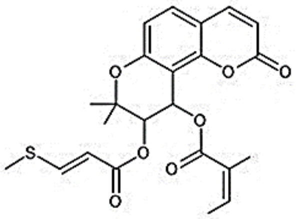

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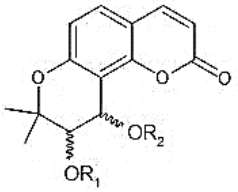
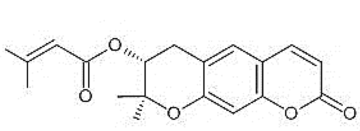


	R1	R2
28 trans-khellactone	H	H
18 cis-khellactone	H	H
29 3'-senecioyl-cis-khellactone	$\mathrm{COCH{=}C(Me)_2}$	H
30 3'-senecioyl-4'-acetyl-cis-khellactone	$\mathrm{COCH{=}C(Me)_2}$	COMe
31 4'-senecioyl-cis-khellactone	H	$\mathrm{COCH{=}C(Me)_2}$
32 3'-acetyl-4'-senecioyl-cis-khellactone	COMe	$\mathrm{COCH{=}C(Me)_2}$
33 3',4'-di-isovaleryl-cis-khellactone	$\mathrm{COCH_2CH(Me)_2}$	$\mathrm{COCH_2CH(Me)_2}$
34 3',4'-disenecioyl-cis-khellactone	$\mathrm{COCH{=}C(Me)_2}$	$\mathrm{COCH{=}C(Me)_2}$
35 3'-angeloyl-4'-isovaleryl-cis-khellactone	COC(Me)=CHMe	$\mathrm{COCH_2CH(Me)_2}$
36 3'-isovaleryl-4'-angeloyl-cis-khellactone	$\mathrm{COCH_2CH(Me)_2}$	COC(Me)=CHMe



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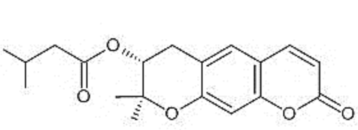

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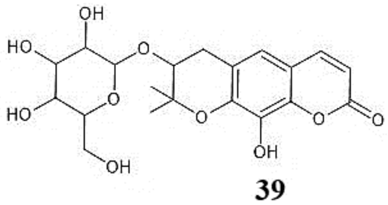

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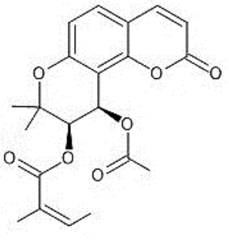

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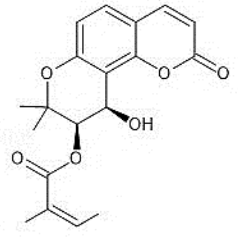

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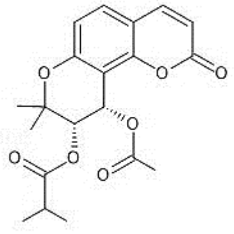

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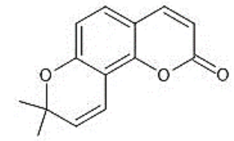

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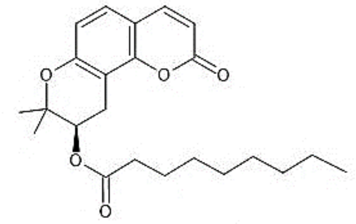

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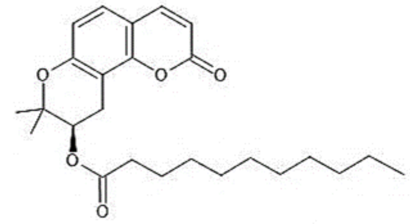

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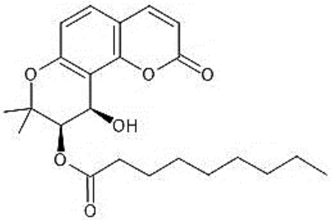

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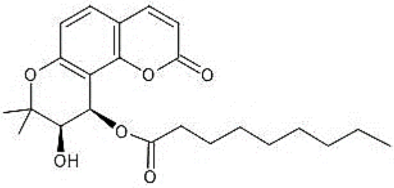

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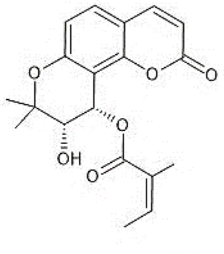

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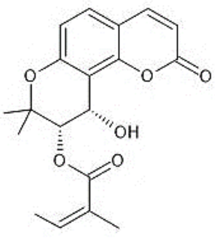

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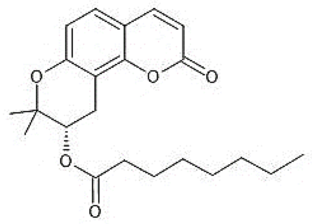

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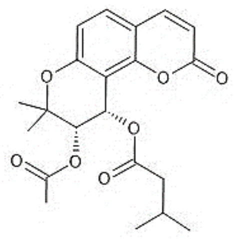

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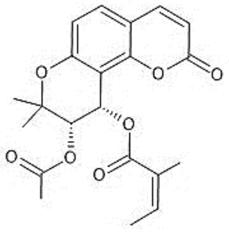

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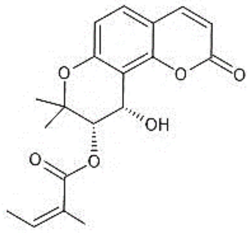

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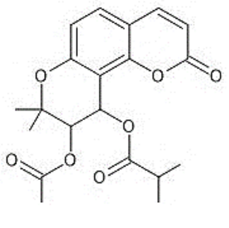

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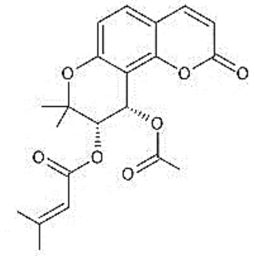

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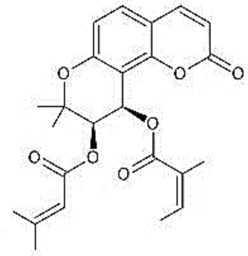

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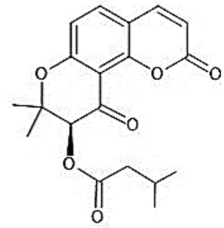

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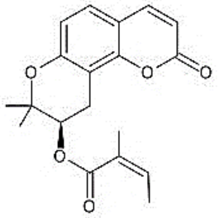

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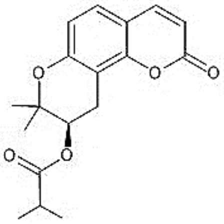

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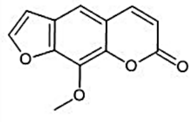
Fig. 4. The pyranocoumarins in *Seseli* species

5.2.2. Furanocoumarin derivatives

Many types of furanocoumarins (Fig. 5), such as xanthotoxin (**60**), bergapten (**61**) and psoralen (**62**) were found in the roots of *S. libanotis* (L.) W.D.J. Koch (Lemmich et al., 1966). (2′*S*)-Rutaretin-1″-sulphate (**63),** known as sulfate ester salts derived from coumarin alcohols as an uncommon coumarin, was reported from the roots of *S. libanotis* subsp. *eu-libanotis* (Lemmich and Shabana, 1984). Glowniak et al. (1991) investigated coumarins from the *S. libanotis* (The roots of *Libanotis intermedia*) and found isopeucenidin (**64**) and libanotin (**65**) as dihydrofuranocoumarins (Glowniak et al., 1991). Several common furanocoumarins called isobergapten (**66**), bergapten (**61**), and phellopterin (**67**) were determined from the roots of *S. sibiricum* (L.) Garcke by Kumar (Kumar et al., 1978). Two linear furanocoumarins, deltoin (**68**) and marmesin angelate (**69**), were obtained from the ether extract of the stems of *S. gummiferum* Pall. subsp. *gummiferum* in the 1970s (Nielsen et al., 1970). Bergapten (**61)** and psoralen (**62**) were characterized in the petroleum ether extracts of the roots of *S. coronatum* Ledeb. from Kazakhstan, and seseliflorin (**70**), and secorin (**71**), other furanocoumarins were isolated from the acetone extracts from *S. coronatum* roots (Dukhovlinova et al., 1974). Moreover, seseliflorin (**70**) was reported previously from the MeOH extracts of the roots of *S. sessiliflorum* Schrenk (Savina et al., 1970a). Apterin (**72**) (a glucoside of vaginol) was found in the roots of *S. montanum* L. (Lemmich and Havelund, 1978). The secrolin (**73**) and columbianadin/zosimin (**74**) as angular-furanocoumarins were identified from the roots of *S. mucronatum* (Schrenk) Pimenov & Sdobnina. According to the previous study, secrolin (**73**) was the columbianetin (zosimol) (**75**) *trans*-methylthioacrylate (Dukhovlinova et al., 1979). The imperatorin (**76**), xanthotoxin (**60),** bergapten (**61**), and isopimpinellin (**77**) have also been found in the umbels of *S. sibiricum* (L.) Garcke (Banerjee et al., 1980). Several linear furocoumarins; xanthotoxol (**78**), xanthotoxin (**60**), isopimpinellin (**77**), phellopterin (**67**), isoimperatorin (**79**), alloisoimperatorin (**80**), and oxypeucedanin hydrate (**81**) and sphondin

(**82**) were determined in *S. elatum* subsp. *gouanii* and *S. elatum* subsp. *austriacum*. Two populations are characterized by the absence or presence of xanthotoxin (**60**); the roots by the presence or absence of xanthotoxin (**60**), oxypeucedanin hydrate (**81**), and sphondin (**82**); the stems by phellopterin (**67**); the leaves by isoimperatorin (**79**); the inflorescences by different quantities of phellopterin (**67**); and the fruits by xanthotoxol (**78**) (Coassini Lokar and Delben, 1988). Phellopterin (**67**) was isolated from the air-dried roots of *S. annuum* extracted with chloroform ($CHCl_3$). In the isolation process, the crude extract of the plant was fractionated by dry-column flash chromatography (DCFC), and column chromatography (CC) eluted with dichloromethane (CH_2Cl_2 and gradually increasing polarity adding MeOH (up to 20% MeOH) (Vučković et al., 2010). However, phellopterin (**67**) had also been identified previously from Apiaceae (Kviesis et al., 2019; Han et al., 2018), Moraceae (Heinke et al., 2011) and Rutaceae plants (Zhang et al., 2017). Then, isoimperatorin (**79**) and deltoin (**68**) were reported from the dried roots of *S. resinosum* extracted with *n*-hexane (Tosun et al., 2006b). Deltoin (**68**) was isolated in a different method from the roots of *S. resinosum* following the next study (Shehzad et al., 2013). Moreover, the anomalin (**19**) and deltoin (**68**) in the *n*-hexane extract of the roots and aerial parts of *S. resinosum* were compared quantitatively with HPLC (High-Performance Liquid Chromatography)-chemometric and traditional HPLC methods [75:25 v/v, at a flow rate of 0.8 mL/min, 10 µL] (Tosun et al., 2007a). The aerial parts of *S. hartvigii* were extracted successively with hexane, EtOAc, and MeOH, and the linear furanocoumarins, 5-[(2"*E*,6"*R*)-6"-hydroxy-3",7"-dimethylocta-2",7"-dienyloxy] psoralen/hartvigimarin A (**83**) and 5-[(2"*E*,6"*S*)-6"-hydroxy-3",7"-dimethylocta-2",7"-dienyloxy] psoralen/hartvigimarin B (**84**) were first isolated from the *n*-hexane extract of *S. hartvigii*, which is an endemic species in southern parts of Türkiye, together with bergaptol (**85**) and notoptol (**86**) (Zhang et al., 2010). Bergapten (**61**), isopimpinellin (**77**), and isorutarin (**87**) were also separated from the seeds of *S. diffusum* (Roxb. ex Sm.) Santapau & Wagh sold in the local markets in Karachi/Pakistan as

Indian celery, extracting by hexane, $CHCl_3$, acetone, and MeOH under reflux and eluted with the hexane: EtOAc and EtOAc: MeOH gradient systems (Abbaskhan et al., 2012). In recent a work, Angelicin (**88**) was isolated from the hexane extract of *S. petraeum* aerial parts (Onder et al., 2022).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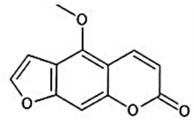
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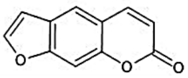
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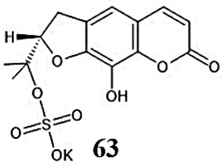

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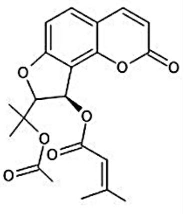
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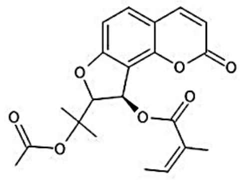
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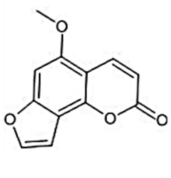
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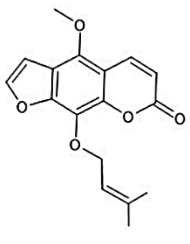
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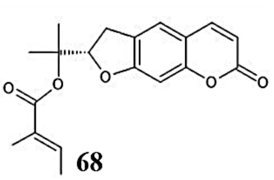
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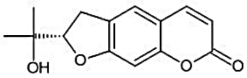

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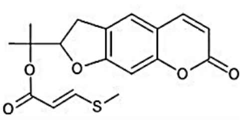

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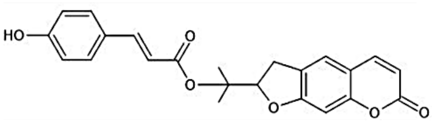

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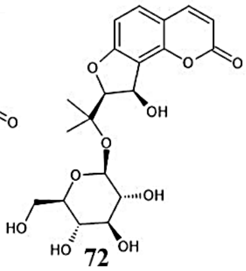

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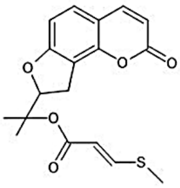

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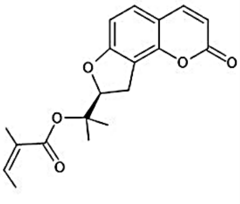
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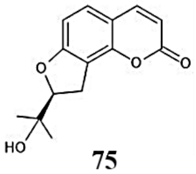

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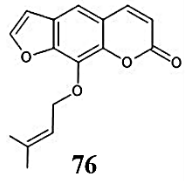
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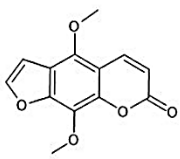
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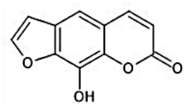

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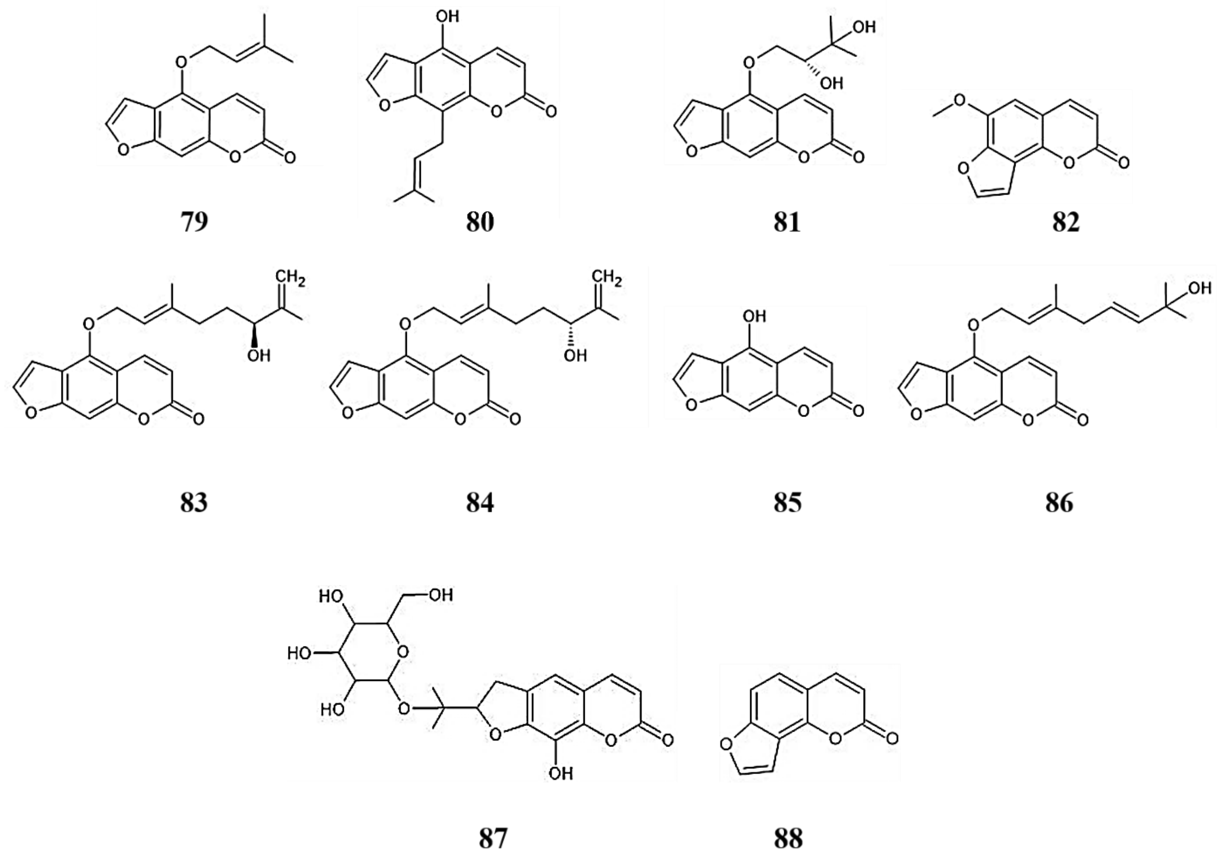
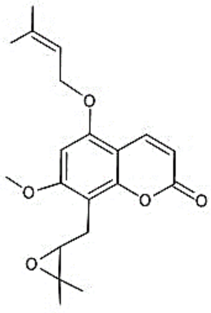


Fig. 5. The furanocoumarins from *Seseli* species

5.2.3. The simple coumarins and derivatives

The simple coumarins, common in many plants containing coumarins, do not seem to be found often in *Seseli* species (Fig. 6). Sesebrin [7-methoxy-5-(3-methylbut-2-enyloxy)-8-(3-methyl-2,3-epoxybutyl) coumarin] (**89**), sesebrinol [7-methoxy-5-(3-methylbut-2-enyloxy)-8-(3-methyl-2,3-dihydroxybutyl) coumarin] (**90**) and sibiricol [7-methoxy-5-hydroxy-8-(3-methylbut-2-enyl) coumarin] (**91**) were determined together with sibiricin (**92**), coumurrayin (**93**), osthenol (**94**) and meranzin hydrate (**95**), from the roots of *S. sibiricum* by Kumar (Kumar et al., 1978), besides osthol (**96**) from the roots of *S. sibiricum* (Kapoor et al., 1968). In HPLC analysis, the *n*-hexane extracts of the aerial and underground parts of three different *Seseli* species with current names *S. corymbosum*, *S. resinosum*, and *S. hartvigii*, were investigated relating to the presence of major coumarins (osthol **96** and corymbocoumarin **51**) by normalphase HPLC (Tosun et al., 2007b). The simple coumarin glycosides as 3′-*O*-2′-*O*- (**97**) and the 7-*O*-*β*-D- (**98**) glucopyranosides of 2′(*R*)-6-(2′,3′-dihydroxy-3′-methylbutyl)-7-hydroxy-coumarin were isolated from the roots of *S. montanum*. The (*R*)-configuration was assigned to the aglycone, also known as (+)-peucedanol (**99**), and its 7-methyl ether, (+)-ulopterol (**100**), by chemical correlation (Lemmich and Havelund, 1978) and with a simple coumarin ostruthin (**101**) having been identified from the roots of *S. mucronatum* (Schrenk) Pimenov & Sdobnina (Dukhovlinova et al., 1979). The seselinal (**102**), sesibiricol (**103**), and sibirinol (**104**), characterized as 5,7-dimethoxy-8-(2-methyl-2-formylpropyl)-2H-1-benzopyran-2-one, 5-(3-methylbut-2-enyloxy)-7-methoxy-8-(2-hydroxy-3-methylbut-3-enyl)-2H-1-benzopyran-2-one and 5,7-dimethoxy-8-(2-hydroxy-3-methylbut-3-enyl)-2H-1-benzopyran-2-one have been isolated from the umbels of *S. sibiricum*. The rest of the coumarins were sesibiricin (**105**), isosibiricin (**106**), osthol (**96**), coumurrayin (**93**), sesebrin (**89**), sesebrinol (**90**), sibiricin (**92**) and mexoticin (**107**) (Banerjee et al., 1980). Tortuoside (**108**) is known as a simple coumarin glycoside due to its 7,8-disubstituted coumarin nucleus and a *β*-glycoside unit, as evidenced from the large ^{1}H coupling constant (7.6 Hz) of the anomeric proton (4.56), namely [7-hydroxy-8- [(2'*R*)-hydroxy-3'-0-*β*-D-glucopyranosy1-3'-methylbutyl-coumarin], purified from the aerial parts of *S. tortuosum* (Ceccherelli et al., 1990). Osthol (**96**) was also reported from the hexane extract of the aerial parts of *S. corymbosum* (previously *S. gummiferum* Pall. ex Sm. subsp. *corymbosum* in Turkish Flora) in quite a high amount (Tosun et al., 2005a). The simple coumarins, such as 6-(3'-methylbutenyl)-7-methoxycoumarin (suberosin) (**109**) and 5,7-dimethoxy-8-(3'-methyl-2',3'-dihydroxybutenyl)-coumarin (mexoticin) (**107**) were determined from the *n*-hexane extract of the aerial parts of *S. hartvigii* (Tosun, 2006). Also, a simple prenylated-coumarin, umbelliprenin (**110**) was found in the $CHCl_3$ extract of the aerial parts of *S. annuum* fractionated by DCFC on the silica column (Vučković et al., 2007). In addition, 3',2'*S* epimer of 8-(2,3-dihydroxy-3-methylbutyl)-7-hydroxychromen-2-one (devenyol) (**111**), its two *O*-monoglucosides at position 3' named devenyoside A (**112**), at position 7 named devenyoside B (**113**) and a di-glucoside, 3',7-*O*-diglucoside called devenyoside C (**114**) from the powdered and ripened fruits of *S. devenyense* Simonk. were obtained by extracting petroleum ether and then MeOH in a Soxhlet apparatus using medium-pressure liquid chromatography (MPLC) (Widelski et al., 2005). Devenyol (**111**) was also isolated from *S. devenyense* fruits by the CCC method (Widelski et al., 2021b). The extraction of the aerial parts of *S. hartvigii* gave a simple coumarin as 6-(3'-methyl-2'-oxo-3'-butenyl)-7-methoxycoumarin (**115**) and a known simple coumarin called tamarin (**116**) (Zhang et al., 2010).



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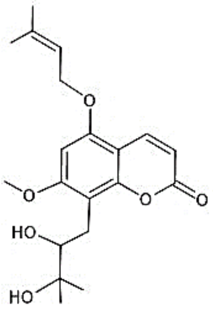

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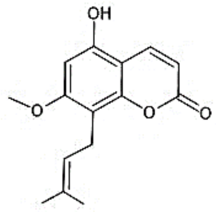

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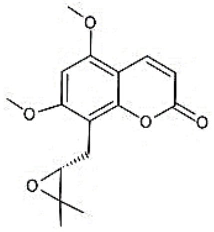

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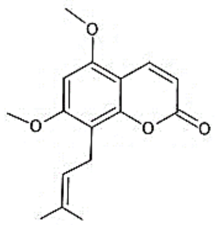

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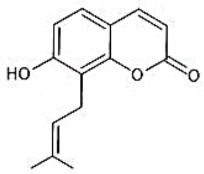

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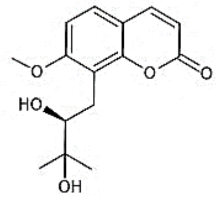

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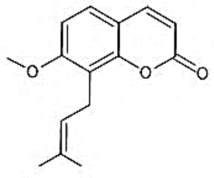

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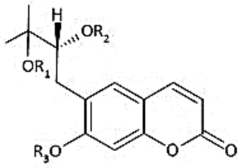
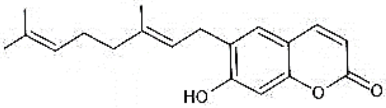


	R1	R2	R3
97 3′-O-2′-O-2′(R)-6-(2′,3′-dihydroxy-3′-methylbutyl)-7-hydroxy-coumarin	Glc	H	H
98 7-O-β-D-2′(R)-6-(2′,3′-dihydroxy-3′-methylbutyl)-7-hydroxy-coumarin	H	H	Glc
99 (+)-peucedanol	H	H	H
100 (+)-ulopterol	H	H	CH_3



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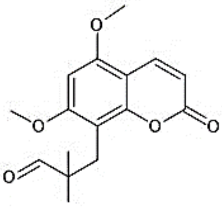

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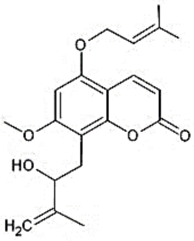

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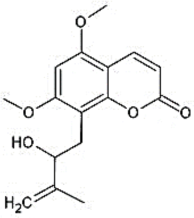

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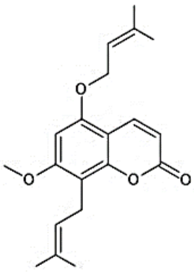

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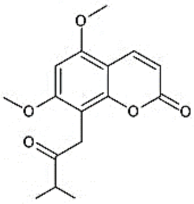

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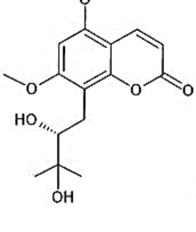

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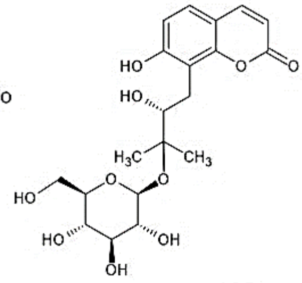

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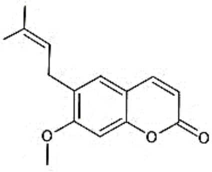

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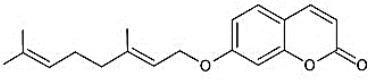

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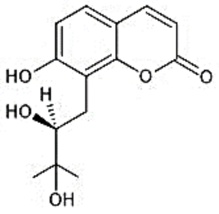

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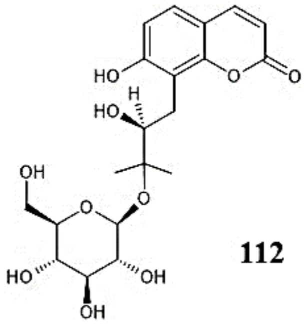

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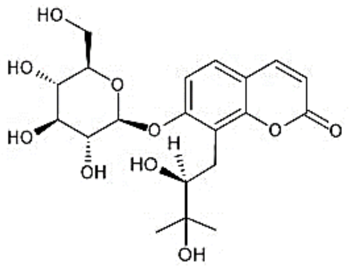

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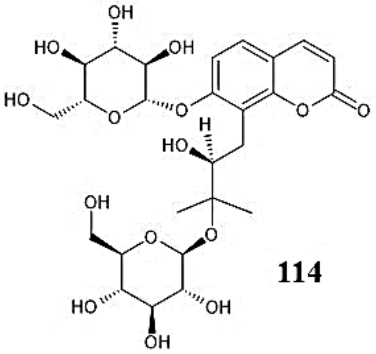

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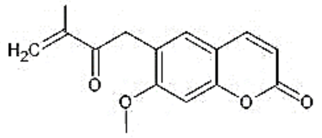

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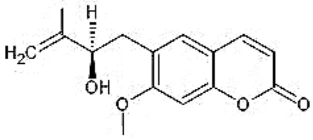

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Fig. 6. The simple coumarins in *Seseli* species

Table 4

The coumarin composition of *Seseli* species

Species	Plant Part Used	Solvent System	Coumarins	References
S. annuum	Roots	$CHCl_3$	Phellopterin, umbelliprenin	Vučković et al., 2007 Vučković et al., 2010
S. bocconi subsp. *bocconi*	Aerial parts	Et_2O	3',4'-diangeloyl-*cis*-khellactone (anomalin) 3'-angeloyI-4'acetyl-*cis*-khellactone (isopteryxin)	Lemmich et al., 1966 Bellino et al., 1986
subsp. praecox			Praeruptorin [(+)-enatiomer of isopteryxin], 3'-isobutyl-4'-acetyl-*cis*-khellactone (bocconin)	
S. coronatum	Roots	Petroleum Ether Acetone	Seselirin, anomalin, seseliflorin, secorin, psoralen, bergapten	Dukhovlinova et al., 1974
S. corymbosum (*S. gummiferum* subsp. *corymbosum*)	Aerial parts	Hexane	Corymbocoumarin [(−)-(*3′S,4′S*)-3′-acetoxy-4′-isovaleryloxy-3′,4′-dihydroseselin], (−)-(*3′S,4′S*)-3′-acetoxy-4′-angeloyloxy-3′,4′-dihydroseselin, (+)-(*3′S,4′S*)-3′-hydroxy-4′-angeloyloxy-3′,4′-dihydroseselin(d-laserpitin) (−)-(*3′S,4′S*)-3′-angeloyloxy-4′-hydroxy-3′,4′-dihydroseselin**,** 3′-acetoxy-4′-isobutyloxy-3′,4′-dihydroseselin, osthole	Tosun et al., 2005a
S. devenyense	Fruits	Petroleum Ether MeOH	Decanoic and dodecanoic esters of (+)-lomatin, the decanoates of (+)-*cis*-khellactone 3' and 4' esters, 2'*S* epimer of 8-(2,3-dihydroxy-3-methylbutyl)-7-hydroxychromen-2-one (devenyol), devenyosides A, devenyosid B, devenyoside C, *cis*-khellactone, d-laserpitin, isolaserpitin, octanoyllomatin	Widelski et al., 2005 Widelski et al., 2021b
S. diffusum	Fruits	Hexane $CHCl_3$ Acetone MeOH	Seselin, bergapten, isopimpinellin, anthriscinol	Abbaskhan et al., 2012
S. elatum subsp. *gouanii*	Aerial parts (stems, leaves, inflorescence, fruits), Roots	MeOH	Xanthotoxol, isopimpinellin, phellopterin, isoimperatorin, alloisoimperatorin, oxypeucedanin hydrate, seselin	Coassini Lokar & Delben, 1988
S. elatum subsp. *austriacum*	Aerial parts (stems, leaves, inflorescence, fruits), Roots	MeOH	Xanthotoxol, isopimpinellin, phellopterin, isoimperatorin, alloisoimperatorin, oxypeucedanin hydrate, seselin	Coassini Lokar & Delben, 1988

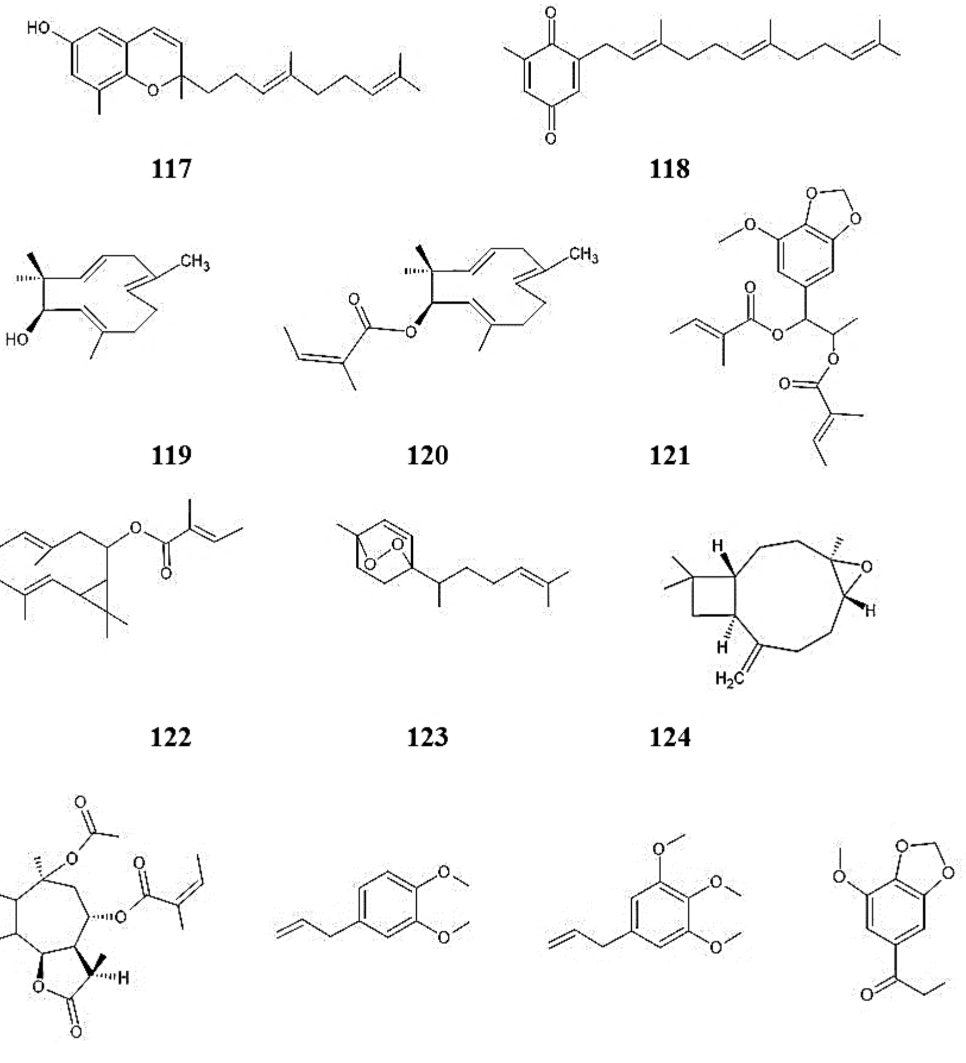
S. grandivittatum	Roots	CHCl$_3$	(-)-3'*R*-decursinol, its angelate, grandivittin (3'-senecioyloxy-3',4'-dihydro-3'R-xanthyletin), grandivittinol [7-hydroxy-6-(3'-hydroxy-2'-senecioyloxyisopentyl) coumarin]	Abyshev et al., 1977
S. gummiferum subsp. *corymbosum* (*Syn: S. corymbosum*)	Aerial	Hexane	Corymbocoumarin (−)-(*3′S,4′S*)-3'-acetoxy-4'-isovaleryloxy-3′,4′-dihydroseselin, (−)-(*3′S,4′S*)-3′-acetoxy-4′-angeloyloxy-3′,4'-dihydroseselin, (+)-(*3′S,4′S*)-3′-hydroxy-4′-angeloyloxy-3′,4'-dihydroseselin (d-laserpitin), (−)-(*3′S,4′S*)-3′-angeloyloxy-4′-hydroxy-3′,4′-dihydroseselin**,** 3′-acetoxy-4′-isobutyloxy-3′,4′-dihydroseselin, osthole	Tosun et al., 2005a
S. gummiferum (*S. gummiferum* subsp. *gummiferum*)	Stems	Et$_2$O	3'(*R*)-(+)-3'-hexanoyloxy-3',4'-dihydroseselin, 3'(*R*)-(+)-3'-octanoyloxy-3',4'-dihydroseselin, 3'(*R*)-(+)-3'-*cis*-4-octenoyloxy-3',4'-dihydroseselin, deltoin, marmesin --- (3'*R*,4'*R)*-3'-isovaleryloxy-4'-angeloyloxy-3',4'-dihydroseselin; (3'*R*,4'*R)*-3'-senecioyloxy-4'-angeloyloxy-3',4'-dihydroseselin; (3'*R*,4'*R)*-3'-acetoxy-4'-senecioyloxy-3',4'-dihydroseselin; (+)-*cis*-khellactone, *cis*-khellactone mixtures	Nielsen et al., 1970 Nielsen et al., 1971
S. hartvigii	Aerial	Hexane	*cis*-(3'*R*,4'*R*)-3'-Angeloyloxy-4'-acetyloxy-3',4'-dihydroseselin (isopteryxin), two simple coumarins, 6-(3'-methylbutenyl)-7-methoxycoumarin (suberosin), 5,7-dimethoxy-8-(3'-methyl-2',3'-dihydroxybutenyl)-coumarin (mexoticin)	Tosun, 2006
			5-[(2"*E*,6"*R*)-6"-Hydroxy-3",7"-dimethylocta-2",7"-dienyloxy] psoralen, 5-[(2"*E*,6"*S*)-6"-hydroxy-3",7"-dimethylocta-2",7"-dienyloxy] psoralen, 6-(3'-methyl-2'-oxo-3'-butenyl)-7-methoxycoumarin, tamarin, bergaptol, notoptol	Zhang et al., 2010
S. libanotis	Root	Et$_2$O	(3'*S*, 4'*S*)-3',4'-disenecioyloy-3',4'-dihydroseselin, (3'*S*,4'*S*)-3'-acetoxy,4'-senecioyloy-3',4'-dihydroseselin, (-)-3'-hydroxy,3',4'-dihydroxhanthyletin and its angeloly ester isopeucenidin, libanotin	Lemmich et al., 1966 Glowniak et al., 1991
S. libanotis subsp. *eu-libanotis*	Root	MeOH	(2′*S*)-Rutaretin-1″-sulphate, (3′*R*)-lomatin-3′-sulphate and (3′*R*,4′*R*)-khellactone-3′-sulphate	Lemmich and Shabana, 1984
S. montanum	Roots	MeOH:Et$_2$O	3′-*O*-,2′-*O*-, and the 7-*O*-β-D-glucopyranosides respectively of 2′(*R*)-6-(2′,3′-dihydroxy-3′-methyl butyl)-7-hydroxy-coumarin, apterin, (+)-peucedanol, (+)-peucedanol-7-methyl ether, (+)-ulopterol	Lemmich & Havelund, 1978
S. mucronatum	Roots	-	Secrolin/columbianetin (zosimol/trans-methylthioacrylate), ostruthin, columbianadin (zosimin), anomalin, pteryxin	Dukhovlinova et al., 1979

S. petraeum	Aerial parts	Hexane	Petracoumarin (3'-isovaleryl-4'-oxo-lomatin), cis-khellactone, anomalin, 3'-senecioyl-cis-khellactone, 4'-senecioyl-cis-khellactone, 3'-angeloyl-4'-isovaleryl-cis-khellactone, 3'-isovaleryl-4'-angeloyl-cis-khellactone, octanoyllomatin, samidin, calipteryxin, selinidin, 3'-isobutryl-lomatin, angelicin	Onder et al., 2022
S. peucedanoides	Roots	-	Seseloside (3'-O-β-D-glucopyranosyloxy-8-hydroxy-2',2'-dimethyl-3',4'-dihydro pyrano-5',6':6,7-coumarin)	Bagirov and Belyi, 1981
S. resinosum	Root	Hexane	(+)-Samidin [(3'*S*,4'*S*)-32-senecioyloxy-4'-acetoxy-3',4'-dihydroseselin], (-)-anomalin [(3'*R*,4'*R*)-3',4'-diangeloyloxy-3',4'-dihydroseselin], calipteryxin (3'*R*,4'*R*)-3'-angeloyloxy-4'-senecioyloxy-3',4-dihydroseselin, isoimperatorin, deltoin	Tosun et al., 2006b Tosun et al., 2007a
			d-Laserpitin, (3'*S*,4'*S*)-3'-angeloyloxy-4'-hydroxy-3',4'-dihydroseselin, (+)-samidin, (3'*S*,4'*S*)-3'-acetoxy-4'-angeloyloxy-3',4'-dihydroseselin, deltoin, calipteryxin, (3'*S*,4'*S*)-3',4'-disenecioyloxy-3',4'-dihydroseselin, (-)-anomalin	Shehzad et al., 2013
S. sessiliflorum	Roots	MeOH	Sessiliflorin, floroselin [3′-angeloyloxy-2′,2′-dimethyl-4′-(*trans*-3-methylthioacryloyloxy)-3′,4′-dihydropyrano-5′,6′:8,7-coumarin]	Savina et al., 1970
S. sibiricum	Roots, Umbels	Petroleum ether, Hexane and benzene, Hexane	Seselinal, sesibiricol and sibirinol, characterized as 5, 7-dimethoxy-8-(2-methyl-2-formylpropyl)-2H-1-benzopyran-2-one, 5-(3-methylbut-2-enyloxy)-7-methoxy-8-(2-hydroxy-3-methylbut-3-enyl)-2H-1-benzopyran-2-one and 5,7-dimethoxy-8-(2-hydroxy-3-methylbut-3-enyl)-2H-1-benzopyran-2-one, sesibiricin, isosibiricin, osthol, coumurrayin, sesebrin, sesebrinol, sibiricin, imperatorin, bergapten, xanthotoxin, isopimpinellin, mexoticin, sesebrin (7-methoxy-5-[3-methylbut-2-enyloxy]-8-[3-methyl-2,3-epoxybutyl] coumarin), sesebrinol (7-methoxy-5-[3-methylbut-2-enyloxy]-8-[3-methyl-2,3-dihydroxybutyl] coumarin), sibiricol (7-methoxy-5-hydroxy-8-[3-methylbut-2-enyl] coumarin), isobergapten, bergapten, phellopterin, sibiricin, coumurrayin, osthenol and meranzin hydrate, osthol	Kapoor et al., 1968 Kumar et al., 1978 Banerjee et al., 1980 Banerjee et al., 1987
S. tenuisectum	Roots Aerial parts	MeOH:Et$_2$O	Anomalin together with (+)-*cis*-methylkhellactone, 3'-angeloyloxy-4'-hydroxy-3',4'-dihydroseselin, 4'-angeloyloxy-3'-hydroxy-3',4'-dihydroseselin (pteryxin) and 7,8-substituted coumarins	Aminov & Nikonov, 1972
S. tortuosum	Aerial parts	Acetone	(-)-2'-Senecioyloxy-1',2'-dihydroxanthyletin, (-)-2'-isovaleryloxy-1'-2'-dihydroxanthyletin, Tortuoside[7-hydroxy-8-[(2'R)-hydroxy-3'-0-*β*-D-glucopyranosy1-3'-methylbutyl]-coumarin	Ceccherelli et al., 1990

S. tortuosum	Aerial parts	Et_2O	*trans*-khellactone, *cis*-khellactone, 3'-senecioyl-*cis*-khellactone, 3'-senecioyl-4'-acetyl-*cis*-khellactone, 4'-senecioyl-*cis*-khellactone, 3'-acetyl-4'-senecioyl-*cis*-khellactone, 3',4'-di-isovaleryl-*cis*-khellactone, 3',4'-disenecioyl-*cis*-khellactone, 3'-angeloyl-4'-isovaleryl-*cis*-khellactone, 3'-isovaleryl-4'-angeloyl-*cis*-khellactone	Gonzáles et al., 1979
S. tschuense	Root	MeOH	Sechulin based on a 2,3-dimethyl dihydro pyranocoumarin	Aminov and Nikonov, 1974

5.3. Terpenes and others

The ether extract from the leaves of *S. farrenyi* Molero & J. Pujadas, an endemic species in Spain, afforded 7-demethylplastochromenol-2 (**117**) (which is thought to be an artifact), a known sesquiterpene-substituted quinone, monoterpenes and sesquiterpenes. It was indicated that the sesquiterpene quinone identified as 2-farnesyl-6-methyl-benzoquinone (**118**), was previously isolated from *S. elatum* L. (= *S. longifolium* L.). However, methyl farnesyl quinone, important chemotaxonomically for the *Seseli* genus, has been found in *S. longifolium* L., *S. gouani* W.D.J. Koch, and *S. leucospermum* Waldst. & Kit. (Muckensturm et al., 1997). In addition, 10-hydroxy-α-humulene (**119**), 10-angeloyloxy-α-humulene (**120**) and 2-epilazerine (**121**) were reported from the hexane extract of *S. vayredanum* Font Quer. aerial parts, together with some sesquiterpenes called 8α-angeloyloxy-bicyclogermacrene (**122**), 3,6-epidioxy-bisabol-1,10-diene (**123**), caryophyllene oxide (**124**), 10-acetoxy-8α-angeloyloxy-3-ene-6,12-olide (**125**), eugenol methyl ether (**126**), elemicin (**127**) and latifolon (**128**) (Barrero et al., 1992). Another study of the same species was carried out again with the aerial part hexane extract and some sesquiterpenoid compounds were detected (Barrero et al., 1994). The structures regarding the terpenic compounds of the *Seseli* species have been given in Fig. 7.

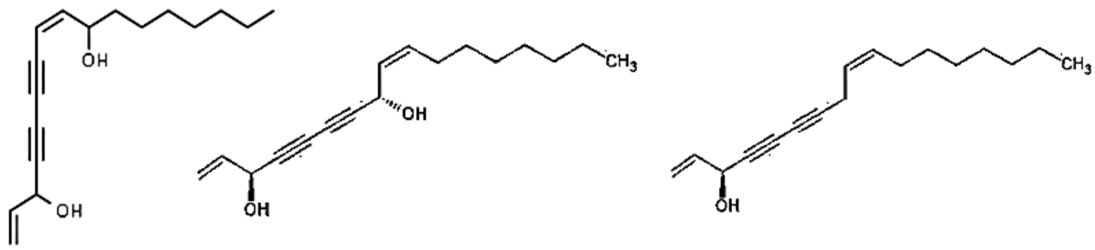


117 **118** **119** **120** **121** **122** **123** **124** **125** **126** **127** **128**

Fig. 7. Terpenes in *Seseli* species

5.4. Polyacetylenes

In the beginning, seselidiol (**129**), a polyacetylene called heptadeca-1,8(Z)-diene-4,6-diyne-3,10-diol, had been reported from the roots of *Seseli mairei* (Hu et al., 1990). Afterward, the roots of *S. annuum* L. were extracted with CHCl$_3$, and the crude extract was subjected to DCFC and CC by the gradual elution with CH$_2$Cl$_2$: MeOH up to 20% MeOH. In the end, falcarinol (**130**) and falcarindiol (**131**) (Fig. 8), which are known polyynes polymers and different from polyacetylenes (polyethynes), with the polymerization of acetylenes, have been obtained (Vučković et al., 2010). The CH_2Cl_2 extract from the stems of *S. praecox* (Gamisans) Gamisans (an endemic species) was also afforded a serial of polyyne-type components (Leonti et al., 2010).

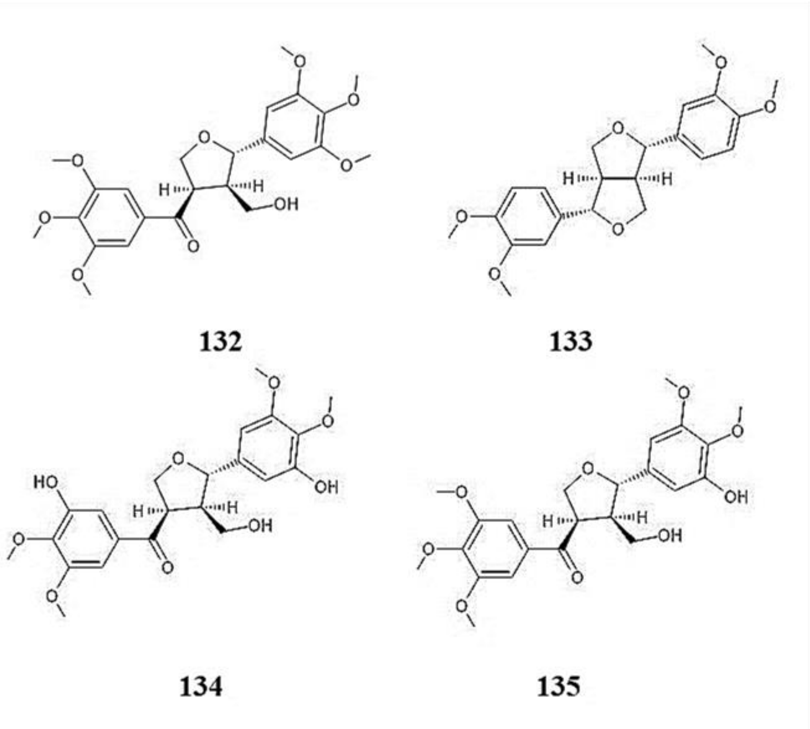


129 **130** **131**

Fig. 8. Polyacetylenes in *Seseli* species

5.5. Lignans

There is only one study on *Seseli* lignans. A tetrahydrofuranoid lignan named seselinone (**132**) together with other lignans such as eudesmin (**133**), magnone A (**134**), and hernone (**135**) (Fig. 9) were isolated from the $CHCl_3$ extract of *S. annuum* L. herbal parts on DCFC on silica using the increasing polarity of petroleum ether: Et_2O: MeOH (Vučković et al., 2007).


132 133

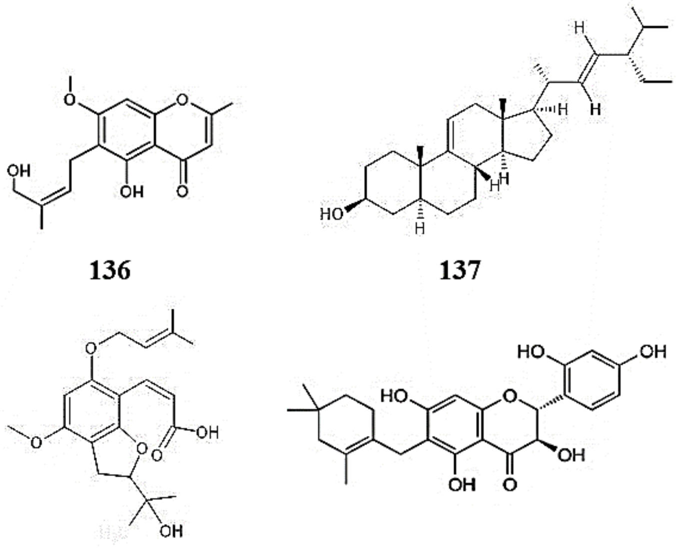
134 135

Fig. 9. Lignans in *Seseli* species

5.6. Miscellaneous compounds

An isopropenylated chromone (5-hydroxy-6-(2-*Z*-butenyl-3-hydroxymethyl)-7-methoxy-2-methylchromone) (**136**) has been characterized from the stems of *Seseli praecox* (Gamisans) Gamisans, an endemic Sardinia species (Leonti et al., 2010). Moreover, a sterol called indosterol (**137**) was obtained from the petroleum ether extract from the stems of *S. indicum* Wight & Arn. (Gupta and Gupta, 1974). The sesebrinic acid (**138**) as a cinnamic acid derivative was isolated (Fig. 10) from the aerial parts of this plant (Banerjee et al., 1987).

In general, the *Seseli* species are poor in flavonoids but have plenty of coumarins and phenolic compounds (Crowden et al., 1969). Seselinonol (**139**) is the only known prenylated flavanonol, isolated from the $CHCl_3$ extract of the roots of *S. annuum* L. (Vučkovič et al., 2010). Also, the aerial parts of several *Seseli* species have been evaluated regarding their phenolic and flavonoid content on the MeOH extract, and the highest phenolic content was found in aerial parts of *S. libanotis* subsp. *intermedium* (Rupr.) P.W. Ball (with 2 mg/mL extract concentration) and the flavonoid content were also the highest (with 3 mg/mL extract concentration) in the *S. pallasii* Besser (Matejić et al., 2012).



136 **137**

138 **139**

Fig. 10. The miscellaneous compounds in *Seseli* species

6. Pharmacological studies

The literature survey indicated that *Seseli* species have many important biological activities (Fig. 11) but limited studies. The papers dealing with the biological activities of *Seseli* species have been discussed in the following subsections, as stated below.

6.1. Antimicrobial and antifungal activity

Like other plant species, antimicrobial activity has been frequently studied on the *Seseli* species, especially on their essential oils. For example, in a screening study, the *n*-hexane extracts from the aerial parts, roots, and essential oils of some *Seseli* species (*S. resinosum, S. hartvigii, S. gummiferum*) at 0.1 mg/mL concentrations were investigated *in vitro* by the agar disk diffusion method, against Gram (–) (*Escherichia coli, Pseudomonas aeruginosa*), Gram (+) (*Staphylococcus aureus, Enterococcus faecalis, Bacillus subtilis, B. cereus*) and a fungus (*Candida albicans*). All the samples showed antimicrobial activity but were not very strong (Tosun et al., 2004).

The essential oil comprising mainly germacrene D (29.8%) from the *S. annuum* aerial parts exhibited antifungal activity in the modified mycelial growth test against many fungi species with MICs (Minimum Inhibitory Concentrations) ranging between 12.5–50.0 μL/mL. In this test, the essential oil was found to be highly active when compared with the commercial fungicidal agent with 1% (w/v) of bifonazole in EtOH (in higher MICs 25.0–100.0 μL/mL) (Milosavljević et al., 2007). The fruit essential oils of *S. petraeum* did not exhibit antimicrobial activity against *Paenibacillus larvae,* but *S. tortuosum* oil did. On the other hand, the fruit oil of *S. andronakii* displayed potent antibacterial activity against the tested larvae in the agar diffusion and microdilution methods (Özkırım et al., 2012). The petroleum ether and MeOH fruit extracts of *S. devenyense* exerted antimicrobial activity against the *Staphylococcus aureus* strain, especially the petroleum ether extract, which showed strong activity (Widelski et al., 2015). Moreover, the volatile constituents of aerial parts with fruits of *S. devenyense* and *S. libanotis* exhibited vigorous antimicrobial activity against human pathogenic Gram (+) bacteria strains at MIC values 0.90–1.20 mg/mL (Widelski et al., 2021a).

The essential oils from the fruits of several Apiaceae spices, including *S. indicum*, have been evaluated for antibacterial activity against *Corynebacterium diphtheriae, S. aureus, Streptococcus haemolyticus, B. subtilis* Gram (+), *Pseudomonas aeruginosa, E. coli, Klebsiella species,* and *Proteus vulgaris* Gram (–), which cause infections in the human body, using the filter paper disk agar method. *S. indicum* oil in low concentration was equally or more active when compared with standard antibiotics (Singh et al., 2002). The *S. indicum* fruit oil was also investigated for its antibacterial activity by a punched-hole method, which is mentioned in the

Pharmacopoeia of India/1996. The essential oil was nearly active against *S. aureus* at low concentration (50 µL/mL) and moderately active at high concentration (100 µL/mL), moderately active against *B. subtilis* at low concentrations, and highly active in both low and high concentrations against *E. coli* (Singh et al., 2012). The fruit essential oil of *S. indicum* was fungistatic at 8.0 × 100 ü/L against *Aspergillus flavus*, *A. niger*, and *Fusarium oxysporum*, stable by temperature, and the oil was not phytotoxic to seed germination and seedling growth of *C. arietinum* (chickpea) and C. *cajan* (pigeon pea) (Chaturvedi and Tripathi, 1989).

Stojković et al. (2008) evaluated the antibacterial activity of *S. globiferum* oils by the microdilution test. In this study, strong activity was documented against *Micrococcus flavus* (MIC=4.8–10.3 µL/mL; MBC=9.7–28.3 µL/mL). While the oils from unmatured and mature fruits of *S. globiferum* exhibited strong fungistatic and fungicidal effects (Most sensitive against *Penicillium ochrochloron* MIC=MFC=0.5 µL/mL), the oil from unmatured fruits exhibited a higher antibacterial activity than that of mature fruits, when compared to the commercial drug streptomycin (Stojković et al., 2008). On the other hand, the microbial growth-inhibitory features of the *S. globiferum* essential oil against several bacterial species, such as *Salmonella typhimurium*, *E. coli*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Bacillus cereus*, *S. aureus*, *S. epidermidis*, *Micrococcus flavus*, besides three fungal species called *Aspergillus niger*, *A. versicolor*, *Trichoderma viride*, and *Penicillium funiculosum*, indicated that the most potent activity was against *P. aeruginosa* in the broth microdilution method, depending on the sabinene (38.0%) content (Janaković et al., 2011). The MIC value was found only against *E. coli* (500 µg/mL) using the broth microdilution method on the essential oil of *S. gracile* (Suručić et al., 2021).

The evaluation of the antibacterial activity on a MeOH extract (at 31.25-500 µg/mL) and essential oil of the aerial parts from *S. libanotis* using the disk diffusion and the minimum inhibitory concentration (MIC) assays showed a broad-spectrum (>14 mm inhibition zone in diameter) against *Bacillus cereus, B. dipsauri, B. lentimorbus, B. sphaericus, B. subtilis, Corynebacterium ammoniagenes, Kocuria rosea, Neisseria subflava,* and *Micrococcus lylae.* The effect of the essential oil emerged from *trans*-caryophyllene, *β*-farnesene, euasarone and spathulenol (Öztürk and Ercişli, 2006). Matejić et al. (2012) also demonstrated the antimicrobial activity of MeOH extracts of *S. pallasii* together with *S. libanotis* subsp. *libanotis* and *S. libanotis* subsp. *intermedium* collected from Serbia using a micro-well dilution assay against the most common human gastrointestinal pathogenic bacterial strains (*E. coli*, *P. aeruginosa*, *Salmonella enteritidis*, *B. cereus*, *Listeria monocytogenes*, *S. aureus*, and *C. albicans*. The favorable results of the tested *Seseli* species showed that the species might be good antimicrobial agents (Matejić et al., 2012). The essential oils obtained from different parts of the *S. pallasii* (fruits, stems, and roots) exhibited almost good antimicrobial activity (MIC=21.9-416 µg/mL and MBC=54.2-582.4 µg/mL) against tested strains (Stankov-Jovanović et al., 2016). The fruit essential oil of *S. libanotis* obtained by different methods showed notable antibacterial activity against *S. aureus* strains, for example, against the Gram (+) bacteria (MICs =0.15-1.25 mg/mL) and the Gram (–) bacteria (MICs=1.25-2.5 mg/mL) (Skalicka-Woźniak et al., 2010). In addition, the antimicrobial effect of essential oil from Polish *S. libanotis* fruits was tested against *S. aureus,* and the MIC value was found to be 600 ppm (Syed et al., 1989). *S. rigidum* essential oil (*α*-pinene 48.5%) was active against *B. subtilis* (MIC=50 µL/mL; MBC=75 µL/mL). *Micrococcus flavus,* and *Staphylococcus epidermidis* were the most resistant bacterial species with MIC=MBC of 100 µL/mL. The essential oil from the flowers exhibited notable antifungal activity against *Aspergillus fumigatus* (MIC=10 µL/mL; MFC=25 µL/mL). *Penicillium ochrochloron* and *A. niger* were also found to be the most resistant fungal species with MIC=MFC at 50 µL/mL compared with commercial antifungal drug bifonazole (Stojković et al., 2009).

When the essential oils and extracts (preparing different polarity of solvent) from *S. rigidum* (root, leaf, flower, and fruit) were evaluated for antimicrobial activity against a few Gram (–) (*Escherichia coli, Pseudomonas aeruginosa*) and Gram (+) (*Staphylococcus aureus*, *Bacillus cereus*) bacterial strains besides fungal (*Candida albicans* and *Aspergillus niger*) strains, the inhibition concentration range of the extracts was found 0.01–1.50 mg/Ml (Stankov-Jovanović et al., 2015). Ilić et al. (2015) also evaluated the antimicrobial potential of *S. rigidum* essential oil by comparing the samples collected from post-fire and control areas. The fruit essential oils (from post-fire and control areas) of *S. rigidum* exhibited antimicrobial activity dominantly against tested microbial strains, frequently causing food spoilage and gastrointestinal illness in humans (Ilić et al., 2015).

In another study, the antifungal potency of the essential oils of *S. tortuosum* and *S. montanum* were compared with each other. The essential oil of *S. tortuosum* showed higher antifungal activity (especially against *Candida neoformans* and dermatophyte strains) than that of *S. montanum.* Furthermore, evaluation of MIC-MLC of the oils showed the variability of inhibition ranging from 0.64 to 1.25 µL/mL may have been adequate due to α-pinene in the composition of *S. tortuosum* (MIC and MLC ranging from 0.08 to 2.5 µL/mL) (Gonçalves et al., 2012). In addition, the essential oil from *S. montanum* subsp. *tommasinii* have medium to strong antimicrobial activity against food pollutants with fungi, plant and animal pathogens (Šiljegović et al., 2011). The antimicrobial and antifungal activity studies on *Seseli* essential oils are summarized in Table 5.

Table 5

The antimicrobial activities of *Seseli* species

Species	**EO/Extract**	**Strains**	**Effects**	**Methods**	**Doses and results**	**References**
S. resinosum *S. hartvigii* *S. gummiferum*	AE, R-EO, *n*-hexane extracts	Gram (–) (*Escherichia coli*, *Pseudomonas aeruginosa*) Gram (+) (*Staphylococcus aureus*, *Enterococcus faecalis*, *Bacillus subtilis*, *B. cereus*) Fungus (*Candida albicans*)	+	Agar disk diffusion	0.1 mg/mL	Tosun et al., 2004
S. annuum	AE-EO, germacrene D	Fungal strains	+	Mycelial growth	MICs=12.5–50.0 µL/mL	Milosavljević et al., 2007
S. petraeum *S. resinosum* *S. andronakii* *S. tortuosum*	Fr-EO	*Paenibacillus larvae*	- - + +	Agar disk diffusion Microdilution	MID=- MID=- MID=9.77 mm MID=6.85 mm	Özkırım et al., 2012
S. indicum	Fr-EO	Gram (+) (*Corynebacterium diphtheriae*, *Staphylococcus aureus*, *Streptococcus haemolyticus*, *Bacillus subtilis*) Gram (–) (*Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella species*, *Proteus vulgaris*)	+	Agar disk diffusion	-	Singh et al., 2002
S. indicum	Fr-EO	*Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*	+	Punched-hole	50-100 µL/mL	Singh et al., 2012
S. indicum	Fr-EO	*Aspergillus flavus*, *A. niger*, *Fusarium oxysporum*	+	-	8.0 × 100 ü/L	Chaturvedi & Tripathi, 1989
S. globiferum	Fr-EO	*Micrococcus flavus*		Microdilution test	MIC=4.8–10.3 µL/mL MBC=9.7–28.3 µL/mL	Stojković et al., 2008
S. globiferum	AE-EO, sabinene	*Salmonella typhimurium*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Enterobacter cloacae* (clinical isolates), *Bacillus cereus* (clinical isolates), *Staphylococcus aureus*, *S. epidermidis*, *Micrococcus flavus*, *Aspergillus niger*, *A. versicolor*,	+	Broth microdilution	15 mg/mL	Janaković et al., 2011

		Trichoderma viride, *Penicillium funiculosum*				
S. gracile	EO	Gram (+) bacteria (*Staphylococcus aureus*, *Enterococcus faecalis*, *Bacillus subtilis*), Gram (−) bacteria (*Escherichia coli*, *Klebsiella pneumoniae*, *Salmonella enterica* subsp. *enterica*, *Pseudomonas aeruginosa*), yeasts (*Candida albicans*)	+	MIC assay	500 µg/mL	Suručić et al., 2021
S. libanotis	Methanol extract AE-EO *Trans*-caryophyllene, *β*-farnesene, euasarone, spathulenol	*Bacillus cereus*, *B. dipsauri*, *B. lentimorbus*, *B. sphaericus*, *B. subtilis*, *Corynebacterium ammoniagenes*, *Kocuria rosea*, *Neisseria subflava*, *Micrococcus lylae*	+	Disk diffusion, MIC assay	31.25-500 µg/mL	Öztürk and Ercişli, 2006
S. pallasii *S. libanotis* subsp. *libanotis* *S. libanotis* subsp. *intermedium*	AE-Methanol extracts	*Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella enteritidis*, *Bacillus cereus*, *Listeria monocytogenes*, *Staphylococcus aureus*, and *Candida albicans*	+	Micro-well dilution	Gram (+) MIC=0.78-12.5 mg/ml MBC=6.25- 50.0 mg/ml	Matejić et al., 2012
S. pallasii	Fr, S, R-EO	*Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus cereus*, *Staphylococcus aureus*, *Candida albicans* and *Aspergillus niger*	+	Microdilution test	MIC=21.9-416 µg/mL MBC=54.2-582.4 µg/mL	Stankov-Jovanović et al., 2016
S. libanotis	Fr-EO	*Staphylococcus aureus*	+	Broth microdilution	MICs=0.15-1.25 mg/mL MICs=1.25-2.5 mg/mL	Skalicka-Woźniak et al., 2010
S. libanotis	Fr-EO	*Staphylococcus aureus*	+	-	MIC=600 ppm	Syed et al., 1989
S. rigidum	*α*-pinene F-EO	*Bacillus subtilis*, *Micrococcus flavus* *Staphylococcus epidermidis* *Aspergillus fumigatus* *Penicillium ochrochloron* and *Aspergillus niger*	+	Microdilution test	MIC=50 µL/mL MBC=75 µL/mL MIC=MBC: 100 µL/mL MIC=10 µL/mL MFC=25 µL/mL MIC=MFC: 50 µL/mL	Stojković et al., 2009
S. rigidum	Fr-EO	Gram (–) (*Escherichia coli*, *Pseudomonas aeruginosa*	+	Micro-well dilution	0.03-6.50 µL/ mL	Ilić et al., 2015

		Gram (+) (*Staphylococcus aureus*, *Bacillus cereus*) Fungus (*Candida albicans* and *Aspergillus niger*)				
S. rigidum	R, L, F, Fr-EO extracts	Gram (–) (*Escherichia coli*, *Pseudomonas aeruginosa*) Gram (+) (*Staphylococcus aureus*, *Bacillus cereus*) Fungus (*Candida albicans* and *Aspergillus niger*)	+	Microdilution test	0.01–1.50 mg/Ml	Stankov-Jovanović et al., 2015
S. tortuosum *S. montanum*	Umbels with seed-EO, *α*-pinene	*Candida neoformans* and dermatophyte strains	+ +	Macrodilution broth	MIC=0.64-1.25 µL/mL MLC=0.08-2.5 µL/mL	Gonçalves et al., 2012
S. montanum subsp. *tommasinii*	AE-EO	food pollutants Bacteria (*Micrococcus flavus*, *Salmonella typhimurium*, *S. enteritidis*, *Enterococcus faecalis* clinical isolate) Fungus (*Aspergillus ochraceus*, *A. fumigatus*, *Penicillium ochrochloron*, *Trichoderma viride*)	+	Disk diffusion	MIC=1.6-30 µL/mL and MBC=3.1-75 µL/Ml MIC=25 µL/mL MFC=50-100 µL/mL	Šiljegović et al., 2011

AE: Aerial parts, F: Flowers, Fr: Fruits, R: Roots, S: Stems, EO: Essential oil

6.2. Antioxidant activity

Natural antioxidants are protective by preventing oxidation in many chronic diseases (Neha et al., 2019). Moreover, plants are a very rich source of antioxidants (Barnard et al., 2019) and due to their low toxic side effects, they have also been preferred in the food industry (Lourenço et al., 2019). There are some studies on the antioxidant effects of *Seseli* species; for example, the water-soluble fraction of *S. diffusum* seeds exhibited potent antioxidant activity. The isorutarin showed notable radical scavenging activity in a DPPH assay (Abbaskhan et al., 2012). The antiradical activities of *S. globiferum* oils were not found significant in DPPH radical scavenging test (SC_{50}=446.7 for unripe fruit oil and 373.2 µL/mL for ripe fruit oil) (Stojković et al., 2008). The moderate antiradical activity of the essential oil of *S. gracile* was determined with SC_{50}=78.60 µg/mL in the DPPH assay (Suručić et al., 2021). However, the flower essential oil of *S. rigidum* exhibited a lower potency for free radical scavenging activity on DPPH assay. The oil concentration was 50% of DPPH scavenging (SC_{50}=24.5 µL/mL), when compared to ascorbic acid (SC_{50}=4.1 µg/mL) or gallic acid (SC_{50}=1.5 µg/mL) (Stojković et al., 2009). On the other hand, the DPPH effects from the different extracts of *S. rigidum* ranged from 46.15 to 1436.45 µg/mL, but the highest activity was observed in the water extract (Jakovljević et al., 2015). The antioxidant effect of the *S. rigidum* essential oils was also evaluated using three different methods compared with post-fire areas and areas not affected by the fire. For example, the DPPH assay of the concentrations of the oils (DPPH radical; SC_{50}=18.75±0.39 mg/mL and 53.42±1.12 µL/mL) for post-fire places. The value of ABTS+ radical was 0.66±0.01 µg/mL Trolox equivalent. The total reducing power of *S. rigidum* fruit essential oil evaluated by Fe(II) reducing power assay (as ascorbic acid equivalents) was 0.24±0.01 and 0.30±0.02 µg/mL for the samples (Ilić et al., 2015). Extracts of *S. rigidum* from different parts like root, leaf, flower, and fruit were also investigated by antioxidant assays, and the essential oils obtained from all parts showed weak antioxidant potency (Stankov-Jovanović et al., 2015). Živković et al. (2015) also evaluated the oil from the different parts of *S. rigidum* tested for potential genotoxic and antigenotoxic activities against H_20_2-induced DNA damage in human blood cells *in vitro* by the comet assay. The essential oil contains high amounts of falcarinol in the root oil, but the fruit oil and aerial parts oil have α-pinene as the major component. The oils' antioxidant activity (established by the FRAP and DPPH tests) was weak; all oils demonstrated a strong antigenotoxic effect on the stimulation of DNA repair mechanisms. The circumstances did not affect the antigenotoxic properties of the oils (Živković et al., 2015). The MeOH extracts of Serbian *Seseli* species (*S. pallasii*, *S. libanotis* subsp. *libanotis,* and *S. libanotis* subsp. *intermedium*) have been analyzed for antioxidant activity using BHA and Vit C as controls [IC_{50} =0.46-4.63 mg/mL and 1.98-2.19 mg Vit C -Vitamin C)/g] when tested with the DPPH and ABTS reagents *in vitro* (Matejić et al., 2012). The DPPH radical scavenging activity of the MeOH extract of *S. tortuosum* was dependent on the tested concentration (38.48±4.17-92.75±0.61), and the FRAP activity was found as 65.2 mg TE/g. The CUPRAC activity of the species was observed depending on the concentration when compared with Trolox (0.375±0.01-1.885±0.01) (Uysal et al., 2017). In a recent study, the *Seseli* species have been screened for antioxidant capacity using various *in vitro* assays. The antioxidant capacity of *S. andronakii*, *S. campestre*, *S. corymbosum*, *S. gummiferum*, *S. hartvigii*, *S. libanotis, S. petraeum*, *S. peucedanoides*, *S. resinosum* and *S. tortuosum* have been examined using DPPH radical scavenging and lipid peroxidation (LPO) inhibition assays. The highest activity of DPPH radicals scavenger was found in the EtOAc extracts of *S. peucedanoides* (IC_{50}=0.49 mg/mL) and *S. libanotis* (IC_{50}=0.75 mg/mL). On the other hand, in the LPO assay, the highest activities were concluded in EtOAc and MeOH extracts (at 5 mg/mL) of *S. tortuosum* and *S. libanotis* (84-94%) (Önder et al., 2020). In a recent study, the methanolic extract of *S. transcaucasicum* (1.18 ± 0.12 mmol TE/g) has the highest antioxidant potency in the phosphomolybdenum assay followed by the methanolic extract of *S.*

gummiferum (0.90 ± 0.09 mmol TE/g). In addition, the total antioxidant capacity of *S. gummiferum* and *S. transcaucasicum* aqueous extracts were 0.78 and 0.66 mmol TE/g, respectively (Zengin et al., 2021).

6.3. Anti-inflammatory and antinociceptive activity

The anti-inflammatory effect is an important biological activity for coumarins and coumarin-containing plants, verified in many articles. Especially pyranocoumarins have been tested for this activity in various studies (Kirsch et al., 2016). As the screening study, the EtOAc and MeOH (80%) extracts from *Seseli* L. species growing in different localities of Türkiye, exhibited anti-inflammatory and antinociceptive activities (Küpeli et al., 2006). In the ongoing study, isolated coumarins from the aerial parts of *S. corymbosum*, such as (−)-(3'S,4'S)-3'-acetoxy-4'-angeloyloxy-3',4'-dihydroseselin (46), 3'-acetoxy derivatives such as corymbocoumarin/(−)-(3'S,4'S)-3'-acetoxy-4'-isovaleryloxy-3',4'-dihydroseselin (45) demonstrated potent antinociceptive and anti-inflammatory effects (Tosun et al., 2009). The anti-inflammatory activity of the essential oils from *S. corymbosum* and *S. gummiferum* were also examined on LPS-stimulated RAW 264.7 cells with the dose-dependent decreases of inducible nitric oxide synthase (iNOS), and cyclooxygenase-2 (COX-2) protein expressions. The oils inhibited nitric oxide (NO) production by suppressing NF-κB activation. The IC_{50} values were found as 56.1 and 108.2 μg/mL, prostaglandin E2 (PGE2) with 49.4 μg/mL and 95.5 μg/mL, respectively (Tosun et al., 2016).

The effect of anomalin (**19**) (which appears as the main compound in many *Seseli* species) has been investigated on the production of inflammatory molecules in LPS-stimulated murine macrophages to explain the mechanisms of cellular signaling of anti-inflammatory effect. It was indicated that the anomalin inhibited iNOS and COX-2 mRNA and protein expression in LPS-stimulated RAW 264.7 macrophage, depending on the dose. Several pro-inflammatory cytokines, such as tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6), were decreased by anomalin (**19**) using quantitative real-time polymerase chain reaction (qRT-PCR), correlated with the down-regulation of the NF-κB signaling pathway. In addition, anomalin suppressed the LPS-induced phosphorylation and degradation of IκBα (Khan et al., 2011). In another study, a pyranocoumarin derivative-samidin (**55**) isolated from *S. resinosum* markedly inhibited NO production, the gene expression levels of iNOS, and COX-2. Samidin (**55**) was also found to be a potent anti-inflammatory agent like anomalin (**19**) (Khan et al., 2014). In addition to anomalin (**19**) and samidin (**55**), calipteryxin (**56**) and (3'*S*,4'*S*)-3',4'-disenecioyloxy-3',4'-dihydroseselin (**2**) from *S. resinosum* showed notable inhibitory effects on pro-inflammatory enzymes and cytokines associated with molecular signaling pathways decreasing the production of NO, TNF-α and IL-1β, depending on the dose. Also, these coumarins inhibited the LPS-induced protein, mRNA expression levels of iNOS, and COX-2 in RAW264.7 cells (Khan et al., 2015). Moreover, this study was extended to investigate the anti-inflammatory activity of corymbocoumarin (**45**), a pyranocoumarin, from *S. corymbosum* in LPS-stimulated RAW 264.7 macrophages. The corymbocoumarin (**45**) prevented NO, PGE2, mRNA expression of iNOS and COX-2 production. Corymbocoumarin (**45**) also reduced TNF-α (Chun et al., 2016).

6.4. Antiproliferative activity

Seselidiol (**129**), a polyacetylene-type compound, and its acetate from *Seseli mairei* roots exhibited moderate cytotoxicity on KB, P-388, and L-1210 tumor cells (Hu et al., 1990). On the other hand, lignan-type compounds called seselinone (**132**) and eudesmin (**133**) isolated from the aerial parts of *S. annuum* showed the cytotoxic effect to C6 rat glioma cell cultures on MTT assay (Vučković et al., 2007). In a similar study, seselinonol (**139**) (a prenylated flavononol) and phellopterin (**67**), from the roots of *S. annuum* were evaluated *in vitro* for protecting effect on chromosome aberrations on human peripheral lymphocytes using cytochalasin-B blocked micronucleus assay. Seselinonol (**139**) employed significant activity by attenuation of DNA damage on human lymphocytes (Vučković et al., 2010). The essential oils from several aromatic and medicinal plants, including *S. tortuosum* exhibited cytotoxic effects on macrophage cells (IC_{50}=10-25 µg/mL) (Costa et al., 2018). The essential oils from *S. tortuosum* and *S. montanum* subsp. *peixotoanum* (1.25 µL/mL and 0.64 µL/mL) decreased MTT reduction by keratinocytes to 4.3 ± 2.3% ($p < 0.001$) and 60.6 ± 18.2% ($p < 0.05$) of the control, respectively. Therefore, *S. tortuosum* essential oil has been found to be cytotoxic against human keratinocyte cell lines in concentrations of 0.64 µL/mL (Gonçalves et al., 2012). Moreover, the essential oil of *S. tortuosum* L. exhibited promising antiproliferative properties *in vitro* using breast and colorectal cancer 2D and 3D spheroid cell lines related to the increased p21 expression and induction of apoptosis with the lowest IC_{50} values, 0.0086 µL/mL (Beeby et al., 2020).

In a different study, the MeOH-water extract (80%) of the fruits of *S. diffusum* (Roxb. ex. sm.) Santapau & Wagh showed significant cytotoxicity in the mechanism-based bioassay, using DNA repair-deficient (rad 52Y) and repair-proficient (RAD+) yeast strains. The hexane and $CHCl_3$ extracts of the fruits exhibited cytotoxicity against only yeasts. The hexane fraction was the most active in this assay as the most nonpolar fraction. Seselin (**43**) and anthriscinol methyl ether in the hexane fraction exhibited selective cytotoxicity in some yeast strains (Abbaskhan et al., 2012). In a recent study, the n-hexane extract from the *S. petraeum* roots inhibited A549 cancer cell growth at 3.432 mg/mL. Moreover, the hexane extract exhibited cytotoxic activity against the suppression at the G0/G1 phase of the cell cycle and induced apoptosis on DNA damage of A549 cells (Cinar et al., 2020). The cytotoxic activity of the *S. petraeum* fruit essential oil showed potent cytotoxicity against MCF-7 (human breast adenocarcinoma) and A549 (human lung carcinoma) cells, but it was more potent against

MCF-7 cells (IC_{50}=390.38 µg/mL). According to the results, the essential oil has a notable cytotoxic effect against treated cancer cells. This activity is attributed to carotol, the major component in essential oil (Önder et al., 2021). In another recent study, the water extracts from *S. gummiferum* and *S. transcaucasicum* exhibited more cytotoxicity against HaCaT (immortalized skin keratinocyte) cells (IC_{50}=267.8 ± 4.14 µg/mL and 321.41 ± 1.25 µg/mL, respectively) than the methanolic extracts (Zengin et al., 2021)

6.5. Insecticidal activity

In a previous study, the essential oil from *S. indicum* fruits exhibited insecticidal activity against *Callosobrucus chinensis* (Dixit ve ark., 1992). The EtOH extract of the *S. diffusum* fruits highly induced neurobehavioral toxicity against *Aedes aegypti* larvae. Moreover, after 4 h of treatment, a high level of larval knock-down (EC_{50}=238.15 ppm) was observed. After 24 (LC_{50}=126.13 ppm) and 48 h (LC_{50}=112.53 ppm) of treatment, the extract (200 ppm) showed a potent larvicidal effect exhibiting 88 and 96% mortality against 4th instar *A. aegypti*. The EtOH extract of the fruits (seeds) at higher concentrations (4400 ppm) caused 100% mortality in the same conditions, indicating a strong candidate for a new biopesticide (Kabir et al., 2013). In addition, the essential oil of *S. gummiferum* subsp. *ilgazense* showed 100 and 70% mortality against *Aedes aegypti* larvae at 125 and 62.6 ppm, respectively (Kurkcuoglu et al., 2018). Pavela (2009) demonstrated that the MeOH extract obtained from the aerial parts of *S. pallasii* employed the highest larvicidal effect at LD_{50}=6 ppm (Pavela, 2009).

6.6. Vasorelaxant and Spasmolytic activity

There are a few studies on the vasorelaxant activity of the *Seseli* species. The spasmolytic effect on nonpolar and polar fractions of *S. diffusum* fruits was observed in the preliminary screening study, and the seselin was the most active component (Abbaskhan et al., 2012). Suručić et al.

(2017) evaluated the vasorelaxant activity of the essential oil from the aerial parts of *S. pallasii* Besser. The essential oil (α-pinene 48.2%) induced relaxations in a concentration-dependent manner with IC_{50}=3.10 nL/mL (IC_{50}=2.70 µg/mL), by inhibition effect on voltage-dependent Ca^{2+} channels and the release of NO (Suručić et al., 2017). The spasmolytic effect of the essential oil of *S. gracile* was found to be notable with IC_{50}=271.4 nL/mL. The activity has been attributed to the monoterpene composition of the essential oil (Suručić et al., 2021).

6.7. Anxiolytic activity

In a very new study as a first report, several coumarins such as devenyol (**111**) (a simple coumarin), *cis*-khellactone (**18**), d-laserpitin (**48**), isolaserpitin (**49**), and octanoyllomatin (**50**) (pyranocoumarins) from the fruits of *S. devenyense* Simonk exerted a significant influence on the anxiety behavior (anxiolytic activity). The anxiolytic effect, also known as reverse thigmotaxis, was determined using a 5-day post-fertilization *Danio rerio* larva (zebrafish larva) model based on light-dark changes. In this experiment, acute administration of *S. devenyense* fruit methanolic extract (3–12.5 µg/mL) increased the locomotor activity of zebrafish larvae, usually during the 40 min light period. The changing rates in the internal (central) and external environment when evaluated with the time spent in the central domain and the distance moved, the changing rates in the internal (central) and external environment showed a decreased level of thigmotaxis in favor of the central environment and increased anxiolytic activity, especially at higher levels. Except for isolaserpitine (**49**), all other isolated coumarins failed to show a significant effect on spontaneous locomotor activity and thigmotaxis behavior for 40 min on illumination at all concentrations. However, anxiolytic effects have been observed under stress conditions. In the second part of the experiments (during the light-dark struggle), it was determined that diazepam together with devenyol (**111**), d-laserpitin (**48**), isolaserpitin (**49**), and octanoyllomatin (**50**) significantly increased the movement distance of the larvae in the central region and the time they spent in the central part (Widelski et al., 2021b).

6.8. Enzyme inhibitory activity

The fruit oil of *Seseli rigidum* can be considered a neural protective agent because it comprises mainly α-pinene and sabinene from the post-fire area, indicated as a significant inhibitor of human (34.9±0.04%) and horse serum (41.78±0.06%) cholinesterase, referring to neostigmine bromide as reference compound (78.56±0.77% and 98.10±0.83% respectively). On the other hand, the essential oil from the unaffected-fire area showed similarity against humans (33.45±0.02%) and horse serum (40.23±0.04%) cholinesterase inhibition (Ilić et al., 2015). In another study, the root essential oil of *S. rigidum* has the highest percentage of inhibition in humans (38.20%) and horses (48.30%) cholinesterase. The root hexane extract exhibited similar results to the samples mentioned above, at 40.56% and 50.65%, respectively (Stankov-Jovanović et al., 2015). In addition, the essential oil from the aerial parts of *S. pallasii* also exhibited a dose-dependent moderate AChE (acetylcholine esterase) inhibitory activity (IC_{50}=0.33 mg/mL). As a major component in the *S. pallasii* essential oil, spathulenol exhibited the best affiliation in the complex with AChE than captopril, which may be valuable for the treatment of hypertension (Suručić et al., 2017).

The coumarins of *S. petraeum* from aerial parts showed marked inhibitory activity against the α-glucosidase enzyme related to the antidiabetic activity. Moreover, octanoyllomatin (**50**) was the best α-glucosidase inhibitor with an IC_{50} at 69.00 ± 0.43 mg/mL (Onder et al., 2022). In a different study, only the water extract of *S. gummiferum* demonstrated inhibitory activity of the α-amylase and α-glucosidase (0.13 ± 0.01 mmol ACAE/g). The methanolic and water extracts (*S. gummiferum* and *S. transcaucasicum*) exhibited almost equal inhibitory activity against the amylase (0.78 mmol ACAE/g and 0.12 mmol ACAE/g, respectively). The tyrosinase inhibitory activity of the methanolic extracts of *S. transcaucasicum* (109.37 ± 0.38 mg KAE/g) and *S. gummiferum* (107.15 ± 1.38 mg KAE/g) was also reported. The water and methanolic extract of *S. gummiferum* and *S. transcaucasicum* aerial parts inhibited cholinesterases, that is *S. transcaucasicum*-MeOH > *S. gummiferum*-MeOH > *S. gummiferum*-Water > *S. transcaucasicum*-Water (AChE: 0.15–4.53 mg GALAE/g and BChE: 1.66–9.71 mg GALAE/g) (Zengin et al., 2021).

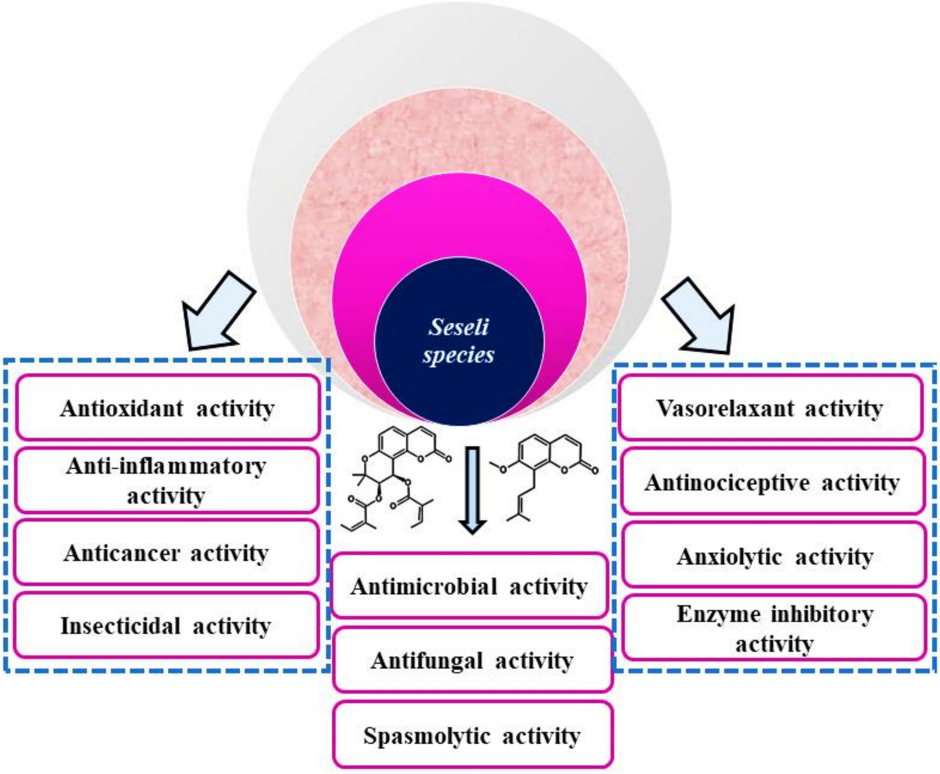


Fig. 11. Schematic representation of medicinal properties of *Seseli* L. genus

7. Toxicological aspects

There is no significant toxicity mentioned in the *Seseli* species. However, no proper studies have been conducted on this subject. In one study, a compound called falcarinol, isolated from *Seseli* species, was found to cause some allergic reactions. Falcarinol is a cannabinoid receptor ligand, isolated from the endemic Sardinian *S. praecox*. It exhibits a binding affinity to both human cannabinoid receptors, leading to releasing pro-allergic chemokines IL-8 and CCL2/MCP-1 in a cannabinoid receptor1-dependent manner in human HaCaT keratinocytes. In addition, falcarinol inhibited the effects of anandamide on TNF-α stimulated keratinocytes. Anti-allergic effects of falcarinol-associated dermatitis can be antagonism of the cannabinoid receptor1 in keratinocytes, increased chemokine expression, and aggravation of histamine action (Leonti et al., 2010). Besides all, furanocoumarins, mostly present in the Apiaceae and the Rutaceae family species, in some cases, may cause photosensitization on the skin defined as a toxic effect (Dugrand-Judek et al., 2015), which is also in *Seseli* species.

8. Conclusion and future perspectives

Phytochemicals have been used in the treatment of various diseases for years. Despite industrialization and technological developments, the cure for most diseases is not available yet, or new diseases are emerging. The *Seseli* is the third-largest genus of the Apiaceae family. In this review, the botanical characteristics, traditional uses, phytochemistry, pharmacology, and toxicity of *Seseli* species growing wild in the world have been explored to the earliest studies in all detail based on the available literature data. The *Seseli* species have been used for various diseases in Europe and Asia for centuries. According to traditional knowledge, *Seseli* species have been used to treat inflammation, edema, rheumatism, pain, and cold and as a sedative, against amenorrhea, urinary discharge, cough, and fever in humans. Although there are different bioactive components in the *Seseli* species, essential oils and coumarins were mainly determined. When the essential oil content was examined, it was found that α-pinene and carotol were dominant in the essential oils of most species. Coumarins were isolated as aglycon and glycosidic types as another dominant secondary metabolite group in the *Seseli* species. The structures of 129 compounds were summarized and presented, among them 106 coumarin-type compounds in the *Seseli* species. Many species belonging to the Apiaceae family have coumarin structures, mostly simple, and furanocoumarins are found in many species of this family. However, what makes *Seseli* species special is that they have coumarins in pyranocomarin structure, in other words–khellactone esters. Although rare, some sulfur-containing coumarins have also been found in this genus. The most important difficulty in the isolation process of such compounds is that they are in ester form, sometimes very close, and sometimes on top of each other in most chromatographic methods. Multiple bioactivities of these components have also been reported, mostly antimicrobial and antifungal activities. However, the anti-inflammatory and anticancer effects of these species also seem too specific to be ignored. It should not be overlooked that it is a rich source of anomalin in the structure of pyranocoumarin, which is especially famous as an anti-inflammatory agent and osthol in the structure of simple coumarins. *Seseli* genus is present with plenty of species in Anatolia, in some places known as Kelemkeşir-kelemenkeşir with a local name. The “herbed cheese” contains some *Seseli* species as a flavoring and protecting agent. The leaves of some species grown in Eastern Anatolia are used as vegetables in salads, suggesting that these types may also be important as functional foods. The pharmaceutical sectors mostly choose cultivated plants used in the applications, and wild plants can be ignored. The fact that *Seseli* species are wild plants and grow as ornamental plants brings to mind the idea that they are suitable for cultivation. Therefore, there is a need for more detailed investigations on *Seseli* species containing such interesting and valuable compounds. Their rich content and high endemisms open new horizons for the isolation of novel compounds to be used in the pharmaceutical, cosmetic and food industries always need new and fresh breath in the chemistry of natural product knowledge.

As a result, *Seseli* species are significant medicinal resources for the prominent components, especially coumarins, with special pharmacological activities. Findings on the phytochemistry and bioactivity of the *Seseli* species have provided a basis for further research on this medicinal and aromatic plant species and its active components. However, prospective studies on the toxicity of *Seseli* plants and clinical trials are much needed to understand the true potential as a source of new pharmaceutical remedies.

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Conflict of interest

The authors declare no conflict of interest.

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