REVIEW ARTICLE

Special Issue-Lamiaceae Family: Phytochemistry, Pharmacology, Ethnopaharmacology, Ethnobotany and as Food Soruce

A C G publications

Rec. Nat. Prod. 19:SI (2025) 350-374

records of natural products

A Mini Review on the Chemodiversity of *Lamiaceae* plants That Are Native to Türkiye and Turkish Republic of Northern Cyprus[#]

İhsan Çalış *

Near East University, Faculty of Pharmacy, Department of Pharmacognosy, Lefkoşa (Nicosia), Turkish Republic of Northern Cyprus

[#] *Dedicated to the memory of Dr. Pharm. Rüştü Akın Çubukçu*

(Received March 13, 2025; Revised April 08, 2025; Accepted April 11, 2025)

Abstract: The mint family (Lamiaceae) is renowned for its aromatic oils, which have played a crucial role in culinary, medicinal, and horticultural practices throughout history. Many species hold significant economic value, serving as sources of wood, ornamental plants, cosmetics, and medicinal and culinary herbs. In Türkiye, Lamiaceae is represented by five of the 12 global subfamilies: Ajugoideae, Lamioideae, Nepetoideae, Scutellarioideae, and Viticoideae. Systematic studies highlight the family's rich diversity, particularly its medicinal and pharmaceutical potential, chemotaxonomic and phylogenetic significance, biodiversity, conservation importance, and ecological roles. Their diverse secondary metabolites and extensive use in traditional medicine make them valuable for drug discovery, natural product chemistry, and sustainable resource management. Given their high endemism (~44.9%) and culinary applications—such as flavoring herbs and herbal teas—Lamiaceae species native to Türkiye and the Mediterranean deserve priority in research. This study presents findings on the non-volatile phytochemicals of selected plants from each subfamily at the genus level.

Keywords: *Lamiaceae;* ajugoideae; lamioideae; scutellarioideae; viticoideae; secondary metabolites.

1. Introduction

The Lamiaceae family, the sixth largest among Angiosperms, comprises about 230 genera and more than 7000 species, found globally and encompassing numerous species of economic and medical significance. Initial infrafamilial classifications within Lamiaceae identified only two subfamilies based on palynological characteristics: Lamioideae, characterised by tricolpate pollen, and Nepetoideae, characterised by hexacolpate pollen. Recent advancements in the past two decades have enhanced its subfamilial classification [1, 2]. Recent studies on taxonomy have categorised the family Lamiaceae into twelve subfamilies: Ajugoideae, Lamioideae, Nepetoideae, Prostantheroideae, Scutellarioideae, Symphorematoideae, Viticoideae, Cymarioideae, Peronematoideae, Premnoideae, Callicarpoideae, and Tectonoideae. A recent study utilised plastome data to assess familial relationships within the Lamiaceae family. Together with newly established tribes, Colquhounieae, Rotheceae, and Betoniceae, the monophyly of 12 subfamilies has been updated by the phylogenomic investigations [3]. This family is represented in the flora of Türkiye with the members of the five subfamilies: Ajugoideae, Lamioideae, Nepetoideae, Scutellarioideae and Viticoideae. In addition, it is a rich resource with a rich diversity in all respects for planned scientific research in different fields

* E-Mail: ihsan.calis@neu.edu.tr

The article was published by ACG Publications
http://www.acgpubs.org/journal/records-of-natural-products June 2025 EISSN:1307-6167
DOI: http://doi.org/10.25135/rnp.516.2503.3458
Available online: June 28, 2025

such as plant chemistry, plant taxonomy and new drug candidate molecule research from natural sources, ethnopharmacological and ethnobotanical studies. The earlier chemotaxonomic studies in respect to the caffeic acid ester distribution in higher plants reported that caffeic acid is a universal constituent of higher plants as a combined form. The plants selected from Lamiacaeae and Apiaceae have been studied in this perspective. These were quinic acid esters such as chlorogenic acid, rosmarinic acid and orobanchin. Orobanchin was later described as phenylethanoid glycoside due to the dihydroxy-phenylethanol as an aglycone. However, these types of glycosides have also been described as phenylpropanoid glycosides due to caffeoyl esters on the diglycosidic sugar moiety [α-L-rhamnopyranosyl-(1→3)-β-D-glucopyranose]. Consequently, it has been proposed that caffeic esters may hold significant relevance in chemotaxonomic research. Iridoids, quinones and flavonoids were thought to be further chemical markers for the caffeic acid ester distribution in the Apiaceae and the Lamiaceae at the generic level [4].

A comparative study of 96 Lamiaceae taxa revealed the presence of rosmarinic and caffeic acids, with the former identified in all species of the subfamily Nepetoideae, but missing in those of the subfamily Lamioideae [5]. This research prompted us to concentrate on the genera characterised by a deficiency or scarcity of volatile oil for subsequent phytochemical research.

The present study reports the results of the phytochemical studies on the plants selected randomly during the 40 years on the genus level which can be classified as the member of Lamioideae, Scutellarioideae, Ajugoideae, Viticoideae subfamilies and tribes recognized by Li et al. [6] and Li and Olmstead [7]. A few examples will be given from the subfamily Nepetoideae which is known for plants rich in essential oil. Most of the plant material chosen for the phytochemical studies has been collected from the flora of Türkiye, in which there are 603 Lamiaceae species with a high endemism ratio (271 endemic species, 44.9%). *Lamium* L. (Lamieae), *Ballota* L., *Marrubium* L. (Marrubieae), *Phlomis* L. (*Phlomideae*), *Stachys* L., *Sideritis* L. (Stachydeae) in Lamioideae, *Scutellaria* L. in Scutellarioideae, *Ajuga* L. and *Teucrium* L. in Ajugoideae, *Clinopodium* L., *Origanum* L., *Thymus* L., *Salvia* L., *Drymosiphon* MELNIKOV and *Satureja* L. (Mentheae) in Nepetoideae) are the largest 15 genera based on taxon number (Table 1) [1].

The preceding study in this context concentrated on the Phlomideae clade under the subfamily Lamiodeae, encompassing the species of *Phlomis* L. and *Eremostachys* Bunge [8].

Table 1. The Subfamilies of Lamiaceae and the genera recorded in the Flora of Türkiye*

Subfamilies	**Tribes**	***Genera* (Taxon number/Species number)**
1. Lamioideae	Lamieae	*Lamium* (26/15)
	Marrubieae	*Ballota* (18/22), *Marrubium* (27/21), *Pseudodictamnus, Molucella*
	Phlomideae	*Phlomis* (53/33), *Eremostachys*, *Phlomoides*
	Stachydeae	*Stachys* (118/90), *Sideritis* (54/45), *Prasium, Melittis*
	Leonureae	*Leonurus,Chaiturus*
	Galeopseae	*Galeopsis*
	Betoniceae	*Betonica*
2. Scutellarioideae		*Scutellaria* (39/17)
3. Ajugoideae	Ajugeae	*Ajuga* (23/13)
	Clerodendreae	*Clerodendrum*
	Teucrieae	*Teucrium* (49/36)
4. Viticoideae		*Vitex*
5. Nepetoidea	Mentheae	*Mentha, Clinopodium* (25/16), *Melissa, Nepeta, Lophantus, Origanum* (31/17), *Thymus* (47/15), *Salvia* (107/100), *Hyssopus, Prunella, Lycopus, Dorystoechas, Rosmarinus, Dracocephalum, Glechoma, Thymbra, Satureja* (17/16), *Cyclotrichium, Lallemantia, Pentapleura, Ziziphora, Micromeria, Hymenocrater, Drymosiphon*
	Ocimeae	*Ocimum, Hyptis, Lavandula*
	Elsholtzieae	*Elsholtzia, Perilla,*

*Table has been prepared according to a tribal classification based on a plastom phylogenomic [1, 2].

2. Results and Discussion

2.1. .Lamioideae – Lamieae

2.1.1. Lamium L.

The genus *Lamium* is herbaceous and includes annual and perennial forms, consisting of approximately 32 species located in the temperate and subtropical regions of Asia, Europe, and Northern Africa. *L. album* L., L. *purpureum* L., and L. *maculatum* are the species that have been extensively researched. The common term for the Lamium species is "dead nettle" due to its superficial resemblance to the stinging *Urtica* species. The species of the genus is traditionally utilised for various purposes, including anti-inflammatory, anti-proliferative, antispasmodic, antiviral, astringent, regulation of sebaceous secretions, and treatment of hypertension, leucorrhea, menorrhagia, uterine haemorrhage, paralysis, prostate issues, scrofula, trauma, and fractures. The genus *Lamium* (Lamiaceae) has 32 species within the flora of Türkiye. Certain of them are utilised in Anatolian traditional medicine. A review on *Lamium* species in the frame of their ethnobotanical uses and pharmacological activities and the results of phytochemical studies including iridoids and secoiridoids, phenylpropanoids, flavonoids, anthocyanins, phytoecdysteroids, betaines, benzoxazinoids, terpenes, and megastigman compounds as well as constituents of the essential oils from *Lamium* between 1967 – 2006 have been reported by Yalçın and Kaya [10]. *L. album*, *L. maculatum* and *L. purpureum* are some of the species used as tonics and astringent in Anatolia [11–13].

The studies on *Lamium eriocephalum* subsp. *eriocephalum* [14] and *Lamium garganicum* subsp. *laevigatum* focused on the iridoid contents [15]. From *L eriocephalum* subsp. *eriocephalum,* in addition two well-known iridoids for *Phlomis* species, lamiide **(1)** and ipolamiide (**2**), eriobioside (**3**) and lamerioside (**4**) were isolated.

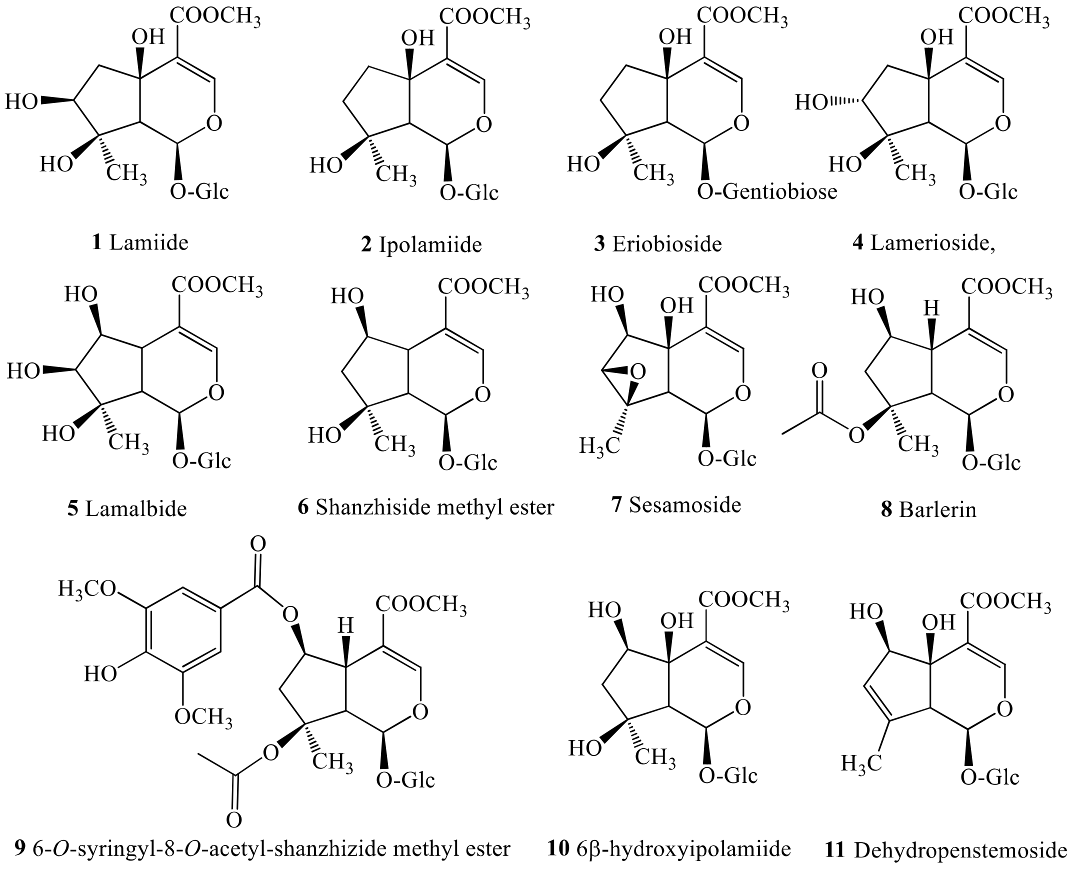
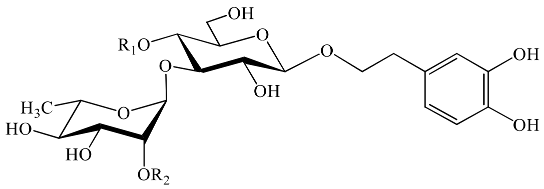


Figure 1. Iridoids from *Lamium* species

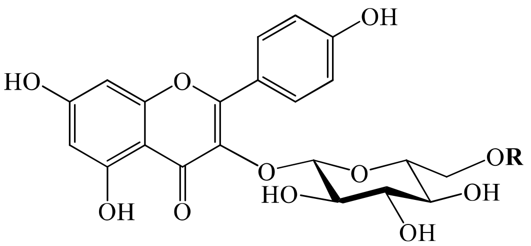
On the other hand, the studies performed on *L garganicum* subsp. *laevigatum* Archangeli resulted in the isolation of seven iridoid glucosides, lamalbide (**5**), shanzhizide methyl ester (**6**), sesamoside (**7**), barlerin (**8**), 6-*O*-syringyl-8-*O*-acetyl-shanzhizide methyl ester (**9**), 6-b-hydroxyipolamiide (**10**) and dehydropenstemoside (**11**) (Figure 1) [14].

Apart from these eleven iridoids, two *Lamium* taxa, *L. garganicum* subsp. *pulchrum* and *L. purpureum* var. *purpureum* were investigated by the help of *HPLC-ESI/MS*. Iridoid content of *the* former was almost similar to those of *L. garganicum* subsp. levigatum except lacking of shanzhizide methyl ester (**6**) and dehydropenstemoside (**11**), while the latter was poorest one among the four taxa containing only compounds lamalbide (**5**) and shanzhizide methyl ester (**6**) [16].

Until now there is no study for phenylethanoid glycosides on *Lamium* species from the flora of Türkiye. However, studies performed on the *Lamium* species reported some phenylethanoid diglycosides such as verbascoside (= acteoside) (**12**), *cis*-acteoside (**13**) and triglycoside, lamalboside (**14**) (Figure 1) [12].



	PhEts (Groups A – C)	R_1	R_2
12	Verbascoside (= Acteoside)	*E*-Caffeoyl	H
13	*cis*-Acteoside	*Z*-Caffeoyl	H
14	Lamalboside	*E*-Caffeoyl	β-D-galactopyranose



(**15**) 3-*O*-rutinosyl kaempferol, **R** = α-L-rhamnopyranosyl
(**16**) 3-*O*-(6''-*O*-p-coumaroyl)-β-D-glucopyranosyl kaempferol, **R** = *p*-coumaroyl

Figure 2. Phenylethanoid and flavonoid glycosides from *Lamium* species

Lamium moschatum Mill. (Musk Deadnettle) is a white flowered species widespread to E. Mediterraenean region from Greece to Palestine including Cyprus [17]. Phytochemical studies on the aerial parts resulted in the isolation of two flavonol glycosides, 3-*O*-rutinosyl kaempferol (**15**) and 3-*O*-(6''-*O*-*p*-coumaroyl)-β-D-glucopyranosyl kaempferol (**16**) [18].

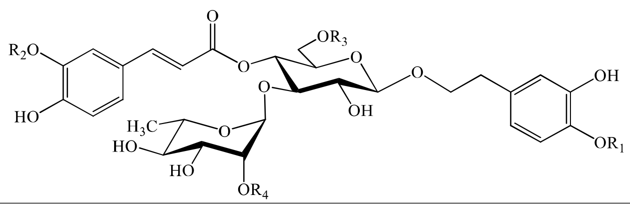
2.1.2. Lamioideae – Marrubieae

2.1.2.1. Marrubium L.

The genus *Marrubium* is represented by 97 species which are widely spread over the temperate and warm regions. Many *Marrubium* species are reported in the literature to be used in folk medicine. Labdane-type diterpenoids such as marrubiin are one of the well-known metabolites isolated from *Marrubium* species. Marrubiin (a diterpene lactone) has been suggested as a potential valuable compound which exists in in many Lamiaceae species and it was demonstrated as a compound with excellent pharmacological properties with high safety margins [19]. The studies on one of the *Marrubium astracanicum* which was collected during the field survey of medicinal plants in Türkiye reported the isolation of similar labdane type diterpenoids, marrubinones A and B [20].

Marrubium alysson L. is a widespread plant in Egypt [21], indigenous to the Mediterranean coastal region from El-Sallum to Rafah and the Sinai desert. Its Arabic name is 'Hashisha Rabiah,' utilised in decoction form as a treatment for asthma and as a diuretic. In North Africa, the tops serve as a flavouring agent.

Previously, the chemical investigation of *M. alysson* has resulted in the isolation of marrubiin, ursolic acid, β-sitosterol, choline, apigenin, apigenin 7-*O*-glucoside, apigenin 7-*O*-arabinoside and. Phytochemical studies on the aerial parts of *M. alysson* resulted in the isolation of phenylpropanoid glycosides; three disaccharide, verbascoside, leucosceptoside A (**17**) and martynoside (**18**) and three trisaccharide esters, forsythoside B (**19**), leucosceptoside B (**20**), alyssonoside (**21**) (Figure 3) [22].



	PhEts (Groups A – C)	R$_1$	R$_2$	R$_3$	R$_4$
17	Leucosceptoside A	H	CH_3	H	H
18	Martynoside	CH_3	CH_3	H	H
19	Forsythoside B	H	H	β-D-apiofuranosyl	H
20	Leucosceptoside B	CH_3	CH_3	β-D-apiofuranosyl	H
21	Alyssonoside	H	CH_3	β-D-apiofuranosyl	H
22	Marruboside	H	H	β-D-apiofuranosyl	β-D-apiofuranosyl
23	Ballotetroside	H	H	β-D-apiofuranosyl	α-L-arabinopyranosyl
24	Arenarioside	H	H	α-L-arabinopyranosyl	H

Figure 3. Phenylethanoid di-, tri- and tetraglycosides isolated from *Marrubium* species

Marrubium species have also been widely studied in respect to phenylpropanoid glycosides and their biological activities. *Marrubium vulgare* L. (White horehound) is prevalent across Europe. The flowering aerial components and their aqueous and hydroalcoholic extracts are utilised in medicine for cough treatment, as a choleretic for digestive and biliary problems and for their neurosedative and anti-inflammatory properties. Two phenylpropanoid tetraglycosides, marruboside (**22**) and ballotetroside (**23**) have been reported from the aerial parts of *Marrubium vulgare* L. in addition to a triglycoside, arenarioside (**24**). The structures of **22** and **23** were established as 3,4-dihydroxy-β-phenylethoxy-*O*-[β-D-apiofuranosyl-(1→2)-α-L-rhamnopyranosyl-(1→3)]-[β-D-apiofuranosyl-(1→6)]-4-*O*-caffeoyl-β-D-glucopyranoside, and 3,4-dihydroxy-β-phenyl-ethoxy-*O*-[β-D-apiofuranosyl-(1→2)-α-L-rhamnopyranosyl-(1→3)]-[β-D-apiofuranosyl-(1→6)]-4-*O*-caffeoyl-β-D-glucopyranoside, respectively. Both are examples for rare tetraglycosidic phenylethanoid glycosides reported [23,24].

However, there is no report for the presence of iridoids from *Marrubium* species.

2.1.3. Lamioideae – Phlomoideae

In Phlomideae six genera were recognized in the tribe: *Eremostachys*, *Lamiophlomis*, *Notochaete*, *Phlomis*, *Phlomoides*, and *Pseuderemostachys*. *Phlomis*, *Eremostachys* and *Phlomoides* are represented in the flora of Türkiye. Phlomideae are typically distinguished by calyx lobes that taper abruptly to a tiny apex and are broadened at the corolla edges, which are adorned with bearded and highly pubescent surfaces, featuring branching hairs [1,2]. *Phlomis tuberosum* and *E. molucelloides* were recently transferred to the genus *Phlomoides*.

2.1.3.1. Phlomis L.

The genus *Phlomis* L. (Turkish sage "Çalba or Şalba") is represented by 53 taxa and 33 species in the flora of Türkiye with a high endemism ratio for all taxa (30 taxa, 57%) and species (16 species, 48%) [1]. The genus *Eremostachys* Bunge is closely related to the genus *Phlomis*. Irano-Turanian region including West and Central Asia are richest zones for this genus with about 60 species [25]. In Türkiye, genus *Eremostachys* is represented by three species *E. moluccelloides*, *E. laciniata* and *E. glabra* [3].

Since the results of the studies performed on the whole species of *Phlomis* L. and two of the three species of *Eremostachys* Bunge were recently reported [8], a summary has been given.

The studies on *Phlomis* species resulted in the isolation of many 21 iridoids and 35 phenylethanoid glycosides. Iridoids are highly oxygenated and biogenetically derived from either 8-epi-loganin without 8-*O*-substitution (Group A) or mussaenoside with 8-*O*-substitution (Group B1) involving further hydroxylation at positions C-5, C-6, and C-7. The third group (B1) was represented only by an example in which a double bond in the pyrane-ring was shifted to the between C-4 and C-5 (Figure 4).

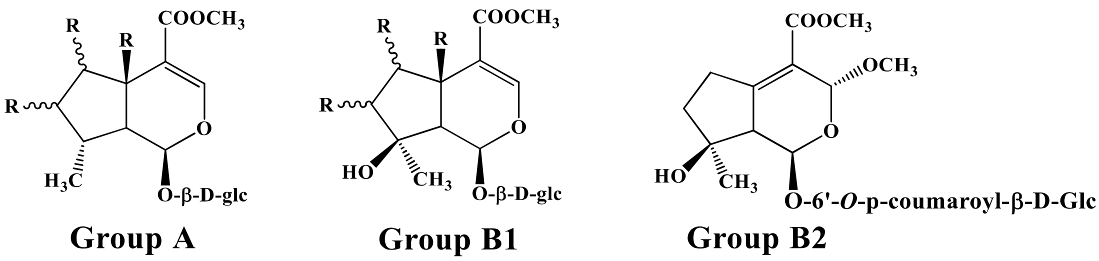


Figure 4. Structural types of *Phlomis* iridoids (R = H or OH)

Iridoids extracted from *Eremostachys* species exhibited a strong similarity to those derived from *Phlomis* species, suggesting a tight phylogenetic link within the Phlomideae tribe.

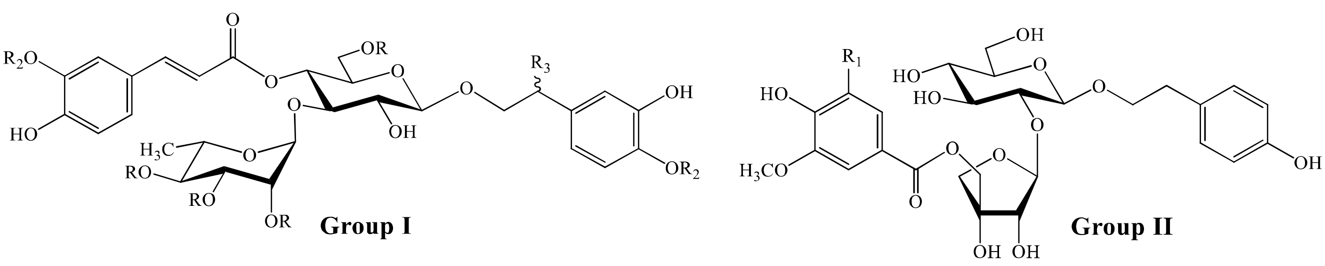


Figure 5. The core structures of the Phenylethanoid glycosides

Group I: R = apiose/arabinose/xylose/rhamnose/glucose, R_1= OH or OMe, R_2 = H or OH
Group II: R = H or OMe

3-*O*-(α-L-rhamnopyranosyl)-β-D-glucopyranose (Group I) and 2-*O*-(β-D-apiofuranosyl)-β-D-glucopyranose (Group II) were the core diglycosidic oligosaccharide moiety of all phenylethanoid glycosides (Figure 5). Tri- and tetraglycosidic phenylethanoid glycosides were the derivatives of the former oligosaccharide. The third and fourth sugar units were apiose, arabinose, xylose, lyxose, rhamnose, or glucose whereas apiose was the most abundant. The glycosidation sites were C-2(OH), C-3(OH) and C-4(OH) of α-L-rhamnopyranose and C-2(OH) and C-6(OH) of the β-D-glucopyranose moieties. Lamiide (**1**) for iridoids, and verbascoside (**12**) and forsythoside B (**19**) were found to be the mostly encountered and phenylethanoid glycosides for the *Phlomis* species. Additionally, these systematic studies on the *Phlomis* species yielded several other types of secondary metabolites such as lignan and neolignane glycosides, flavonoids, quinic acid and shikimic acid esters, mono-, di- and triterpenes and miscellaneous compounds.

2.1.3.2. Phlomoides (Bunge) Salmaki

The studies on *Phlomoides molucelloides* had been published under the name of *Eremostachys molucelloides* Bunge as plant material [25]. However, *Eremostachys molucelloides* Bunge was transferred to the genus *Phlomoides, P. molucelloides* (Bunge) Salmaki [26]. *P. molucelleoides* is native to Altay, Iran, Iraq, Kazakhstan, Kirgizstan, Lebanon-Syria, Mongolia, Tadzhikistan, Transcaucasus, Türkiye, Turkmenistan, Uzbekistan, West Siberia, Xinjiang and accepted as a homotypic synonym of *E. molucelloides.*

The studies on *Phlomoides molucelloides (*previously *E. molucelloides*), *E. laciniata* resulted in the isolation of fourteen iridoid glucosides of which five were common for both species. These were lamalbide (**5**), 5-deoxypulchelloside (**25**), shanzhizide methyl ester (**6**) sesamoside (**7**) and 5-deoxysesamoside (phlorogidoside C) (**26**) [25, 27].

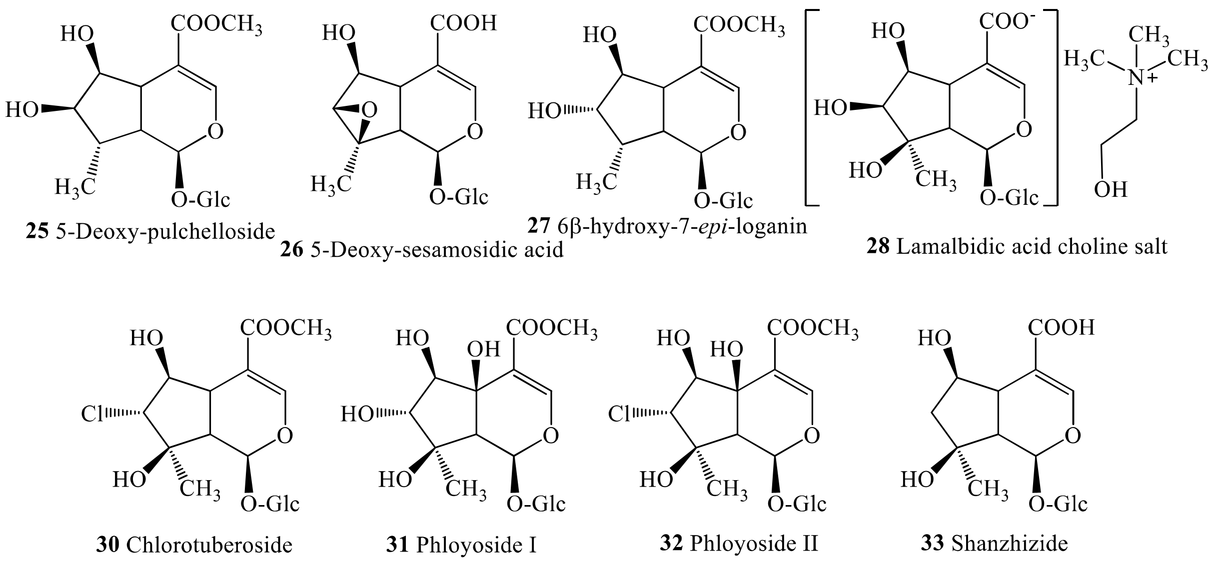


Figure 6. Iridoids from *Eremostachys* species

Additional iridoids were 6β-hydroxy-7-*epi*-loganin (**27**) and lamalbidic acid choline salt (**28**), 5-deoxy-sesamosidic acid (**29**), chlorotuberoside (**30**), Phloyosides I (**31**), II (**32**) and shanzhizide (**33**) (Figure 6).

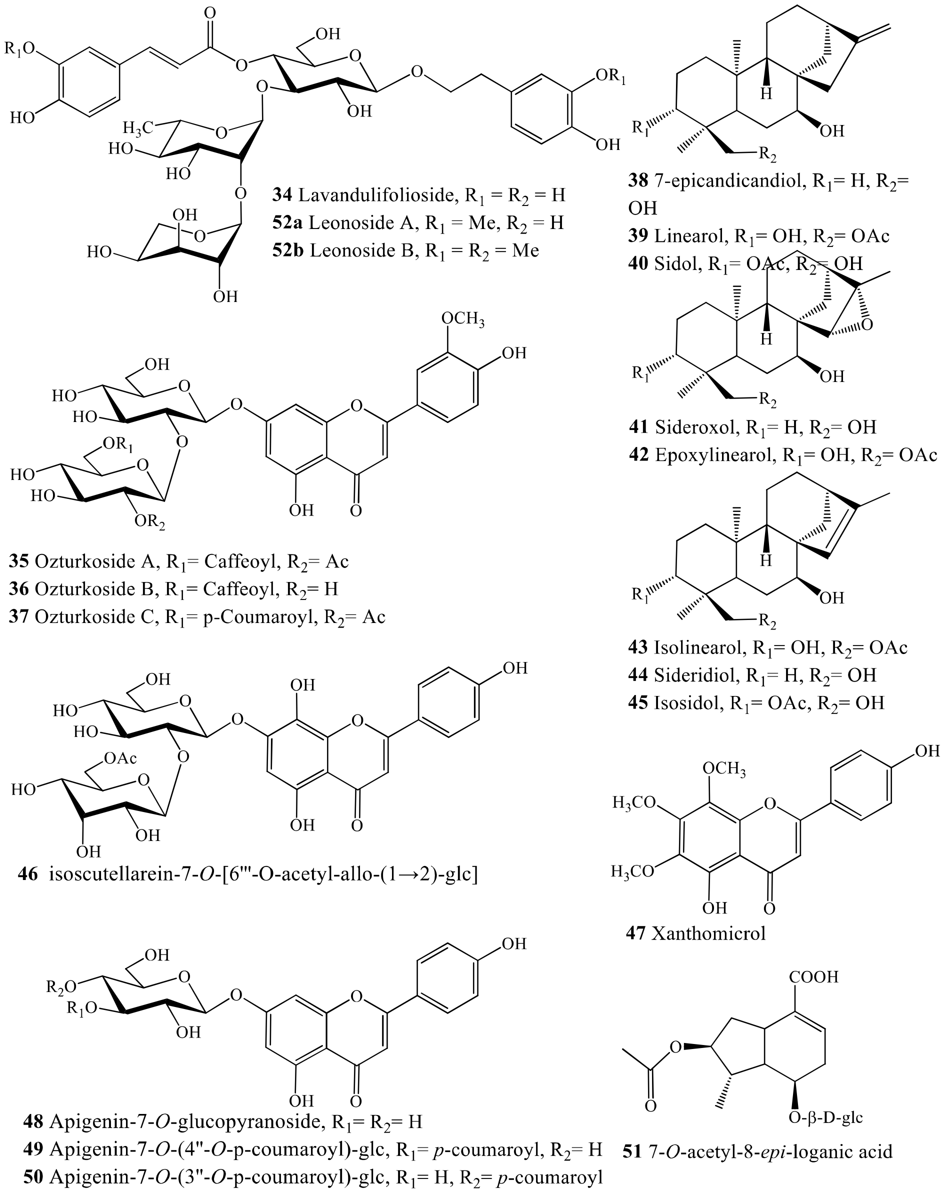
These results suggest that the iridoids isolated from *Eremostachys* and or *Phlomoides* species are closely related to those of *Phlomis* showing close similarity in oxidation pattern on the cyclopentane-pyrane skeleton of the iridoids.

The studies on *Eremostachys laciniata* resulted in the isolation of di- and triglycosidic phenylethanoid glycosides, verbascoside (**12**), leucosceptoside A (**17**), martynoside (**18**) and forsythoside B (**19**) [27]. These results were also in good accordance to those *Phlomis* studies.

2.1.4. Lamioideae – Stachydeae

2.1.4.1. Sideritis L.

The genus *Sideritis* is one of the largest five genera with 54 taxa (45 species) with high endemism in the flora of Türkiye. Endemism ratio is 74% for taxa (45/54) and 80% (36/45) for the species [1]. Some of the species are used as herbal tea throughout Anatolia and consumed under the name of "dağ çayı", "yayla çayı" or "ada çayı" [28, 29]. The genus name *Sideritis* is derived from the Greek word "sideros" (iron) in reference to the use given for these plants since ancient times to heal wounds caused by weapons made with iron. *Sideritis* species are annual and perennial or small shrubs and widely distributed in the Mediterranean region comprising 150 species mainly in the western Mediterranean region, especially Iberian Peninsula (Spain and Portugal) [29]. The *Sideritis* species have been investigated for essential oils, diterpenoids, flavonoids and phenylethanoid glycosides by a large group of scientists.



*Abbreviations: Glc = glucopyranose, allo = allopyranose

Figure 7. Phenylethanoids, flavonoids, diterpenoids and iridoids from *Sideritis* species

As a member of Lamioideae few *Sideritis* species were studied for their chemical constituents. From *S. lycia* four phenylpropanoid glycosides were isolated and their structures were identified as acteoside (**12**), leucosceptoside A (**17**), martynoside (**18**) and lavandulifolioside (**34**) [30]. Lavandulifolioside is a triglycosidic phenylethanoids like the phlinosides from *Phlomis linearis* [31], with the same glycosidation pattern but differing by having α-L-arabinose on the C-2(OH) position of the rhamnose moiety.

Studies on *S. ozturkii* resulted in the isolation of three phenylethanoid glycosides, acteoside (**12**), leucosceptoside A (**17**) and martynoside (**18**), three flavon glycosides, chrysoeriol 7-*O*-[2'''-*O*-caffeoyl-6'''-*O*-acetyl-β-D-glucopyranosyl-(1→2)-β-D-glucopyranoside (**35**), chrysoeriol 7-*O*-[2'''-*O*-caffeoyl-β-D-glucopyranosyl-(1→2)-β-D-glucopyranoside (**36**) and chrysoeriol 7-*O*-[2'''-*O*-p-coumaroyl-6'''-*O*-acetyl-β-D-glucopyranosyl-(1→2)-β-D-glucopyranoside (**37**) (ozturkosides A, B and C, resp.) and five *ent*-kaurane- and epoxykaurane-type diterpenoids, 7-epicandicandiol (**38**), linearol (**39**), sidol (**40**), sideroxol (**41**) and epoxylinearol (**42**) [32,33]. From *S. stricta*, four diterpenes, linearol (**39**), isolinearol (**43**), sideridiol (**44**) and isosidol (**45**), two flavon glycosides, isoscutellaroin 7-*O*-[6'''-*O*-acetyl-β-D-allopyranosyl-(1→2)]-β-D-glucopyranoside (**46**), isoscutellaroin 7-*O*-[6'''-*O*-acetyl-β-D-allopyranosyl-(1→2)]-6''-*O*-acetyl-β-D-glucopyranoside (**47**), a methoxyflavone, xanthomicrol (**47**) and, a PhEts acteoside (**12**) were isolated [34].

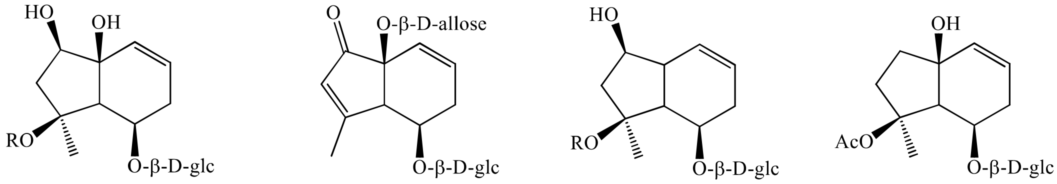
From aerial parts of *S. cypria* endemic in Northern Cyprus, four *ent*-kaurane diterpenes; sidol (**40**) and isosidol (**45**), linearol (**39**) and isolinearol (**43**); four phenylethanoid glycosides; verbascoside (**12**), lavandulifolioside (**34**), leonoside A (**52a**), leucoseptoside A (**17**); four flavone derivatives, isoscutellarein-7-*O*-[6'''-*O*-acetyl-allopyranosyl-(1→2)-glucopyranoside] (**46**), a methoxy-flavon, xanthomicrol (**47**), apigenin-7-*O*-glucopyranoside (**48**), and a mixture of apigenin-7-*O*-(4''-*O*-*p*-coumaroyl)-glucopyranoside (**49**) and apigenin-7-*O*-(3''-*O*-*p*-coumaroyl)-glucopyranoside (**50**) were elucidated. 7-*O*-acetyl-8-*epi*-loganic acid (**51**). Iridoid glycoside (**51**), was reported herein for the first time for genus *Sideritis*. In addition, major compounds of the essential oil were determined as α-pinene (14.73±0.15%), β-pinene (16.60±0.20%), β-phellandrene (17.83±0.23%) and *epi*-cubebol (7.70±0.20%), respectively (Figure 6) [35].

2.1.4.2. Stachys L.

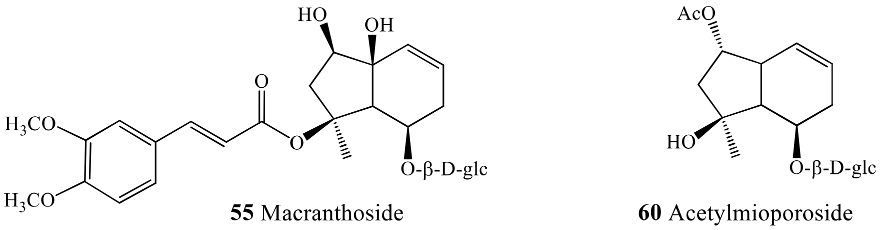
Stachys is one of the largest genera with 300 species throughout the World and largest genus with 118 taxon and 90 species in Türkiye [1]. *S. lavandulifolia* var. *lavandulifolia* is one of the members of Lamiaceae known as “hairy tea” in Türkiye. As a result of an investigation on the water-soluble extract, two PhEts, acteoside (**12**) and lavandulifolioside (**34**) were isolated [36].

In the flora of Türkiye and the East Aegean Islands, Section Betonica has been treated as a *Stachys* subgenus *Betonica* (L.) Bhattacharjee [3]. *Stachys macrantha* (Syn: *Betonica grandiflora* Willd.) one of the species classified in this section was investigated for polar compounds. This study has resulted in the isolation of five aucubin-type iridoids, harpagide (**53**), 8-*O*-acetyl-harpagide (**54**), macranthoside (**55**), allobetonicoside (**56**), ajugol (**57**), ajugoside (**58**), reptoside (**59**) and acetylmioporoside (**60**) (Figure 7)together with three diglycosidic PhEts, acteoside (**12**), leucosceptoside A (**17**), martynoside (**18**) and a triglycosidic PhEt, lavandulifolioside (**34**) [37].

In respect to iridoids, the results were in good accordance with those obtained from *Betonica officinalis*. *Betonica* L. is represented by about twelve species in the vicinities of middle, South and southeast Europe including Türkiye. As a results of a chemotaxonomic studies on *Betonica officinalis*, 8-*O*-acetyl-harpagide (**54**), allobetonicoside (**56**), reptoside (**59**) and acetylmioporoside (**60**) have been reported (Figure 8) [49]. A recent phylogenetic study showed that *Betonica* forms a clade which is sister to Stachydeae under Lamioideae, supporting these similarities in their iridoid constituents [1,2].



53 Harpagide, R= H
54 8-*O*-acetyl-harpagide, R= Ac
56 Allobetonicoside
57 Ajugol, R= H
58 Ajugoside, R= Ac
59 Reptoside



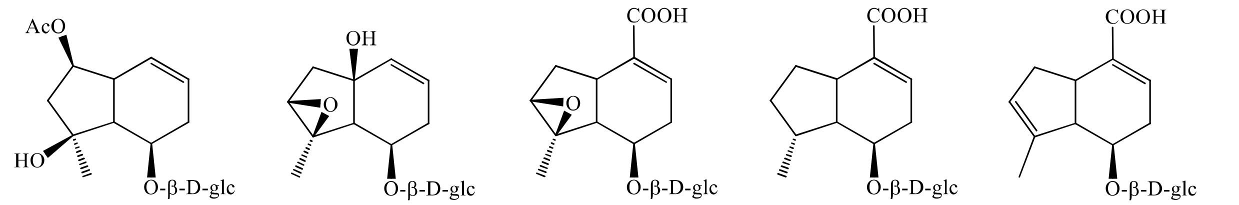
55 Macranthoside
60 Acetylmioporoside

Figure 8. Iridoids from *Stachys macrantha* and *Betonica officinalis*

2.1.5. Lamioideae – Leonureae

2.1.5.1. Leonurus L.

Leonurus (motherwort) species are used for medicinal purposes in Europe as well as in Asia. *L. cardiaca* is one of the species used in European community to treat cardiac problems [38]. *L. japonicus* (syn. *L, heterophyllus, L. artemisia)* is widely used in far-east countries, China, Japan and S. Korea, and known as a panacea to treat diseases related to blood [39]. In the flora of Türkiye, the genus *Leonurus* is represented by five species, *L. marrubiastrum*, *L. cardiaca*, *L. glaucescens*, *L. quinquelobatus* and *L. persicus* [1,3] of which two were choosen for investigation. The studies performed on *L. glaucescens* resulted in the isolation of four phenyethanoid glycosides, verbascoside (**12**), lavandulifolioside (**34**), leonosides A (**52a**) and B (**52b**) [40].



61 6-*O*-acetylajugol
62 Galiridoside
63 7,8-epoxy-8-*epi*-loganic acid
64 10-Deoxy-8-*epi*-loganic acid
65 10-Deoxygeniposidic acid

Figure 9. Iridoids from *Leonurus persicus*

L. persicus was studied in detail [41] yielding iridoids (Figure 9) [42] and labdane-type diterpenoids [43-46]. Aucubin-type iridoids, 6-*O*-acetylajugol (**61**), galiridoside (**62**) and loganin-type of iridoids, 7,8-epoxy-8-*epi*-loganic acid (**63**), 7-deoxy-8-*epi*-loganic acid (**64**) and 10-deoxy-geniposidic acid (**65**) together with a series of labdane-type diterpenoids were isolated (**66-96**). Diterpenoids can be classified as epimeric mixtures of C-15 hemiacetals, C-15 lactone possessing derivatives, prefuranic and furanic labdane and *seco*-labdane derivatives (Figure 9).

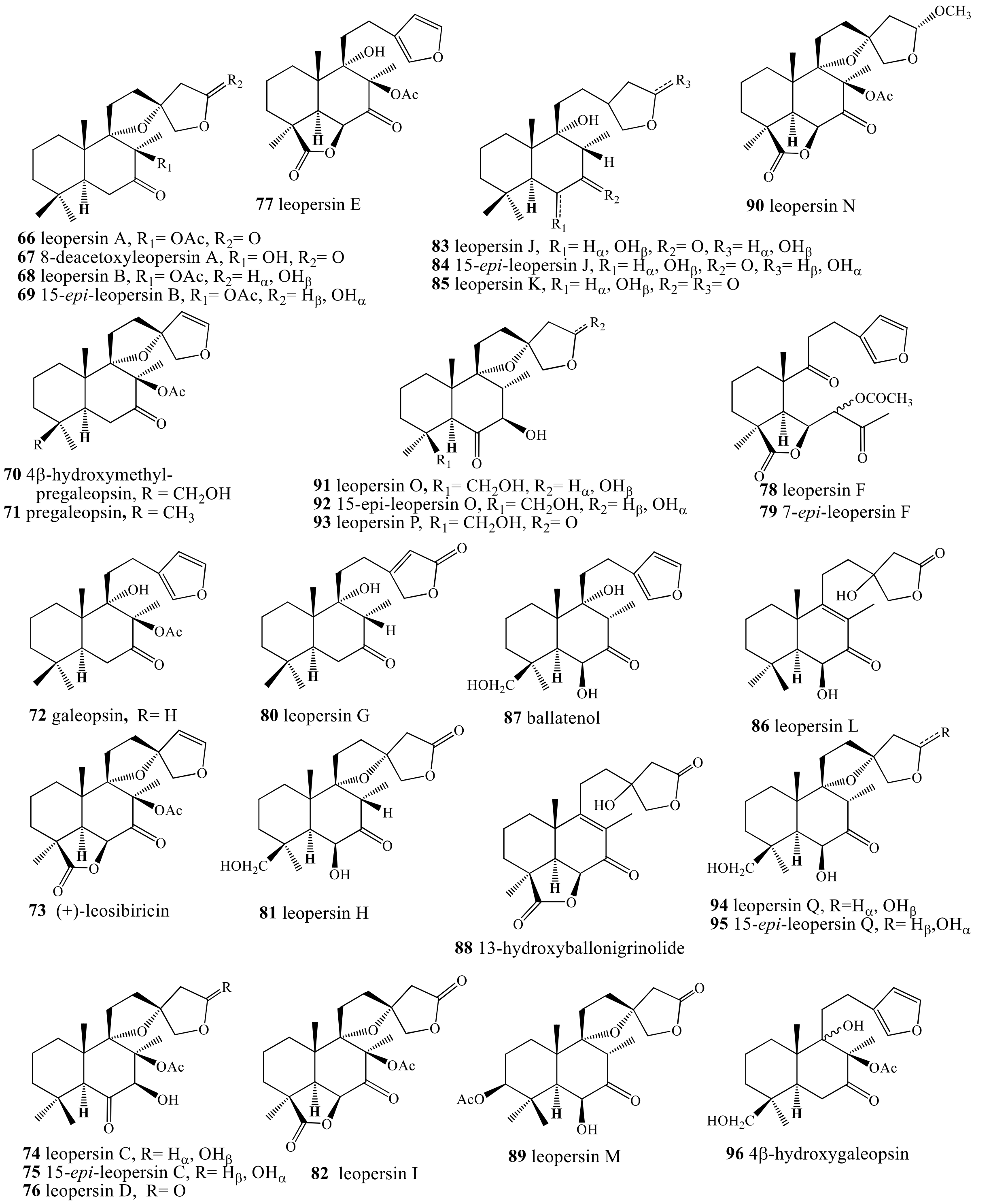


Figure 10. Diterpenoids from *Leonurus persicus*

2.1.6. Lamioideae – Galeopseae

2.1.6.1. Galeopsis Pubescens Besser

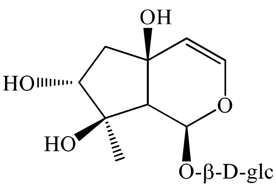
The initial study on *Galeopsis pubescens* resulted in isolation of harpagide (**53**), acetylharpagide (**54**), galiridoside (**62**) and daunoside (**97**) (Figure 11) [4]. Further studies on the uncharacterized fractions of the same plant material resulted in the isolation of two phenylethanoid glycosides, martynoside (**18**) and isomartynoside (**98**) (Figure 9) [48].

This study has been the pioneering one which led us to investigate the distribution of the caffeic acid derivatives and iridoids in the plants of Lamiaceae.

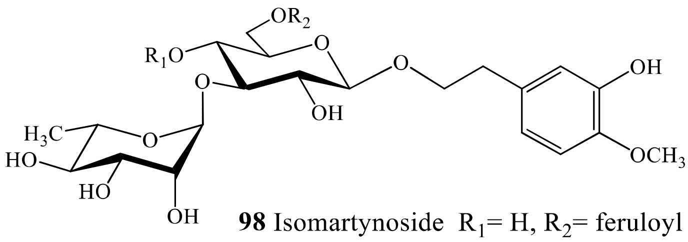
2.1.7. Lamioideae – Betoniceae

2.1.7.1. Betonica Officinalis L.

Betonica L. has approximately twelve species, primarily concentrated in central, southern, and southeastern Europe, as well as Türkiye. It becomes both logical and prudent to distinguish the genus *Betonica* L. from the polymorphic genus *Stachys* L. During chemotaxonomic studies on *Betonica officinalis* L., acetyl-harpagide (**54**), allobetonicoside (**56**), reptoside (**59**) and 6-*O*-acetylmioporoside (**60**). Allobetonicoside (**56**), an iridoid diglycoside has been proposed to be a taxonomic marker for biosystematic investigations of *Betonica officinalis* [49].



97 Daunoside



98 Isomartynoside R_1= H, R_2= feruloyl

Figure 11. Iridoid and phenylethanoid glycosides from *Galeopsis pubescens*

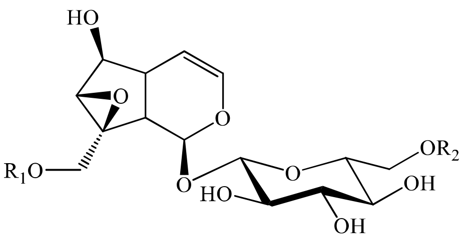
2.2. Scutellarioideae

2.2.1. Scutellaria L.

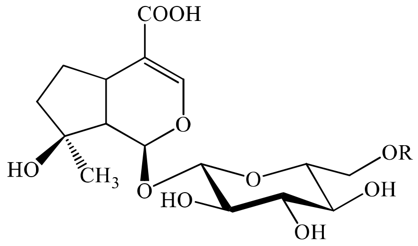
Scutellarioideae consists of ca. 390 species in five genera which are *Holmskioldia* Retz. (1 sp.), *Wenchengia* (1 sp.), *Renschia* Vatke (1 sp.), *Tinnea* Kotschy ex Hook. f. (19 sp.), and *Scutellaria* L. (ca. 360 spp.). *Scutellaria* is the largest and most widely distributed genus, having a cosmopolitan distribution [2].

The genus *Scutellaria* is a sub-cosmopolitan genus of Lamiaceae, subfam. Scutellarioideae [50]. *Scutellaria* and *Apeltanthus* are the two subgenera of *Scutellaria*. A phylogenetic study on the genus has been studied on the 42 Iranian taxa, close to Turkish flora, belonging to subgenera *Apeltanthus* and *Scutellaria*. There are taxa from three section of the genus which are sect. *Scutellaria* and sect. *Salviifoliae* belonging to subgenus *Scutellaria* and sect. *Lupulinaria* belonging to subgenus *Apeltanthus* [50]. A recent phylogenetic study reported *S. baicalensis, S. barbata* and *S. lateriflora* are used for medicinal puposes such as such as antitumor, anti-angiogenesis, hepatoprotective, antioxidant, anticonvulsant, antibacterial and antiviral activities [51]. Phytochemical profiles of different species-groups show also distinct diversity in their constituents. The coexistence of phenylethanoid glycosides, flavonoids (flavones, flavonols, flavanones, flavanonols, biflavonoids, flavonolignans, chalcones), iridoids and neoclerodane-type diterpenoids, triterpenoids, alkaloids as well as essential oils in different species shows variability [51]. In the flora of Türkiye, this genus is represented by 39 taxa and 17 species [1]. *S. orientalis* is recorded as a medicinal plant used as antidiarrheaic, haemostatic and tonic [3].

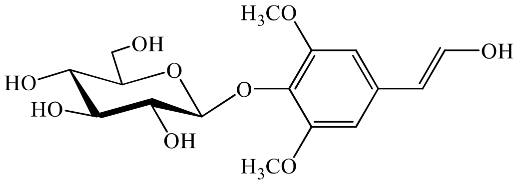
The studies on *S. albida* subsp. *colchica* (Subgenus: *Scutellaria*; Section: Scutellaria) resulted in the isolation of three PhEts, acteoside (**12**), leucosceptoside A (**17**) and martynoside (**18**) together with six iridoids, catalpol (**99**), scalbidoside (**100**), globularin (= scutellarioside I) (**101**), scutellarioside II (**102**) and mussaenosidic acid (**104**) albidoside (**105**) [52, 53].



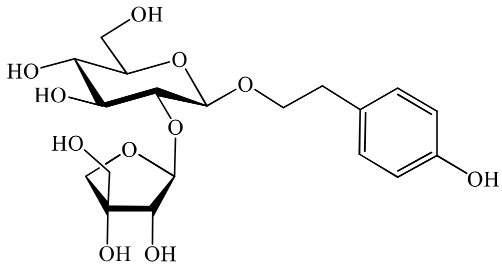
99 Catalpol, R_1= R_2= H
100 Scalbidoside, R_1= (*E*)-cinnamoyl, R_2= α-D-glc
101 Globularin, R_1= (*E*)-cinnamoyl, R_2= H
102 Scutellarioside II, R_1= (*E*)-coumaroyl, R_2= H



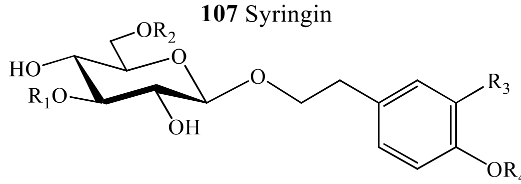
104 Mussaenosidic acid, R= H
118 6'-*O*-caffeoyl-mussaenosidic acid, R= caffeoyl
105 Albidoside, R= (*E*)-coumaroyl



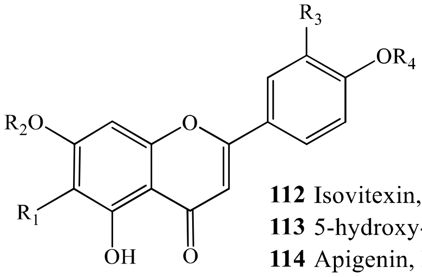
107 Syringin



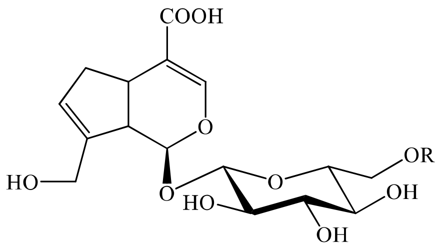
106 Darendoside A



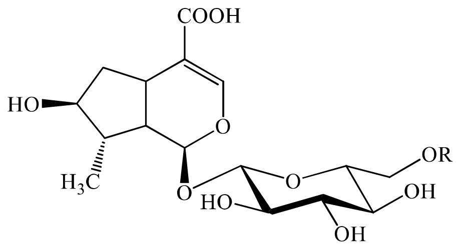
108 Darendoside B, R_1=α-L-rha, R_2= H, R_3= OH, R_4= CH_3
109 2-(4-hydroxyphenyl)-ethyl-(6-*O*-caffeoyl)-β-D-glc
R_1= H, R_2= caffeoyl, R_3= OCH_3, R_4= H
110 calceolarioside B, R_1= H, R_2= caffeoyl, R_3= OH, R_4= H
111 Osmanthuside E, R_1= H, R_2= feruloyl, R_3= OH, R_4= H



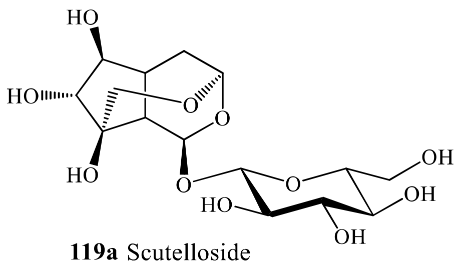
112 Isovitexin, R_1= β-D-glc, R_2= R_3=R_4=H
113 5-hydroxy-7,3',4'-trimethoxyflavone, R_1= H, R_2= R_3=OCH_3, R_4= CH_3
114 Apigenin, R_1= H, R_2= R_3= R_4= H
115 Apigenin-7-*O*-β-D-glc-4'-*O*-methylether, R_1= H, R_2= glc, R_3=H, R_4= CH_3



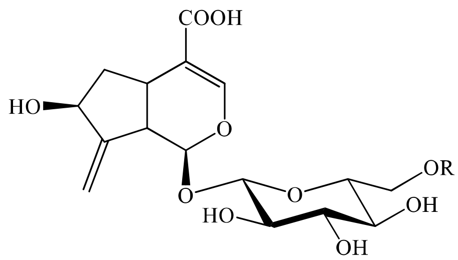
116 6′-*O*-*E*-caffeoyl geniposidic acid, R= Caffeoyl



117 6′-*O*-*E*-caffeoyl 8-*epi*-loganic acid, R= Caffeoyl



119a Scutelloside



119b 6′-*O*-*E*-caffeoyl gardoside, R= Caffeoyl

Figure 12. Iridoids, phenylethanoid-, simple phenol, flavonoid glycosides and flavons from *Scutellaria* species

Darendosides A (**106**) and B (**108**), two deacyl-phenylethanoid glycosides were reported from *S. orientalis* subsp. *pinnatifida* (Subgenus: *Apelthanthus*; Section: Lupulinaria) [54]. A simple phenolic glucoside, syringin (**107**); together with a *C*-glucosyl flavone, isovitexin (**112**); two flavones, 5-hydroxy-7,3′,4′-trimethoxyflavone (**113**); apigenin (**114**); two flavone glucosides, apigenin 7-*O*-b-D-glucopyranoside (**48**); and apigenin 7-*O*-b-D-glucopyranoside-4′-*O*-methylether (**115**); as well as two phenylethanoid glycosides, acteoside (**12**) and martynoside (**18**) were isolated from the aerial parts of *S. pontica* [55]. On the other hand, From the aerial parts of *Scutellaria galericulata* L. (Subgenus: *Scutellaria*; Section: Galericulata), four phenylethanoid glycosides, 2-(4-hydroxyphenyl)-ethyl-(6-*O*-caffeoyl)-b-D-glucopyranoside (**109**), calceolarioside B (**110**), osmanthuside E (**111**) and martynoside (**18**), were isolated [56].

From the aerial parts of *Scutellaria glaphyrostachys* Rech.f., two acylated iridoid glucosides, 6′-*O*-*E*-caffeoyl geniposidic acid (**116**) and 6′-*O*-*E*-caffeoyl 8-*epi*-loganic acid (**117**) in addition to 6′-*O*-*E*-p-coumaroyl 8-*epi*-loganic acid (**118**), catalpol (**99**), scutellarioside I (globularin, **101**), scutellarioside II (**102**), 6′-*O*-*E*-caffeoyl mussaenosidic acid (**118**), albidoside (**105**), scutelloside (**119a**), 6′-*O*-*E*-p-coumaroyl gardoside (**119b**) (Figure 12) [57].
Based on this evidence, isolation of iridoids from the plant belonging to sect. *Scutellaria*, *S. albida* subsp. *colchica* and *S. glaphyrostachys* is important for the chemotaxonomic classification of the genus *Scutellaria*.

2.3.1. Ajugoideae- Clerodendreae

2.3.1.1. Ajuga L.

The genus *Ajuga* L., usually referred to as bugle, consists of roughly 300 species of perennial herbaceous flowering plants predominantly found in the temperate parts of the eastern hemisphere, including Europe, Asia, Australia, North America, and Africa. *Ajuga* species are traditionally used as a treatment for fever, malaria, diarrhea, toothache, diabetes, gastrointestinal problems, and hypertension. *A. decumbens* in China, *A. turkestanica* in Uzbekistan and Tadzhikistan, *A. bracteosa* in Pakistan, China, India, and Malaysia, *A. reptans* in Europe, North America, and West Asia, *A. iva* in Algeria are used traditionally for many purposes. *A. remota*, *A. forrestii* are other species used for the treatment of dysentery, ascariasis, and mastitis in China. Two varieties of *A. macrosperma* which grow in the tropical regions of India, Nepal, and China are also used to alleviate fever and remove phlegm [58]. Phytochemical studies on this genus resulted in the isolation of various bioactive compounds including *neo*-clerodane-type diterpenoids, steroids, ecdysteroids, triterpenoids, iridoids, withanolides, flavonoids, phenylethanoid glycosides. Modern pharmacological activity studies revealed anti-inflammatory, anti plasmodial, anti-platelet, antioxidant, analgesic, anti-diabetic, antifungal, insecticidal and cytotoxic activities of *Ajuga* species [58,59].

In the flora of Türkiye, *Ajuga* is represented by 11 species [3], some of which are traditionally used in wound healing and as a diuretic, as well as against diarrhea and high fever [29]. The studies on *Ajuga salicifolia* collected from the around Ankara in Türkiye, resulted in the isolation of novel sterol glycosides named as ajugasaliciosides A-G (**120-127**). These were mono- (**120, 124, 125** and **126**), di- (**121**, **122**), tri- (123) and tetraglycosidic sterol (**127**) glycosides. Ajugasalicigenin (**128**) was obtained as a non-glycosidic sterol. The most common structural features of these compounds are the epoxidation patterns on side chains of ajugasaliciosides A and B (**121-122**) (Figure 13). Cytotoxicity assays have been conducted on HeLa cells, Jurkat T cells, and peripheral mononuclear blood cells. Ajugasaliciosides A - D **(120-123)** selectively suppressed the viability and proliferation of Jurkat T-leukemia cells at doses under 10 μM. Ajugasalicioside A (**120**; (IC50 6 μM) and C (**122**; (IC50 3 μM) were the most potent compounds. Ajugasalicioside A (**120**) promoted cell-cell contact, suppressed Jurkat T cell proliferation, and elevated mRNA levels of the cell-cycle regulator cyclin D1, potentially indicating cell differentiation. Moreover, 120 decreased the mRNA levels of the NF-κB component p65 in a concentration-dependent manner. The observed effects were absent for ajugasalicioside B (**121**), which contains an extra glucose unit, whereas the beginning of cytotoxicity for **122** (IC50 10 μM) was postponed by 24 hours [60-62].

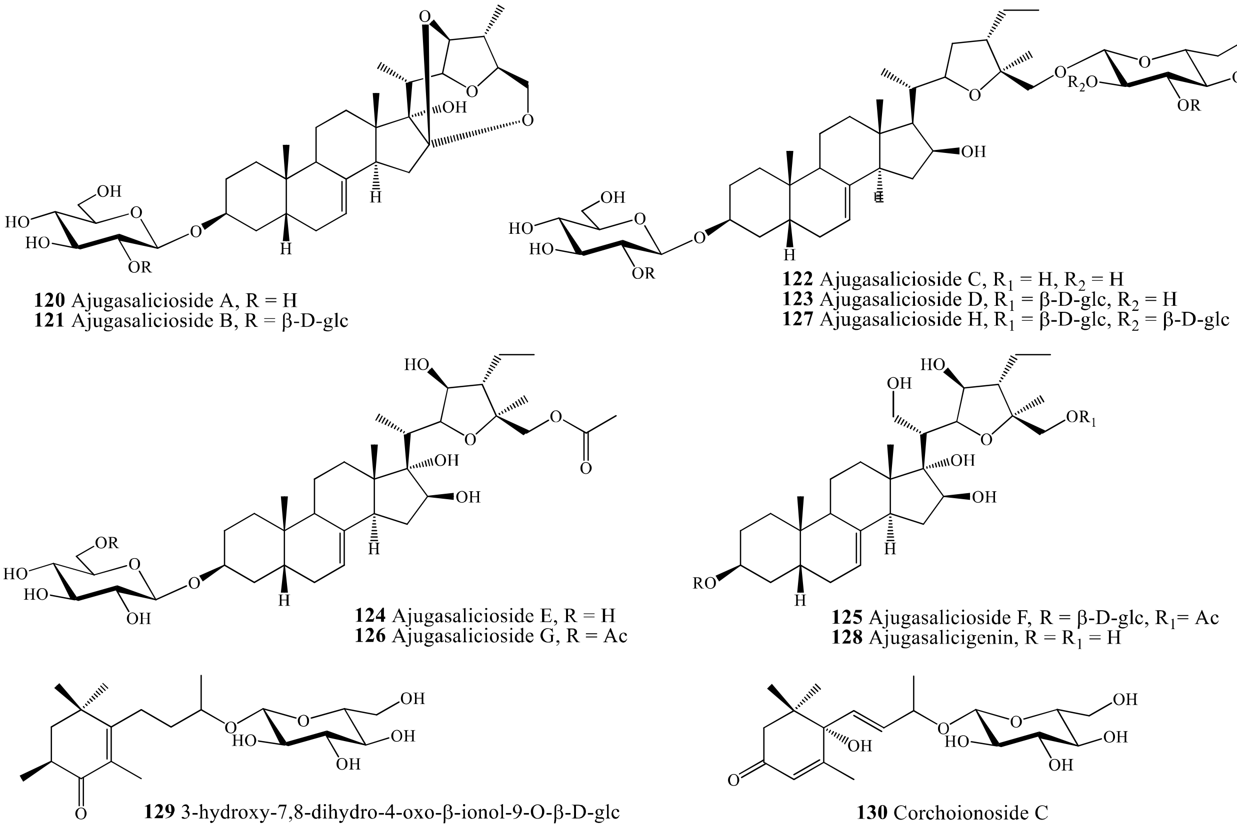


Figure 13. Stigmastane-type sterol, sterol and ionone glycosides from *Ajuga salicifolia*

Further studies on the aerial parts of *Ajuga salicifolia* resulted in the isolation of two ionone glycosides, 3-hydroxy-7,8-dihydro-4-oxo-β-ionol-9-*O*-β-D-glucopyranoside (**129**) and corchoionoside C (**130**) of which the former has firstly been reported in this study [63]. Along these compounds, harpagide (**53**), 8-*O*-acetyl-harpagide (**54**), ajugol (**57**), lavandulifolioside (**34**) and leonosides A and B (**52a, b**) were isolated.

2.3.2 Ajugoideae- Clerodendreae

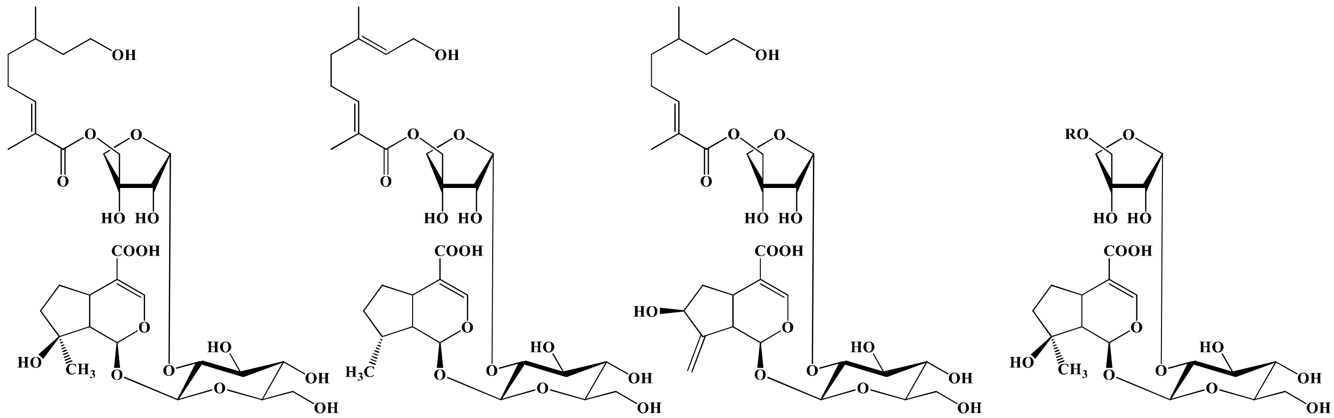
2.3.2.1 Clerodendrum Inerme Gaertn.

The genus *Clerodendrum* L. was previously treated as members of Verbenaceae and was the largest genus of this family. *Clerodendrum* is a widespread genus throughout tropical and subtropical regions of Asia and Mesoamerica. *C. bungei* and *C. trichotomum* have been cultivated as ornamental plants in parks and gardens in Türkiye. *C. bungei* has been naturalized in Black Sea region [64]. However, this genus has been accepted as a member of Clerodendreae tribes under the subfamily Ajugoideae [2]. Tribe Clerodendreae consists of ca. 350 species in ten genera: *Clerodendrum* (ca. 150 spp.), *Volkameria* L. (30 spp.), *Kalaharia* Baill. (1 sp.), *Amasonia* L.f. (8 spp.), *Tetraclea* A. Gray (2 spp.), *Aegiphila* Jacq. (120 spp.), *Ovieda* L. (21 spp.), *Oxera* Labill. (21 spp.), *Hosea* Ridl. (1 sp.), and *Monochilus* Fisch. & C.A. Mey. (2 spp.).

Clereodendrum inerme serves as an army-worm antifeedant in East Africa, whereas in West Africa, the leaf extract is employed to halt bleeding from cuts and wounds, as well as to prevent post-partum hemorrhage. Numerous *Clerodendrum* species have been documented to possess phenylpropanoid glycosides, flavonoids, diterpenes, and iridoids [65, and the references cited therein]. The phytochemical screenings into the secondary metabolite content of *C. inerme* leaves collected from Al-Orman Garden, Giza, Egypt resulted in the isolation of iridoid biglycosides, inerminosides.

The leaves of *C. inerme* have yielded five iridoid biglycosides, inerminosides A, B, C, A1 and D (**131-135**) (Figure 14). Their unique structures have been characterized as 2'-*O*-[5"-*O*-(8-hydroxy-2,6-dimethyl-2(*E*)-octenoyl)-β-D- apiofuranosyl]-mussenosidic acid (inerminoside A, **131**), 2'-*O*-[5"-*O*-(8-hydroxy-2,6-dimethyl-2(*E*),6(*E*)-octadienoyl)-β-D-apiofuranosyl]-8-*epi*-loganic acid (inerminoside B, **132**), 2'-*O*-[5"-*O*-(8-hydroxy-2,6-dimethyl-2(*E*)-octadienoyl)-β-D-apiofuranosyl]-gardoside (inerminoside C, **133**), 2'-*O*-β-D- apiofuranosyl]-mussenosidic acid (inerminoside A1, **134**), and 2'-*O*-[5"-*O*-(*p*-hydroxy-benzoyl)-β-D- apiofuranosyl]-mussenosidic acid (inerminoside D, **135**), respectively [65-66].

The structures of inerminosides A-D (**131-135**) show similarity to those 8-*O*-foliamenthoyl-euphroside, 2',8-di-*O*-foliamenthoyl-euphroside reported from *C. incisum* having an acyclic monoterpene as acyl units [67]. However, acylation sites for inerminosides were on the diglycosidic sugar chain, β-D-apiofuranosyl-(1→2)-β-D-glucopyranose.



131 Inerminoside A **132** Inerminoside B **133** Inerminoside C **134** Inerminoside A1, R = H
135 Inerminoside D, R = *p*-hydroxybenzoyl

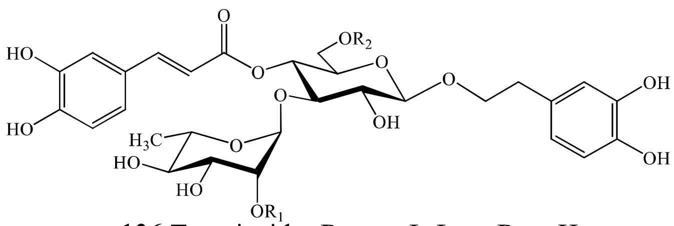
Figure 14. Iridoid biglycosides from *Clerodendrum inerme*

2.3.3. Ajugoideae – Teucrieae

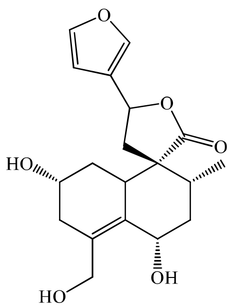
2.3.3.1. Teucrium L.

The tribe Teucrieae has approximately 260 species across three genera: *Teucrium, Schnabelia,* and *Rubiteucris*. Two genera, *Schnabelia* and *Rubiteucris*, are exclusive to East Asia. *Teucrium* exhibits a subcosmopolitan range and is the largest genus, comprising 250 species. The taxa of *Teucrium* are prevalent in the Mediterranean phytogeographic region, exhibiting a significant endemism ratio with *Sideritis, Ballota*, and *Origanum*. The genus *Teucrium* has 35 species, with an endemism ratio of 42%. South America, the mountainous tropical Northeast, South Africa, and Australia are the regions where various species are distributed. Isoprenoids, including iridoids, sesquiterpenoids, diterpenoids, and triterpenoids, as well as phenolic compounds such as flavonoids and phenylethanoid glycosides, are the primary phytochemicals identified in *Teucrium* species. Neo-clerodane diterpenoids have been suggested as promising chemotaxonomic indicators for *Teucrium* species [68, 69]. *Teucrium* species also possess rearranged neo-clerodane or abietane diterpenes, sesquiterpenes, triterpenes, and steroids. The chemical characteristics of neo-clerodanes extracted from *Teucrium* species have been thoroughly studied alongside their stereochemical structures [69]. *Teucrium* species have been used for millennia as therapeutic herbs due to its diuretic, diaphoretic, antiseptic, antispasmodic, antipyretic properties, and hypoglycemic effects in North Africa and Saudi Arabia. *T. polium* L. and *T. chamaedrys* L. are the conventional species used for the treatment of digestive disorders and diabetes. The lack of enough toxicological studies is the gap for the uses of *Teucrium* species as medicinal plants because of some reports on their potential liver and hepatitis toxicity. In some European countries, there are several toxicity reports based on the uses of *Teucrium* species for weight loss program or to treat hypercholesteraemia and diabetes causing chronic hepatitis as well as acute cytolytic hepatitis. Therefore, *Teucrium* species such as *T. chamaedrys, T. polium* and *T. capitatum* which are used as herbal medicines and dietary supplements have been advised to be strictly controlled. Hence, being the responsible compounds, the *neo*-clerodane-type diterpenoids have been the subject of intensive studies [70].

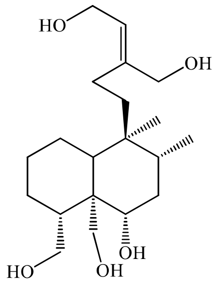
Teucrium chamaedrys and *T. polium* are used in traditional folk medicine, with being one of the most highly investigated species in this genus. Both are used as stimulants, tonics, diaphoretics, diuretics, and treatments for stomach pain. The studies on the aerial parts of *T. chamaedrys* subsp. *syspirense* (C. Koch) Rech resulted in the isolation of a phenylethanoid (= phenylpropanoid) triglycoside, teurioside (**136**) in addition to two *neo*-clerodane-type diterpenes, syspirensins A and B (**137-138**) [71]. Moreover, two *neo*-clerodane-type diterpenes, teulolins A and B (**139-140**) were also isolated from the aerial parts of *T. polium* [72]. Comparative studies on *T. chamaedrys* and *T. polium* in respect to the contents of triglycosidic phenylethanoid derivatives resulted in the isolation of teucrioside (**136**) from poluimoside (**141**), respectively (Figure 14) [73].



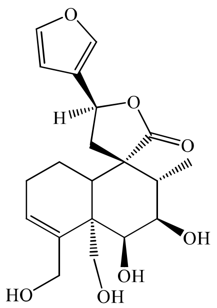
136 Teucrioside, R_1 = α-L-Lyx, R_2 = H
141 Poluimoside, R_1 = H, R_2 = α-L-rha



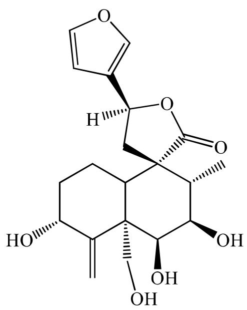
137 Syspirensin A



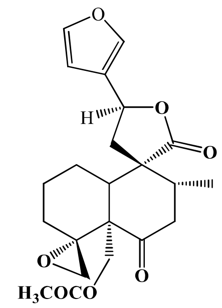
138 Syspirensin B



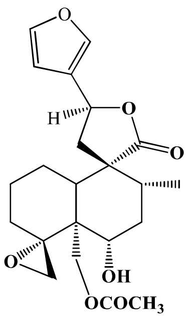
139 Teulolin A



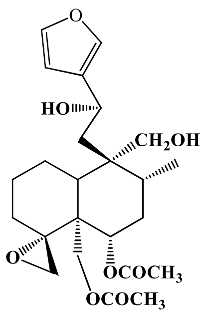
140 Teulolin B



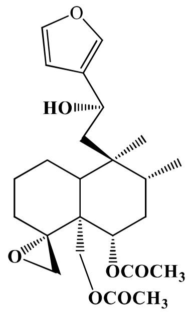
142 Teucrin H3



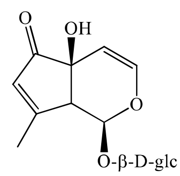
143 Teucjaponin B



144 Teucretol



145 Diacetylteumassulin



146 Teuhircoside

Figure 15. Phenylethanoid and iridoid glycosides and diterpenes from *Teucrium* species
*Abbreviations: Lyx = Lyxose, rha = Rhamnose, glc = Glucose

Contrary the presence of neoclerodane-type diterpenes in both species, the most significant difference between the two *Teucrium* species was observed in the glycosidation patterns of the phenylethanoid triglycosides, teucrioside (**136**) and poluimoside (**141**). A rare sugar α-L-lyxose was the third sugar glycosylated on the C-2(OH) position α-L-rhamnose moiety in teucrioside (**136**) while a second α-L-rhamnose unit was attached to the C-6(OH) of the core sugar β-D-glucose in poluimoside (**141**).

In the flora of Cyprus, *Teucrium* is represented by 9 species which are classified under the five sections, Teucrium (1 spec.), Polium (5 spec.), Chamaedrys (1 spec.), Scorodonia (1 spec.) and Scordium (1 spec., 2 ssps.) [74]. *Teucrium creticum* L. is a member of Teucrium section. From the aerial parts of *T. creticum* L. (Lamiaceae) eight compounds were isolated. Their structures were determined as two phenylethanoid glycosides, verbascoside (= acteoside) (**12**) and lavandulifolioside (**34**), four neoclerodane-type diterpenoids, teucrin H3 (= 19-acetylgnaphalin) (**142**), teucjaponin B (**143**), teucretol (**144**) and diacetylteumassilin (**145**), and two iridoids, 8-*O*-acetylharpagide (**54**) and teuhircoside (**146**) (Figure 14) [75].

2.3.4. Viticoideae

2.3.4.1. Vitex L.

Vitex, *Teijsmanniodendron* and *Pseudocarpidium* are the three genera in Viticoideae. These genera are distributed predominantly in the Tropics with a few species of *Vitex* occurring in temperate regions of the Northern Hemisphere [2]. *Vitex* L. is the unique genera in the subfamily Viticoideae and represented by two species in the flora of Türkiye, *V. agnus-castus* L. and *V. pseudo-negundo* (Hausskn, ex Bornm.) Hard.-Mazz. *Vitex* was one of the three members of Verbenaceae together with *Phyla* Lour. and *Verbena* L. [76]. Recently it was transferred to the Tribe Viticoideae as one of the subfamilies of Lamiaceae [1]. In the flora of Cyprus, it is represented only by one species, *V. agnus-castus* [74].

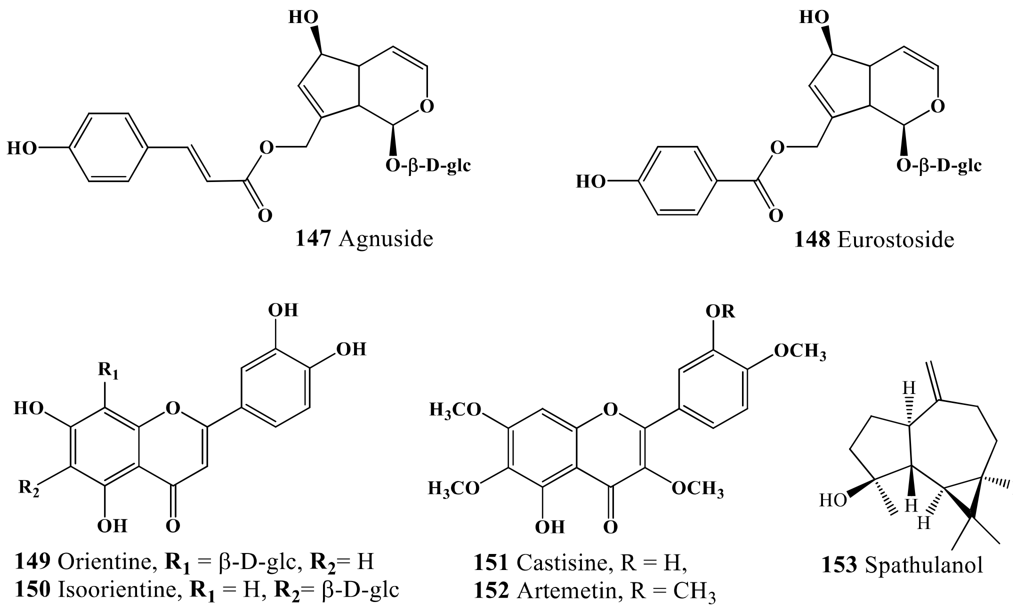


Figure 16. Iridoid glycosides, flavonoids and a sesquiterpene from the fruits of *Vitex agnus-castus*
*Abbreviations: glc = glucose

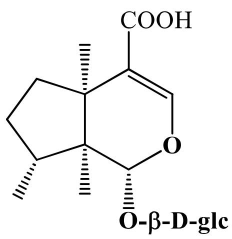
The studies performed on the methanolic extract of the fruits of *V. agnus-castus* collected from the N. Cyprus yielded two iridoids, agnuside (**147**) and eurotoside (**148**) in addition to flavone C-glycosides, orientin (luteolin 8-C-β-D-glucopyranoside) and iso-orientin (luteolin 6-C-β-D-glucopyranoside (**149-150**), two polymethoxy-flavonol derivatives, castisin (3,6,7,4'-tetramethoxy-5,3'-dihydroxy-flavone) (**151**) and artemetin (3,6,7,3',4'-pentamethoxy-5-hydroxy-flavone) (**152**), and a sesquiterpene, spathulanol (**153**) (Figure 16) [77-78]. These results are in accordance with those performed on *Vitex agnus-castus* collected from the flora of Türkiye [79-81].

2.3.5. Nepetoideae - Mentheae

Nepetoideae is represented by three tribes, *Mentheae* (24 species), *Ocimeae* (3 species) and *Escholtzieae* (2 species) (*see* Table 1) [1]. The plants in Nepetoideae are known with their high-level essential oils such as *Mentha*, *Melissa*, *Origanum*, *Rosmarinus*, *Lavandula*. Therefore, only *Origanum* and *Nepeta* species have been studied for their caffeic acid ester glycosides and irioids [82-83].

2.3.5.1. Nepeta

Nepeta is one of the Lamiaceae members which has 46 species and a high endemism ratio (44%) in the flora of Türkiye [1]. *Nepeta caesarea* Boiss. and *N. ucrainica* L. are two species studied for their phytoconstituents. *N. caesarea* was collected from the Turkish flora while *N. ucrainica* from Kazakhistan. Phytochemical analysis of the aerial components of the plant led to the isolation of verbascoside (=acteoside) **(12)** and 1,5,9-epi-deoxyloganic acid (**154**) (Figure 17) [82-83]. The in vitro immunomodulatory effect of verbascoside was studied by evaluating neutrophil function, namely chemotaxis and intracellular killing activity. Verbascoside demonstrated enhanced chemotactic activity at all dosages and positively influenced the respiratory burst of neutrophils. Conversely, an opposing impact with escalating doses, indicating a potential inhibition of neutrophil intracellular killing activity, was noted [83].



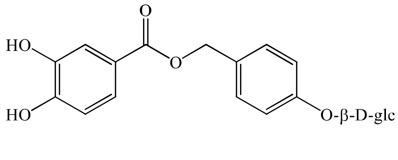
154 1,5,9-epideoxy-loganic acid

Figure 17. 1,5,9-epideoxyloganic acid from *Nepeta* species

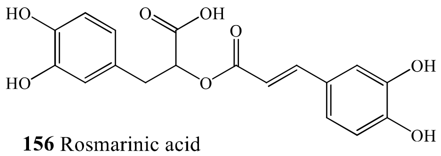
2.3.5.2. Origanum L.

The taxa of *Origanum* are prevalent in the Mediterranean phytogeographic region, exhibiting a significant level of endemism. Species of *Origanum* are frequently used as spices and for their therapeutic properties. The majority of investigations have concentrated on essential oil constituents and terpene compositions. Oregano is among the economically valued spices globally, with about 60 plant species used under this name. *Origanum* (Lamiaceae) and *Lippia* (Verbenaceae) constitute the primary sources of oregano. Their characteristic compounds are carvacrol and thymol which are known as cymyl compounds [84]. These are a group of phenolic monoterpenoids found in the essential oils of plants from the genus *Origanum* such as γ-terpinene, p-cymene, carvacrol and thymol which are responsible for the pungent oregano flavor and are considered valuable for their medicinal and sensory properties, particularly their antimicrobial activity.

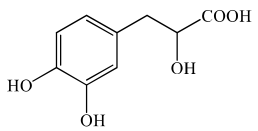
From a different point of view, the compounds responsible for the pharmacological or biological activities of a medicinal plant rich in essential oils can also be non-volatile compounds. With this approach, methanolic extracts of two *Origanum* species were studied.



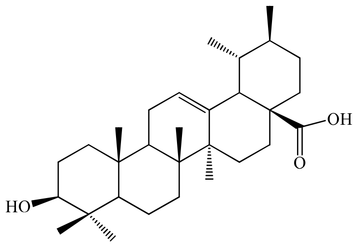
155 4-(3,4-dihydroxy-benzoyl-oxymethyl)-phenyl-β-D-glucopyranoside



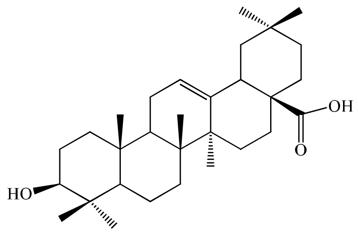
156 Rosmarinic acid



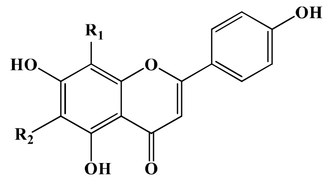
157 3-(3,4-dihydroxyphenyl)-2-hydroxypropionic acid



158 Ursolic acid



159 Oleanolic acid



160 Vicenin-2, $\mathbf{R_1} = \mathbf{R_2}$= β-D-glc

Figure 18. Compounds from *O. micranthum* and *O. minutiflorum*

4-(3,4-dihydroxy-benzoyl-oxymethyl)-phenyl-β-D-glucopyranoside (**155**), rosmarinic acid (**156**), 3-(3,4-dihydroxyphenyl)-2-hydroxypropionic acid (**157**), ursolic acid (**158**), oleanolic acid (**159**) were isolated from *O. micranthum*, rosmarinic acid (**156**), apigenin (**114**) and vicenin-2 (**160**) were isolated from *O. minutiflorum* at the end of the study (Figure 18) [85].

3. Conclusion

During the last four decades, after the first study published in 1984 [48], species of the Lamiaceae family that did not carry essential oils or were poor in essential oils were randomly selected at the genus level. Inspiration of the pioneer study was some reports on the taxonomic approach for the phytochemical studies in respect to caffeic acid ester distribution in the higher plants [4]. Lamiaceae with the earlier name Labiatae was an interesting family with high number of plant species throughout the world as well as for the flora of Anatolia as a part of Eastern Mediterraenean. One of the early infrafamilial classifications within Lamiaceae was recognized to be only two subfamilies based on palynological distinctions, Lamioideae (with tricolpate pollen) and Nepetoideae (with hexacolpate pollen) [86]. A congress on Lamiaceae at 1991 which was held in Kew Garden, London where Cantino et al. published a list of subfamilies and genera of the Lamiaceae including eight subfamilies, Ajugoideae, Chloanthoideae, Lamioideae, Nepetoideae, Pogostomonoideae, Scutellaroideae, Teucrioideae and Viticoidea stimulated the further studies [87]. This classification was evaluated recently based on plastome data to estimate family-wide relationships within Lamiaceae and 12 subfamilies were suggested (Table 1) [1-2].

Hence, the studies on the Lamiaceae plants were presented according to the recent subfamilial classification. Contrary to the content of rich essential oils in the plants of Nepetoideae, the studies performed on the randomly selected plants of other subfamilies afforded mainly iridoid and phenylethanoid glycosides indicating richness in structural diversity. Iridoids are also monoterpene derivatives with a cyclopentane-pyrane ring system. They are mostly monoglucosidic compounds and loganin-type iridoids in the member of Lamiaceae. Rarely aucubin-type iriodids were also isolated. However additional second sugar units such as β-D-apiose can be observed as inerminosides with a diglycosidic sugar chain (**134-135**). Interestingly, these compounds contain additional monoterpene acids as ester moiety [65-66]. Some of the iridoids are also esterified by an acetyl, benzoyl or cinnamoyl derivatives. Allobetonicoside (**56**) is also another example glycosylated at C-1(OH) as usual in addition to a second glycosylation site at C-5(OH). In this case β-D-allose is the second hexose unit [49]. Marruboside (**22**) and ballotetroside (**23**) were reported by Şahpaz et al [23,24]. These tetraglycosidic compounds were added to the study in order to indicate the stuructural diversity.

The second group of compounds, phenylethanoid glycosides, are also known and reported as phenylpropanoid glycosides due to their cinnamoyl esters in the earlier studies. The α-L-rhamnopyranosyl-(1→3)-β-D-glucopyranose is the basic structure for most of the phenylethanoid glycosides. 3,4-dihydroxy-phenylethyl alcohol is the aglycone while caffeic acid as cinnamoyl derivatives (monomeric phenylpropanoid) is the esterified mostly on the C-4(OH) of the core sugar β-D-glucose. Therefore verbascoside (**12**) has been found mostly in all plant species. The site of further glycosidation are observed on the remaining hydroxyl groups of glucose and/or rhamnose moieties. Forsythoside B (**19**), lavandulifolioside (**34**), teucrioside (**136**), poliumoside (**141**) are some of the triglycosidic phenylethanoid glycosides, while marruboside (**22**) and ballotetroside (**23**) are tetraglycosidic. β-D-Apiose, α-L-rhamnose, α-L-arabinose, α-L-lyxose and β-D-xylose are the additional monosaccharides for tri- and tetraglycosidic phenyethanoids.

Further phenolic compounds such as flavonoids and lignans were also isolated

During the studies, labdane-types diterpenes such as prefuranolabdanes, furanolabdanes, $\boldsymbol{\Delta^{8,9}}$**,** 13-furanolabdanes from *Leonurus* species (**66-96**), *neo*-clerodane-type diterpenes from *Teucrium* species (**137-145**), *ent*-kaurene type diterpenes from *Sideritis* species (**38-45**), pimarane type diterpenes [8] from *Phlomis* species were isolated. However, abietane type diterpenoids from *Teucrium* species, clerodane and neo-clerodane type diterpenoids from *Ajuga*, *Salvia*, *Plectranthus, Salvia*, *Scutellaria* and *Teucrium* species were also reported by other research groups [8,70].

As triterpenoids, oleanane, nor-oleanane, ursane and lupane type triterpenes have been reported from the *Phlomis*, *Leonurus* and *Origanum* species [8,85]. Steroids and phytoecdysteroids are another secondary metabolites which are reported mostly from *Lamium* [10] and *Ajuga* [60-62] [90] species.

Another interesting result is the lack of iridoids in *Ballota* and *Marrubium* species (LAMIOIDEAE**:** Marrubieae) species. On the other hand, *Nepeta* species (NEPETOIDEAE: Mentheae) contain 1,5,9-epideoxy-loganic acid, **154**) in addition to nepetalactons.

These studies showed the richness in structural diversity such as iridoids and phenylethanoid glycosides in the plants of the subfamilies of Lamiaceae such as Lamioideae, Scutellarioideae, Ajugoideae and Viticoideae. Iridoids are one of the groups of the secondary metabolites that are responsible for the biological and pharmacological activities of medicinal plants [88]. On the other hand, a series of biological and pharmacological activities of the traditionally used medicinal plants have been attributed to Phenylethanoid glycosides [89].

The rest of the compounds such as diterpenoids, phytoecdysteroids, flavonoids have also been reported as responsible for activities observed in the several plants of Lamiaceae.

Acknowledgments

I would like to thank all of the authors participated in these studies participated as co-authores, my MSc or PhD students as well as senior authors of the other studies in the same field for inviting me as co-worker. I also thank Dr. Kumsal Kocadal Kaymakzade for her feedback on the English quality of the article.

ORCID
İhsan Çalış:0000-0001-5489-3420

References

[1] F. Celep and T. Dirmenci (2017). Systematic and biogeographic overview of *Lamiaceae* in Turkey. *Nat. Volatiles Essent. Oils* **4**, 14–27.

[2] F. Zhao, Y. P. Chen, Y. Salmaki, B. T. Drew, T. C. Wilson, A. C. Scheen, F. Celep, C. Bräuchler, M. Bendiksby, Q. Wang, D. Z. Min, H. Peng, R. G. Olmstead, B. Li and C. L. Xiang (2021). An updated tribial classification of Lamiaceae based on plastome phylogenomics, *BMC Biol.* **19**.

[3] P. H. Davis (1982). LABIATAE (Lamiaceae). *in* Flora of Turkey and the East Aegean Islands. Vol. VII. Edinburgh, University Press, pp. 36–463.

[4] J. B. Harborne (1966). Caffeic acid ester distribution in higher plants, *Z. fur Naturforsch.-B J. Chem. Sci.* **21**, 604–605.
[5] G. Janicsák, I. Máthé, V. Miklóssy-Vari and G. Blunden (1999). Comparative studies of the rosmarinic and cafeic acid contents of Lamiaceae species, *Biochem. Syst. Ecol.* **27**, 733–738
[6] B. Li, P. D. Cantino, R.G. Olmstead, G. L. Bramley, C. L. Xiang, Z. H. Ma, Y. H. Tan and D. X. Zhang (2016). A large-scale chloroplast phylogeny of the Lamiaceae sheds new light on its subfamilial classification, *Sci Rep.* **6**,:34343.
[7] B. Li and R. G. Olmstead (2017). Two new subfamilies in Lamiaceae, *Phytotaxa.* **313**, 222–226.
[8] İ. Çalış and K. H. C. Başer (2021). Review of studies on *Phlomis* and *Eremostachys* species (lamiaceae) with emphasis on iridoids, phenylethanoid glycosides, and essential oils, *Planta Med*. **87**, 1128–1151.
[9] B. Salehi, L. Armstrong, A. Rescigno, B. Yeskaliyeva, G. Seitimova, A. Beyatli, J. Sharmeen, M. F. Mahomoodally, F. Sharopov, A. Durazzo, M. Lucarini, A. Santini, L. Abenavoli, R. Capasso and J. Sharifi-Rad (2019). *Lamium* plants-A comprehensive review on health benefits and biological activities, *Molecules* **24**, 1913.
[10] F. N. Yalçın and D. Kaya (2006). Ethnobotany, pharmacology and phytochemistry of the genus *Lamium* (Lamiaceae), *FABAD J. Pharm. Sci*. **31**, 43–53.
[11] T. Baytop (2021). Therapy with medicinal plants in Turkey (Past and Present), Second Edition. Nobel Tıp Kitabevi: Istanbul: Turkey, pp. 157
[12] D. Kaya (2007). Pharmacognostical Researches on *Lamium garganicum* subsp *laevigatum* Arcangeli. MS Thesis. Hacettepe University Institute of Health Sciences.
[13] E. Küpeli Akkol, F. N. Yalçın, D. Kaya, İ. Çalış, E. Yeşilada and T. Ersöz (2008). In vivo anti-inflammatory and antinociceptive actions of some *Lamium* species, *J. Ethnopharmacol.* **118**, 166–172.
[14] F. N. Yalçın, T. Ersöz, K. Avcı, C. H. Gotfredsen, S. R. Jensen and İ. Çalış (2007). New iridoid glycosides from *Lamium eriocephalum* subsp. *Eriocephalum*, *Helv. Chim. Acta* **90**, 332–336.
[15] T. Ersöz, D. Kaya, F. N. Yalçın, C. Kazaz, E. Palaska, C. H. Gotfredsen, S. R. Jensen and İ. Çalış (2007). Iridoid glucosides from *Lamium garganicum* subsp. *Laevigatum*, *Turk. J. Chem* **31**, 155-162.
[16] F. N. Yalçın, D. Kaya, İ. Çalış, T. Ersöz and E. Palaska. (2008). Determination of iridoid glycosides from four Turkish *Lamium* species by HPLC-ESI/MS, *Turk. J. Chem*. **32**, 457-467.
[17] D. E. Viney (2011). An illustrated flora of North Cyprus: An essential guide to the wildflowers of the eastern Mediterranean. Gantner Verlag, Ruggell, Liechtenstein.
[18] S. Edawdi (2021). Phytochemical Investigation of *Lamium moschatum* subsp. *micranthum*. MSc Thesis, Near East University, Institute of Graduate Studies.
[19] K. Popoola, A. M. Elbagory, F. Ameer and A. A. Hussein (2013). Marrubiin, *Molecules* **18**, 9049–9060.
[20] A. Iida, Y. Tanaka, T. Mihara, M. Tabata, G. Honda, T. Shingu, Y. Takeda, Y. Takaishi, E. Yeşilada, E. Sezik and T Fujita (1995). Marrubinones A and B, new labdane diterpenoids from *Marrubium astracanicum* (Labiatae), *Chem. Pharm. Bull*. **43**, 1454–1457.
[21] V. Tackholm (1956). Student Flora of Egypt. Anglo-Egyptian, Cairo.
[22] İ. Çalış, M. Hosny, T. Khalifa and P. Rüedi (1992). Phenylpropanoid glycosides from *Marrubium alysson*, *Phytochemistry* **31**, 3624–3626.
[23] S. Sahpaz, T. Hennebelle and F. Bailleul (2002). Marruboside, a new phenylethanoid glycoside from *Marrubium vulgare* L, *Nat Prod Lett*. **16**,195–199.
[24] S. Sahpaz, T. Garbacki, M. Tits and F. Bailleul (2002). Isolation and pharmacological activity of phenylpropanoid esters from *Marrubium vulgare*, *J Ethnopharmacol*. **79**, 389–392.
[25] İ. Çalış, A. Güvenç, M. Armağan, M. Koyuncu, C. H. Gotfredsen and S. R. Jensen (2007). Iridoid glucosides from *Eremostachys moluccelloides* BUNGE, *Helv. Chim. Acta* **90**, 1461–1466.
[26] Y. Salmaki, S. Zarre, O. Ryding, C. Lindqvist, A. Scheunert, C. Bräuchler and G. Heubl (2012). Phylogeny of the tribe Phlomideae (Lamioideae: Lamiaceae) with special focus on *Eremostachys* and *Phlomoides*: New insights from nuclear and chloroplast sequences, *Taxon* **61**, 161–179.
[27] İ. Çalış, A. Güvenç, M. Armağan, M. Koyuncu, C. H. Gotfredsen and S. R. Jensen (2008). Secondary metabolites from *Eremostachys laciniata*, *Nat. Prod. Commun.* **3**, 117–124.
[28] F.P. Şahin (2003). Botanical and Phytochemical studies on some *Sideritis* L. species. Hacettepe University, Institute of Health Sciences, PhD Thesis.
[29] E. González-Burgos, M. E. Carretero and M. P.Gómez-Serranillos (2011). *Sideritis* spp.: uses, chemical composition and pharmacological activities-A review, *J. Ethnopharmacol.* **135**, 209–225.
[30] Y. Akcos, N. Ezer, İ. Çalış, R. Demirdamar and B. Tel (2008) Polyphenolic compounds of *Sideritis lycia*: and their anti-inflammatory activity, *Pharm. Biol.* **37**, 118-122.
[31] İ. Çalış, A. A. Basaran, I. Saracoglu, O. Sticher and P. Rüedi (1990). Phlinosides A, B and C, three phenylpropanoid glycosides from *Phlomis linearis*, *Phytochemistry* **29**, 1253–1257.

[32] F. P. Şahin, N. Ezer, İ. Çalış, P. Rüedi and D. Taşdemir (2004). Three acylated flavone glycosides from *Sideritis ozturkii* Aytac & Aksoy, *Phytochemistry* **65**, 2095–2099.

[33] A. Linden, F. P. Şahin, N. Ezer and İ. Çalış (2006). ent-7α,18-Hydroxykaur-16-ene ethanol solvate, *Acta Crystallogr C* **62**, 253–255.

[34] F. P. Şahin, N. Ezer, and İ. Çalış (2006). Terpenic and phenolic compounds from *Sideritis stricta*, *Turk. J. Chem.* **30**, 495–504.

[35] D. Yiğit-Hanoğlu, A. Hanoğlu, H. Yusufoğlu, B. Demirci, K. H. C. Başer, İ. Çalış and D. Özkum-Yavuz (2020). Phytochemical investigation of *Sideritis cypria* post, *Rec. Nat. Prod*. **14**, 105–115.

[36] A. A. Basaran, İ. Çalış, C. Anklin, S. Nishibe and O. Sticher (1988). Lavandulifolioside: A new phenylpropanoid glycoside from *Stachys lavandulifolia*, *Helv. Chim. Acta.* **71**, 1483–1490.

[37] İ. Çalış, A. A. Basaran, İ. Saracoglu and O. Sticher (1992). Iridoid and phenylpropanoid glycosides from *Stachys macrantha, Phytochemistry* **31**, 167–169.

[38] K. Kuchta, J. Ortwein, İ. Çalış, R. B. Volk and H.W. Rauwald (2016). Identification of cardioactive *Leonurus* and *Leonotis* drugs by quantitative HPLC determination and HPTLC detection of phenolic marker constituents, *Nat. Prod. Comm*. **11**, 1129–1133.

[39] L.-L. Miaoa, Q.-M. Zhoua, C. Penga, Z.-H. Liud, L. Xionga (2019). *Leonurus japonicus* (Chinese motherwort), an excellent traditional medicine for obstetrical and gynecological diseases: A comprehensive overview, *Biomed. Pharmacother.* **117**, 109060.

[40] İ. Çalış, T. Ersöz, D. Tasdemir and P. Rüedi (1992). Two phenylpropanoid glycosides from *Leonurus glaucescens, Phytochemistry* **31**, 357–359.

[41] D. Tasdemir (1997). Phytochemical and biological investigations of Turkish *Leonurus* species, emphasizing on the diterpenoids of *Leonurus* species [Dissertation]. Zurich: Swiss Federal Institute of Technology Zurich.

[42] D. Tasdemir, L. Scapozza, O. Zerbe, A. Linden, O. Sticher and İ. Çalış (1999). Iridoid glycosides of *Leonurus persicus*, *J. Nat. Prod.* **62**, 811–816.

[43] D. Tasdemir, A. D. Wright, O. Sticher, İ. Çalış and A. Linden (1995). Detailed ^{1}H- and ^{13}C-NMR investigations of some diterpenes isolated from *Leonurus persicus, J. Nat. Prod*. **58**, 1543–1554.

[44] D. Tasdemir, A. D. Wright, O. Sticher and İ. Çalış (1996). New furanoid and seco-labdanoid diterpenes from *Leonurus persicus*, *J. Nat. Prod.* **59**, 131–134.

[45] D. Tasdemir, O. Sticher, İ. Çalış and A. Linden (1997). Further labdane diterpenoids isolated from *Leonurus persicus*, *J. Nat. Prod*. **60**, 874–879.

[46] D. Tasdemir, İ. Çalış and O. Sticher (1998). Labdane diterpenes from *Leonurus persicus*, *Phytochemistry.***49**, 137–143.

[47] E. Rogenmoser (1975). Isolierung,Charakterisierung und Strukturaufklärung der Iridoidglucoside von *Galeopsis pubescens* Besser. [Dissertation] Zürich: ETH No: **5574** Juris Druck + Verlag Zürich.

[48] İ. Çalış, M. F. Lahloub, E. Rogenmoser and O. Sticher (1984). Isomartynoside, a phenylpropanoid glycoside from *Galeopsis pubescens, Phytochemistry* **23**, 2313–2315.

[49] M. Jeker, O. Sticher, İ. Çalış and P. Rüedi. (1989). Allobetonicoside and 6-*O*-Acetylmioporoside: Two new iridoid glycosides from *Betonica officinalis* L., *Helv. Chim. Acta.* **72**, 1787–1791.

[50] A. Paton (1990). A global taxonomic investigation of *Scutellaria* (Labiatae), *Kew Bull*. **45**, 399–450.

[51] X. Shang, X. He, X. He, M. Li, R. Zhang, P. Fan, Q. Zhang and Z. Jia (2010). The genus *Scutellaria* an ethnopharmacological and phytochemical review, *J. Ethnopharmacol*. **128**, 279–313.

[52] İ. Saracoğlu, T. Ersöz and İ. Çalış (1992). Phenylpropanoid from *Scutellaria albida* subsp *colchica, Hacet. Univ. J. Fac. Pharm* **12**, 65–70.

[53] İ. Çalış, T. Ersöz, İ. Saracoglu and O. Sticher (1993). scalbidoside and albidoside, two new iridoid glycosides from *Scutellaria albida* subsp. *Colchica, Phytochemistry* **32**, 1213–1217.

[54] İ. Çalış, İ. Saracoglu, A. A. Basaran and O. Sticher (1993). Two Phenethyl alcohol glycosides from *Scutellaria orientalis* subsp. *Pinnatifida, Phytochemistry* **32**, 1621–1623.

[55] T. Ersöz, Ü. Ş. Harput, İ. Saracoglu, İ. Çalış and Y. Ogihara (2002). Phenolic compounds from *Scutellaria pontica, Turk. J. Chem*. **26**, 581–588.

[56] T. Ersöz, D. Taşdemir, İ. Çalış and C. M. Ireland (2002). Phenylethanoid glycosides from *Scutellaria galericulata, Turk. J. Chem*. **26**, 465–471.

[57] Z. Dogan, K. Ishiuchi, T. Makino and İ. Saracoglu (2019). New acylated iridoid glucosides from *Scutellaria glaphyrostachys* Rech.f. and chemotaxonomic importance for the genus *Scutellaria, Phytochem. Lett*. **32**, 157–161.

[58] F. Luan, K. Han, M. Li, T. Zhang, D. Liu, L. Yu and H. Lv (2019). Ethnomedicinal uses, phytochemistry, pharmacology, and toxicology of species from the genus *Ajuga* L.: A systematic review, *Am. J. Chin. Med.* **47**, 959–1003.

[59] K. Nagarkoti, J. Kanyal, O. Prakash, R. Kumar, D. S. Rawat and A. K. Pant. (2021). *Ajuga* L.: A systematic review on chemical composition, phytopharmacological and biological potential, *Curr. Bioact. Compd.* **17**, 11–37.

[60] P. Akbay (2002). Phytochemical and Biological Investigations on a Turkish *Ajuga* species, *Ajuga salicifolia*. DISS. ETH Nr. **14816**.

[61] P. Akbay, J. Gertsch, İ. Çalış, J. Heilmann, O. Zerbe, and O. Sticher (2002). Novel antileukemic sterol glycosides from *Ajuga salicifolia, Helv. Chim. Acta* **85**, 1930–1942.

[62] P. Akbay, İ. Çalış, J. Heilmann and O. Sticher (2003). New stigmastane sterols from *Ajuga salicifolia*, *J. Nat. Prod.* **66**, 461-465.

[63] P. Akbay, İ. Çalış, J. Heilmann and O. Sticher (2003). Ionone, iridoid, and phenylethanoid glycosides from *Ajuga salicifolia*, *Z. fur Naturforsch. - C J. Biosci. **58**,* 177–180.

[64] S. Arslan, B. Şahin and M. Vural (2009). On the Turkish *Clerodendrum* L. (Verbenaceae), *Biol. Diversity Conversation* **2**, 10-13.

[65] İ. Çalış, M. Hosny, A. Yürüker, A. D. Wright and O. Sticher (1994). Inerminosides A and B, two novel complex iridoid glycosides from *Clerodendrum inerme*, *J. Nat. Prod.* **57**, 494–500.

[66] İ. Çalış, M. Hosny and A. Yürüker (1994). Inerminosides A1, C and D, three iridoid glycosides from *Clerodendrum inerme*, *Phytochemistry.* **37**, 1083–1085.

[67] E. Stenzel, H. Rimpler and D. Hunkler (1986). Iridoid glucosides from *clerodendrum incisum, Phytochemistry.* **25**, 2557–2561.

[68] Z. Sadeghi, J.-Li Yang, A. Venditti and M. M. Farimani (2022). A review of the phytochemistry, ethnopharmacology and biological activities of *Teucrium* genus (Germander), *Nat. Prod Res.* **36**, 5647-5664.

[69] A. Ulubelen, G. Topçu and U. Sönmez (2000). Chemical and biological evaluation of genus *Teucrium*. In: Studies in Natural Products Chemistry, ed: Atta-ur Rahman, Elsevier Science, Amsterdam, Netherlands, pp 591 – 648.

[70] M. E. Grafakou, C. Barda and H. Skaltsa (2020). Secondary Metabolites of *Teucrium* species with toxic effects. In: *Teucrium* Species: Biology and Applications, ed: Milan Stanković, Springer Nature, Switzerland, Cham, pp.211-230.

[71] İ. Çalış, E. Bedir, A. D. Wright and O. Sticher, (1996). Neoclerodane diterpenoids from *Teucrium chamaedrys* subsp. *Syspirense, J. Nat. Prod*. **59**, 457–460.

[72] E. Bedir, D. Tasdemir, İ. Çalış, O. Zerbe, and O. Sticher (1999). *Neo*-clerodane diterpenoids from *Teucrium polium*, *Phytochemistry.***51**, 921–925.

[73] E. Bedir and İ. Çalış (1997). *Teucrium polium* ve *Teucrium chamaedrys* subsp. *syspirense*'den elde edilen fenilpropanoit heterozitleri, *Hacettepe Univ. J. of Faculty of Pharmacy* **17**, 9–16.

[74] R.D. Meikle (1985). Flora of Cyprus. The Bentham-moxon trust, Royal Botanic Gardens, Kew, 2, 833-1969. ISBN 0 9504876 43, Clark Constable, Edinburgh, London, Melbourne

[75] A. Hanoğlu, D. Y. Hanoğlu, N. Demirel, H. S. Yusufoğlu and İ. Çalış (2021). Secondary metabolites from *Teucrium creticum* L., *Rec. Nat. Prod*. **15**, 487–502.

[76] P.H. Davis (1982). VERBENACEAE. *in* Flora of Turkey and the East Aegean Islands. Vol. VII. Edinburgh, University Press, pp. 31-35.

[77] R. Kassam, A. Hanoğlu and İ. Çalış (2024). *Vitex agnus-castus* Meyvaları Üzerinde Fitokimyasal Çalışmalar. BİHAT-XXV. Bitkisel İlaç hammaddeleri Toplantısı, P-6, Lefkoşa, TRNC.

[78] R. Kassam (2025). Phytochemical Studies on the Fruits of *Vitex agnus-castus* L. Master Thesis, Institute of Graduate Studies. Near East University.

[79] A. Kuruüzüm-Uz, K. Ströch, L. Ö. Demirezer and A. Zeeck (2003). Glucosides from *Vitex agnus-castus, Phytochemistry* **63**, 959–964.

[80] A. Kuruüzüm-Uz, Z. Güvenalp, K. Ströch, L.Ö. Demirezer and A. Zeeck (2008). Antioxidant potency of Flavonoids from *Vitex agnus-castus* L. growing in Turkey. *FABAD J. Pharm. Sci.* **33**, 11–16.

[81] N. Küçükboyaci and B. Şener (2010). Two major flavonoids from the fruits of *Vitex agnus-castus* L., *Turk J. Pharm. Sci*. **7**, 119–126.

[82] İ. Saracoglu, A. A. Basaran, İ. Çalış, W. Ad, and S. Otto (1990). 1,5,9-epideoxyloganic acid: an iridoid glucoside isolated from *Nepeta caesarea* Boiss Lamiaceae, *Hacet. Univ. J. Fac. Pharm.* **10,** 57–64.

[83] P. Akbay, İ. Çalış, Ü. Ündeğer, N. Başaran and A. A.Başaran (2002). *In vitro* immunomodulatory activity of verbascoside from *Nepeta ucrainica* L., *Phytother. Res.* **16**, 593–595.

[84] C C. Franz and J. Novak (2016). Sources of essential oils. In Handbook of Essential Oils. Science, Technology, and Application. Second Edition. Eds. K.H.C. Başer and G. Buchbauer. CRC Press. Taylor and Francis Group. 6000 Broken Sound Parkway NW. pp. 43–86.

[85] E. S. Karaoğlan, U. Özgen, İ. Çalış and C. Kazaz (2020). Isolation of major compounds of *Origanum micranthum* and *Origanum minutiflorum*, *FABAD J. Pharm. Sci.* **45**, 135–143.

[86] G. Erdtman (1945). Pollen morphology and plant taxonomy. IV. Labiatae, Verbenaceae and Avicenniaceae, *Svensk. Bot. Tidskr.* **39**, 277–285.
[87] P.D. Cantino, R.M. Harley and S.J. Wagstaff SJ (1992). Genera of Labiatae: status and classification. In: R. Harley and T. Reynolds, Editors. Advances in Labiatae science. London: Royal Botanic Gardens, Kew, pp. 511–522.
[88] B. Dinda (2019). Pharmacology and applications of naturally occurring iridoids. Springer Cham, Switzerland.
[89] İ. Çalış (2002). Biodiversity of Phenylethanoid glycosides. biodiversity: biomolecular aspects of biodiversity and innovative utilization. Edited by B. Şener, Kluwer Academic/Plenum Publishers, pp. 137-149.
[90] R. Lafont, C. Balducci and L. Dinan (2021). Ecdysteroids, *Encyclopedia* **1**, 1267–1302.