FABAD J. Pharm. Sci., 31, 43-52, 2006

SCIENTIFIC REVIEW

Ethnobotany, Pharmacology and Phytochemistry of the Genus *Lamium* (Lamiaceae)

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Ethnobotany, Pharmacology and Phytochemistry of the Genus Lamium (Lamiaceae)
Summary
The genus Lamium (Lamiaceae) is represented by 30 species in the flora of Turkey. Lamium album, L. maculatum and several Lamium species have been used in Anatolian folk medicine. In this study, the genus Lamium is evaluated from the viewpoint of ethnobotany, pharmacology and phytochemistry.
Key Words: *Lamium, Lamiaceae, dead nettle.*
Received : 15.02.2007
Revised : 25.06.2007
Accepted : 05.07.2007

Lamium (Lamiaceae) Cinsinin Etnobotanik, Farmakolojik ve Fitokimyasal Yönden Değerlendirilmesi
Özet
Lamium (Lamiaceae) cinsi Türkiye bitki örtüsünde 30 tür ile temsil edilmektedir. Lamium album, L. maculatum ve diğer bazı Lamium türleri Anadolu'da geleneksel tıpta tonik olarak kullanılmaktadır. Bu çalışmada Lamium cinsi etnobotanik, farmakolojik ve fitokimyasal açıdan değerlendirilmiştir.
Anahtar Kelimeler: *Lamium, Lamiaceae, Dead nettle.*

INTRODUCTION

A member of the Lamiaceae family, *Lamium* L. (dead nettle), has been described as perennial and annual herbs. Leaves are ovate to reniform, crenate to dentate. Verticillasters are dense or remote, 2-12 flowered. Calyx is tubular or campanulate, 5-veined, with 5 equal or subequal teeth. Corolla is purple mauve, pink, cream or rarely white, 2-lipped; upper lip hooded; lower lip obcordate or broadly obovate with or without small lateral lobes. Nutlets are triquetrous, usually truncate at apex[1].

The genus Lamium contains almost 40 species, native to Europe, Asia, and North Africa[2], some of which are well-known: *L. album* L., *L. purpureum* L., and *L. maculatum* L. The common name "dead nettle" refers to their superficial resemblance to the unrelated stinging nettles, but unlike those, they do not have stinging hairs and as such are harmless or apparently "dead". Some *Lamium* plants have been used in folk medicine worldwide as remedy in the treatment of several disorders, such as trauma, fracture, paralysis, hypertension, menorrhagia, and uterine hemorrhage[3,4].

The focus of this review is to provide information of the ethnobotanical uses and pharmacological activities of *Lamium* species and the structures of the compounds isolated and identified from *Lamium* since 1967.

Ethnobotanical uses and pharmacological activities of *Lamium* species

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Traditional medicinal uses of *Lamium* have been reported. *L. album* is considered as the most popular species. The dried flowers of this plant exhibited uterotonic, astringent, antispasmodic and anti-inflammatory activities and therefore are utilized in menorrhagia, uterine hemorrhage, vaginal and cervical inflammation and leukorrhea treatment[4]. *L. maculatum* has been used in Chinese folk medicine in the treatment of trauma, fracture, paralysis, and hypertension[5]. *L. album* flowers have been reported to possess antioxidant, free radical scavenging and antiproliferative properties[6-8]. *L. purpureum* flowers also exhibited antioxidant and free radical scavenging activities[7]. The essential oil from *L. garganicum* L. subsp. *laevigatum* Arcangeli was reported to possess bacteriostatic activity against Gram-positive and -negative bacteria[9]. Of the 30 species growing in the flora of Turkey[1,10], the whole plants of *L. album* and some other *Lamium* species are used to relieve pain in rheumatism and other arthritic ailments in Western Anatolia[11], and *L. album*, *L. maculatum*, and *L. purpureum* have been reported to be used as tonics and in the treatment of constipation as home remedies[12]. Different extracts prepared from the over ground parts of *L. eriocephalum* Bentham subsp. *eriocephalum, L. garganicum* subsp. *laevigatum*, *L. garganicum* L. subsp. *pulchrum* R. Mill., and *L. purpureum* L. var. *purpureum* exhibited anti-inflammatory[13], antinociceptive[13], antimicrobial[14], and free radical scavenging[14] activities.

Phytochemistry of *Lamium* species

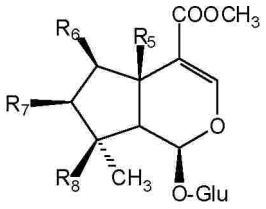
The medicinal properties of *Lamium* species and their traditional usage worldwide have attracted significant attention and this has led to intensive phytochemical investigations. The phytochemistry of the genus *Lamium* has been extensively studied since 1967. During the past 40 years, iridoids and secoiridoids, phenylpropanoids, flavonoids, anthocyanins, phytoecdysteroids, betaines, benzoxazinoids, terpenes, and megastigmen compounds as well as essential oils have been recognized from *Lamium* species. Structures of the compounds are given in Figures 1-5. Table 1 lists the compounds reported in *Lamium*, including the species from which they have been isolated.

I. Iridoids and secoiridoids

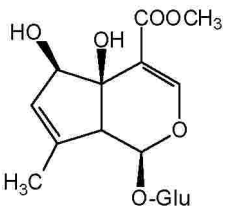
The most prominent compounds in *Lamium* species are iridoid glucosides. *Lamium* species contain C_{10} or C_9 iridoids. The C_{10} cyclopentane pyrane ring is usually characterized by a 11–COOR (1-15, 21) or 11–CH_3 (16-20) substitution. One of the earlier phytochemical reports on the phytochemistry of *Lamium* species revealed the isolation of two iridoid glucosides, lamiol (16) and lamioside (17), from *Lamium amplexicaule*[15]; however, today over 20 iridoids have been isolated and identified from *Lamium* species. Iridoids are also recognized as valuable taxonomic markers for the genus[16]. Deacetylasperulosidic acid (21), characterized from *L. amplexicaule*[17], is the only representative of a C-11 carbocyclic iridoid isolated from a *Lamium* species to date. The remainder of the related iridoids are substituted by a $COOCH_3$ function at C-4 position. As in dehydropenstemoside (13) and deacetyl asperulosidic acid (21), a double bond can take a place between C-7 / C-8 carbon atoms or this position is occupied by an epoxy function, as in sesamoside (14). 6-*O*-syringyl-8-*O*-acetylshanzhiside methyl ester (12) isolated from *L. garganicum* subsp. *laevigatum*[18] is the only example of the *Lamium* iridoids with further esterification at C-6 position. To date, *Lamium* species have been reported to contain iridoids with a β hydroxylation at C-5, 6, 7 or 8 atoms. However, lamerioside (6) reported from *L. eriocephalum* subsp. *eriocephalum*[19], an a-epimer of a well-known iridoid, lamiide (7), is the first example of a *Lamium* iridoid with an α-C-7(OH) function. C_9 iridoids had more restricted distribution within the genus *Lamium*. Harpagide (22) and 8-*O*-acetylharpagide (23), isolated from L. *galeobdolon* L. subsp. *galeobdolon*[17], are the only C_9 iridoids isolated from *Lamium* plants. Almost all *Lamium* iridoids are monoglucosidic compounds with a β-glucopyranose moiety linked to C-1 position. However, recently Yalç›n and co-workers[19] reported the isolation of eriobioside (15) from *L. eriocephalum* subsp. *eriocephalum* . This is the first iridoid diglycoside to be isolated from the genus *Lamium* characterized by the occurrence of a gentiobiosyl moiety on its structure.

The secoiridoid glucosides, albosides A (24) and B

(25) isolated from a Danish population of *L. album*[20], are the only examples of the secoiridoids reported from a plant belonging to the genus *Lamium*. Alboside A has a structure of sweroside-type, whereas Alboside B is a morroniside-type secoiridoid glucoside (Fig. 1, Table 1).



1	R_5= OH	R_6= H	R_7= H	R_8= OH
2	R_5= OH	R_6= H	R_7= H	R_8= OAc
3	R_5= OH	R_6= OH	R_7= H	R_8= OH
4	R_5= H	R_6= H	R_7= OH	R_8= OH
5	R_5= H	R_6= OH	R_7= OH	R_8= OH
6	R_5= OH	R_6= H	R_7= α-OH	R_8= OH
7	R_5= OH	R_6= H	R_7= OH	R_8= OH
8	R_5= OH	R_6= H	R_7= OH	R_8= H
9	R_5= OH	R_6= OH	R_7= H	R_8= H
10	R_5= H	R_6= OH	R_7= H	R_8= OH
11	R_5= H	R_6= OH	R_7= H	R_8= OAc
12	R_5= H	R_6= O-syringyl	R_7= H	R_8= OAc



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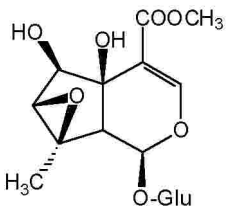

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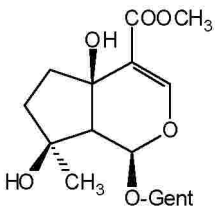

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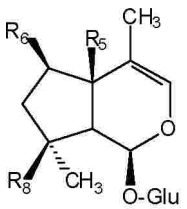
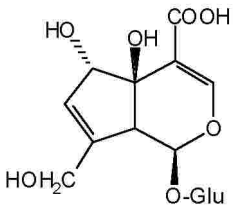


16	R_5= OH	R_6= OH	R_8= OH
17	R_5= OH	R_6= OH	R_8= OAc
18	R_5= H	R_6= OH	R_8= OH
19	R_5= H	R_6= OH	R_8= OAc
20	R_5= OH	R_6= H	R_8= OAc



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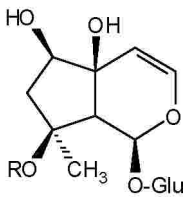
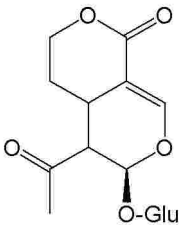


22 R= H
23 R= Ac



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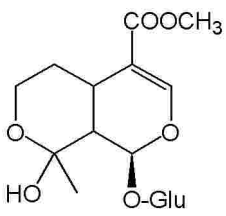

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Figure 1. Iridoids and secoiridoids from *Lamium*

Table 1. Compounds found in *Lamium* species

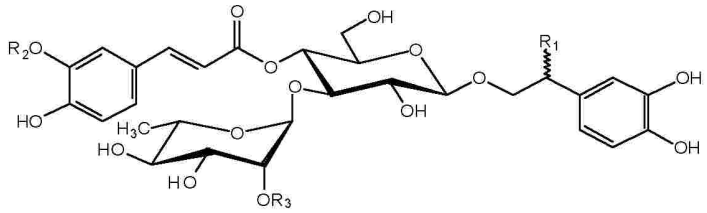
Compounds	Plants and references	Compounds	Plants and references
Ipolamiide (1)	*L. eriocephalum* subsp. *eriocephalum*[19], *L. amplexicaule*[33]	**Rutin (=** rutoside) **(40)**	*L. album*[21], *L. maculatum* var. *kansuense*[22], *L. maculatum*[23]
Ipolamiidoside (2)	*Lamium amplexicaule*[33]	**3'-*O*-Methyl quercetin 3-rutinoside (41)**	*L. maculatum* var. *kansuense*[22]
6-β-OH ipolamiide (3)	*L. garganicum* subsp. *laevigatum*[18]	**Quercetin 3-*O*-glucoside (42)**	*L. album*[21]
Caryoptoside (4)	*L. album*[34,16,20]	***trans* Tiliroside** (= kaempferol 3-*O*-β-(6'''-*O*-*trans*-*p*-coumaroyl)-glucopyranoside) **(43)**	*L. album*[21]
Lamalbide (= lamiridoside) **(5)**	*L. album*[34,16,20,35,36], *L. amplexicaule*[16,17,37], *L. garganicum*[16, 17], *L. maculatum*[34, 16], *L. purpureum*[16]	***cis*-Tiliroside** (= kaempferol 3-*O*-β-(6'''-*O*-*cis*-*p*-coumaroyl)-glucopyranoside) **(44)**	*L. album*[21]
Lamerioside (6)	*L. eriocephalum* subsp. *eriocephalum*[19]	**Quercitroside (45)**	*L. maculatum* var. *kansuense*[38]
Lamiide (7)	*L. maculatum* var. *kansuense*[19,33]	**3,7-Dimethoxy quercetin (46)**	*L. maculatum*[23]
5-OH-8-*epi*-Loganin (8)	*L. maculatum* var. *kansuense*[38]	**Cyanidin 3-glucoside (47)**	*L. amplexicaule*[25]
Penstemoside (9)	*L. maculatum*[34]	**Cyanidin 3,5-diglucoside** (= cyanin) **(48)**	*L. amplexicaule*[25], *L. garganicum*[25]
Shanzhiside methyl ester (10)	*L. album*[16], *L. amplexicaule*[16,17,37], *L. garganicum*[16,17], *L. maculatum*[16], *L. maculatum* var. *kansuense*[38], *L. purpureum*[16], *L. garganicum* subsp. *laevigatum*[18]	**Cyanidin 3-(6''-*p*-coumaroyl glucoside)-5-(6''' malonyl glucoside) (49)**	*L. garganicum*[25]
8-*O*-Acetylshanzhiside methyl ester (= barlerin) **(11)**	*L. amplexicaule*[37], *L. garganicum*[17,39]	**Cyanidin 3-(6''-*p*-coumaroylglucoside)-5-glucoside)** (= perillanin) **(50)**	*L. grandiflorum*[25]
6-*O*-Syringyl-8-*O*-acetylshanzhiside methyl ester (12)	*L. garganicum* subsp. *laevigatum*[18]	**Cyanidin 3-(6''-malonylglucoside)-5-(6'''-malonylglucoside) (51)**	*L. grandiflorum*[25], *L. maculatum*[25]
Dehydropenstemoside (13)	*L. garganicum* subsp. *laevigatum*[18]	**Peonidin 3,5-diglucoside (= peonin) (52)**	*L. amplexicaule*[25]
Sesamoside (14)	*L. amplexicaule*[16,17], *L. garganicum*[16,17], *L. maculatum*[16]	**Peonidin 3,5-monomalonyldiglucoside (53)**	*L. amplexicaule*[25]
Eriobioside (15)	*L. eriocephalum* subsp. *eriocephalum*[19]	**Peonidin 3-(6''-malonylglucoside)-5-glucoside (54)**	*L. amplexicaule*[25]
Lamiol (16)	*L. album*[16], *L. amplexicaule* (*L. amplessicaule*[‡]) [15,16,40,41‡], *L. maculatum*[16,34], *L. purpureum*[16, 17]	**20-hidroksiekdizon (55)**	*L. maculatum*[23], *L. purpureum*[26]
Lamioside (17)	*L. amplexicaule* (*L. amplessicaule*[‡])[15,17,37,40,41‡], *L. purpureum*[17]	**Polipodin B** (= 5β, 20-dihidroksiekdizon) **(56)**	*L. album*[26], *L. maculatum* var. *kansuense*[38]
5-Deoxylamiol (18)	*L. amplexicaule*[16], *L. maculatum*[16,34], *L. purpureum*[16,17]	**Abutasteron (57)**	*L. album*[26]
5-Deoxylamioside (19)	*L. amplexicaule*[40,42]	**Inokosteron (58)**	*L. album*[26]
6-Deoxylamioside (20)	*L. amplexicaule*[40]	**Pterosteron (59)**	*L. album*[26]
Deacetylasperulosidic acid (21)	*L. amplexicaule*[17]	**24-*epi*-pterosteron (60)**	*L. purpureum*[17]
Harpagide (22)	*L. galeobdolon* subsp. *galeobdolon*[17]	**β-Sitosterol (61)**	*L. maculatum* var. k*ansuense*[22]
8-*O*-Acetyl harpagide (23)	*L. galeobdolon* subsp. *galeobdolon*[17]	**Daucosterol (62)**	*L. maculatum* var. k*ansuense*[22]
Alboside A (24)	*L. album*[20]	**Stigmasterol (63)**	*L. maculatum* var. k*ansuense*[22]
Alboside B (25)	*L. album*[20]	**Hemialboside (64)**	*L. album*[43]
Verbascoside (= acteoside) **(26)**	*L. album*[21], *L. garganicum*[17], *L. maculatum* var. k*ansuense*[22], *L. maculatum*[23], *L. purpureum*[17,24]	**9-*O*-β-D-glucopyranosyloxy-5-megastigmen-4-on (65)**	*L. album*[27]
Lamalboside (= lamiuside A) **(27)**	*L. album*[21], *L. purpureum*[24]	**Blepharin (66)**	*L. galeobdolon*[17]
***cis*-Acteoside (28)**	*L. album*[21]	**2-*O*-β-D-Glucopyranosyl-6-hydroxy-2*H*-1,4-benzoxazin-3(4*H*)-on (67)**	*L. galeobdolon*[17]
Lamiuside B (29)	*L. purpureum*[24]	**2-*O*-β-D-Glucopyranosyl-7-hydroxy-2*H*-1,4-benzoxazin-3(4*H*)-on (68)**	*L. galeobdolon*[17]
Lamiuside C (30)	*L. purpureum*[24]	**2-*O*-β-D-Glucopyranosyl-4-hydroxy-2*H*-1,4-benzoxazin-3(4*H*)-on (69)**	*L. galeobdolon*[17]
Lamiuside D (31)	*L. purpureum*[24]	**4-Hydroxy-2*H*-1,4-benzoxazin-3(4*H*)-on (70)**	*L. galeobdolon*[17]
Lamiuside E (32)	*L. purpureum*[24]	**Pipecolic acid betaine (71)**	*L. maculatum*[29,44], *L. galeobdolon*[44]
Leucosceptoside A (33)	*L. purpureum*[24]	***trans*-4-Hydroxypipecolic acid betaine (72)**	*L. maculatum*[29,44], *L. galeobdolon*[44]
Isoacteoside (34)	*L. purpureum*[24]	**Proline betaine (73)**	*L. album*[44], *L. galeobdolon*[44], *L. maculatum*[28,29,44], *L. purmpureum*[44]
6''-*O*-glucosyl martynoside (35)	*L. purpureum*[24]	***trans*-4-Hydroxyproline betaine (74)**	*L. album*[44], *L. galeobdolon*[44], *L. maculatum*[28,29,44], *L. purmpureum*[44]
Salidroside (36)	*L. galeobdolon* subsp. *galeobdolon*[17]	**Trigonelline (75)**	*L. album*[44], *L. galeobdolon*[44], *L. maculatum*[28,44], *L. purmpureum*[44]
Chlorogenic acid (37)	*L. album*[21]	**Allantoin (76)**	*L. maculatum* var. *kansuense*[22]
Liriodendrin (38)	*L. maculatum* var. *kansuense*[22, 38]	**Uridine (77)**	*L. maculatum* var. *kansuense*[38]
Kaempferol 3-*O*-glucoside (= astragalin) **(39)**	*L. album*[21]		

II. Phenylpropanoids

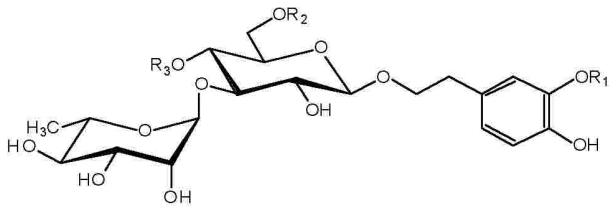
Phenylpropanoids isolated from *Lamium* species are given under the following titles:

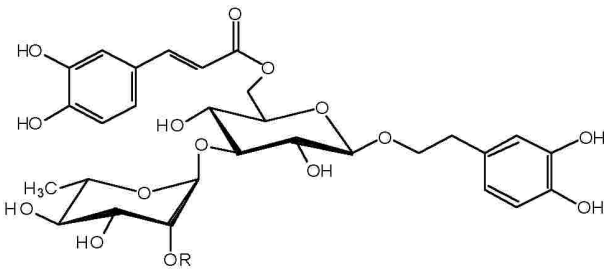
IIa. Phenylethanoid glycosides

In previous reports, three phenylethanoid glycosides, verbascoside (= acteoside: 3,4 dihydroxy-β-phenyletoxy-*O*-α-rhamnopyranosyl-(1→3)-4-*O*-caffeoyl-β-glucopyranoside) (26), lamalboside (27) and *cis*-acteoside (28) were reported from *L. album*[21], *L. garganicum*[17], *L. maculatum* L. var. *kansuense*[22], *L. maculatum* L.[23], and *L. purpureum*[17]. Recently Ito and colleagues[24] reported the isolation of five new phenylethanoid glycosides, lamiusides A-E (27, 29-32), together with four known phenylethanoid glycosides (26, 33-35) from the whole plants of *L. purpureum*. However, lamiuside A (27) is identical to that of lamalboside, previously isolated from *L. album*[21]. The phenylethanoid glycosides isolated from *Lamium* species are all di- or triglycosidic compounds. In lamiuside C (30) and isoacteoside (34), the acyl moiety was attached to the C-6' position of the core glucose; however, in the remaining glycosides, the acyl unit was linked to C-4' carbon atom of the core sugar (Fig. 2, Table 1).



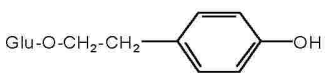
26 R_1= H R_2= H R_3= H
27 R_1= H R_2= H R_3= β-galactopyranosyl
29 R_1= H R_2= CH_3 R_3= β-galactopyranosyl
31 R_1= OCH_3 R_2= H R_3= β-galactopyranosyl
33 R_1= H R_2= CH_3 R_3= H





28 R_1= H R_2= H R_3= cistine-caffeic acid
32 R_1= CH_3 R_2= β-glucopyranosyl R_3= cistine ferulic acid
35 R_1= CH_3 R_2= β-glucopyranosyl R_3= transtine-ferulic acid

30 R= β-galactopyranosyl
34 R= H



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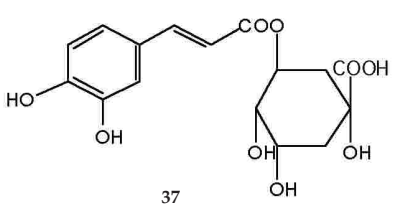

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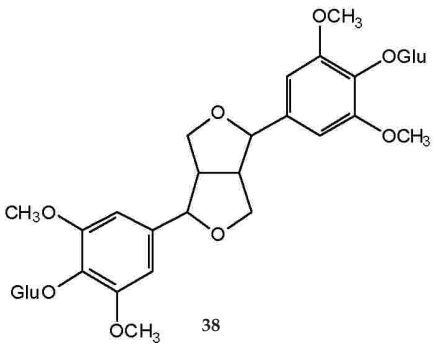

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Figure 2. Phenylethanoid glycosides and phenylpropanoids from *Lamium* species.

IIb. Monomeric and dimeric phenylpropanoids

Lamium species contain some monomeric or dimeric phenylpropanoids. Salidroside (36) was reported from *L. galeobdolon* subsp. *galeobdolon*[17] and chlorogenic acid (37) was isolated from *L. album*[21]. In addition to these monomeric phenylpropanoids, a dimeric phenylpropanoid glucoside, liriodendrin (38), has been characterized from *L. maculatum* var. *kansuense*[38]. Liridodendrin is the only lignan glycoside reported in the genus (Fig. 2, Table 1).

IIc. Flavonoids

To date, seven flavonol glycosides, kaempferol 3-*O*-glucoside (39), rutoside (40), 3'-*O*-methyl quercetin 3-rutinoside (41), quercetin 3-*O*-glucoside (42), *trans*-tiliroside (43), *cis*-tiliroside (44), quercitroside (45) and a flavonol, 3,7-dimethoxy quercetin (46), have been obtained from the flowers of *L. album*[21], *L. maculatum* var. *kansuense*[22,38], and *L. maculatum*[23] (Fig. 3, Table 1).

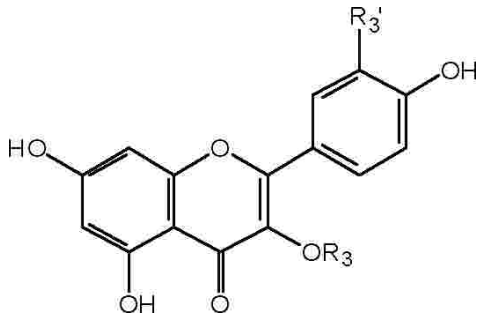
IId. Anthocyanins

A total of eight anthocyanins were variously identified from the fresh flowers of *L. amplexicaule*, *L. garganicum*, *L. grandiflorum*, and *L. maculatum*[25]. Five of the antocyanins were cyanidin derivatives (47-51) and three were peonidin glycosides (52-54). Anthocyanins with malonyl residues attached to the glucose in the 5-position are unique to Lamiaceae[25]. Two of the *Lamium* anthocyanins wer e substituted with a malonyl moiety at C-5(OH) (49), or on the C-3 of the glucose unit (54), whereas two glycosides (51, 53) wer e malonylated both at C-5(OH) and C-3 of the glucose moiety. Two of the cyanidin glycosides (49, 50) wer e coumaroyl substituted. Of the eight anthocyanins, two (48, 52) wer e isolated as cyanidin and peonidin diglucosides (Fig. 3, Table 1).

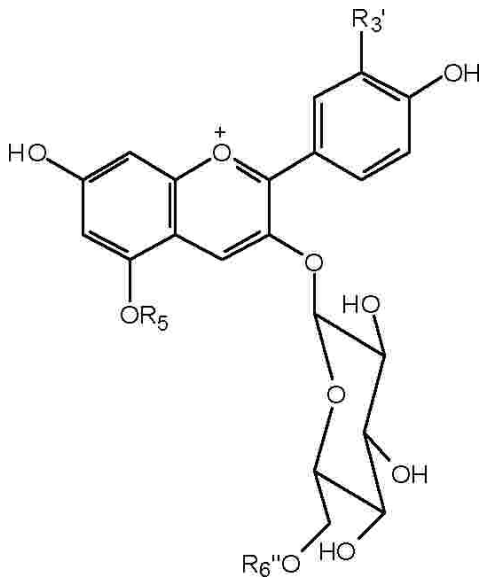
III. Steroids

IIIa. Phytoecdysteroids

Phytoecdysteroids are insect hormone analogues



39	R_3= β-glucopyranoside	$R_{3'}$= H
40	R_3= 6"-α-rhamnosyl-β-glucopyranoside	$R_{3'}$= OH
41	R_3= 6"-α-rhamnosyl-β-glucopyranoside	$R_{3'}$= OCH_3
42	R_3= β-glucopyranoside	$R_{3'}$= OH
43	R_3= 6"-coumaroyl-β-glucopyranoside	$R_{3'}$= H
44	R_3= 6"-coumaroyl-β-glucopyranoside	$R_{3'}$= H
45	R_3= α-rhamnoside	$R_{3'}$= H



46	R_3= CH_3	R_7= CH_3	$R_{3'}$= OH
47	$R_{3'}$= H	R_5= H	$R_{6''}$= H
48	$R_{3'}$= H	R_5= β-glucopyranoside	$R_{6''}$= H
49	$R_{3'}$= H	R_5= 6'''-malonylglucopyranside	$R_{6''}$= coumaroyl
50	$R_{3'}$= H	R_5= β-glucopyranoside	$R_{6''}$= coumaroyl
51	$R_{3'}$= H	R_5= 6'''-malonyl glucopyranoside	$R_{6''}$= malonyl
52	$R_{3'}$= OCH_3	R_5= β-glucopyranoside	$R_{6''}$= H
53	$R_{3'}$= OCH_3	R_5= 6'''-malonyl glucopyranoside	$R_{6''}$= malonyl
54	$R_{3'}$= OCH_3	R_5= β-glucopyranoside	$R_{6''}$= malonyl

Figure 3. Flavonoids and anthocyanins from *Lamium* species.

secreted by some plant species. They constitute a qualitative defense against phytophagous insects. *Lamium* species are considered as ecologically important hosts for a number of insect species, e.g. *L. album* and *L. purpureum* ar e hosts on which the lepidopterans *Arctica caja, euplagia quadripunctaria* and *Phragmatobia fuliginosa* feed[26]. Based on the investigations on plant phytoecdysteroids, six ecdysteroids (55-60) were reported from *L. album*[26], *L. maculatum*[23,26], *L. maculatum* var. *kansuense*[22,38], and *L. purpureum*[17] (Fig. 4, Table 1).

IIIb. Sterols

Deng et al.[22] reported β-sitosterol (61), daucosterol (62) and stigmasterol (63) from *L. maculatum* var. *kansuense* (Fig. 4, Table 1).

IV. Hemiterpenes

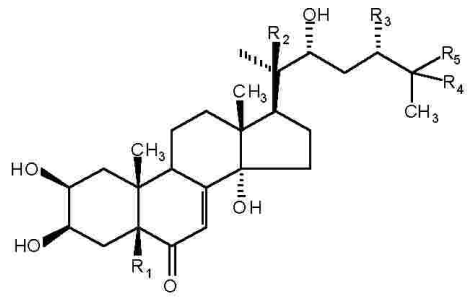
There is only one report which implies a hemiterpene glucoside, hemialboside (64), was isolated from *Lamium album*[43] (Fig. 4, Table 1).

V. Megastigmens

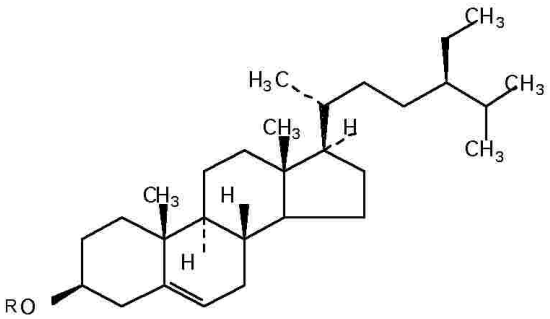
Sarker and co-workers[27] isolated and characterized a novel "megastigmen" class of glycoside, 9-*O*-β-D-glucopyranosyloxy-5-megastigmen-4-on (65) from the leaves of *Lamium album* (Fig. 4, Table 1).

VI. Nitrogen-containing compounds

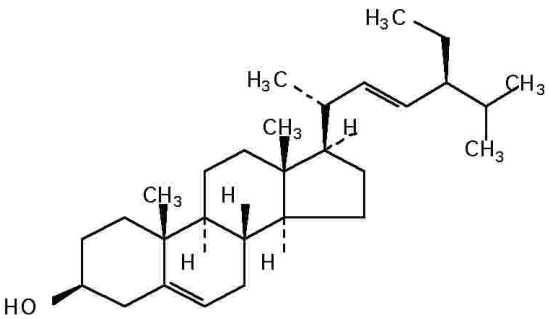
There are a few reports on the isolation and identification of some nitrogenous compounds from some *Lamium* species.



55	R_1= H	R_2= OH	R_3= H	R_4= OH	R_5= CH_3
56	R_1= OH	R_2= OH	R_3= H	R_4= OH	R_5= CH_3
57	R_1= H	R_2= OH	R_3= OH	R_4= OH	R_5= CH_3
58	R_1= H	R_2= OH	R_3= H	R_4= H	R_5= CH_2OH
59	R_1= H	R_2= OH	R_3= OH	R_4= H	R_5= CH_3
60	R_1= H	R_2= OH	R_3= OHa	R_4= H	R_5= CH_3



61 R= H
62 R= β-glucopyranoside



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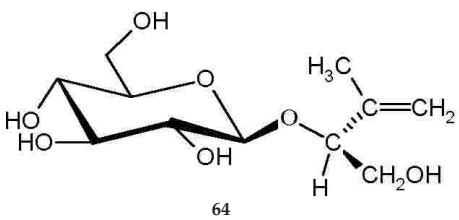

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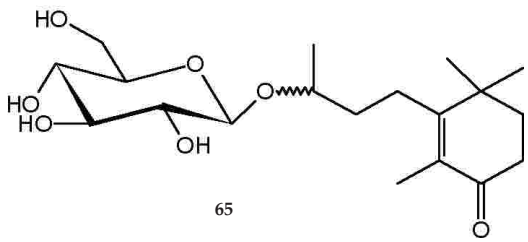


65

Figure 4. Steroids, terpenes and megastigmens from *Lamium* species.

VIa. Benzoxazinoids

Benzoxazinoids are arylhydroxamic acid derivatives and play a role in the protection of plants against bacteria, fungi and insects in many crop plants. Alipieva and colleagues[17] reported the isolation of five benzoxazinoids (66-70) from *L. galeobdolon* subsp. *galeobdolon* (Fig. 5, Table 1).

VIb. Betaines

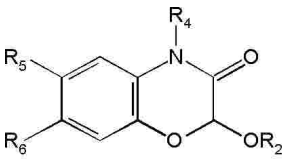
Betaines are naturally occurring compounds that have an important role in osmotic stress resistance in a variety of organisms, including bacteria, algae, mammals, and plants[28]. Betaines are also being considered as taxonomic markers for some plant families[29]. To date, two pipecolic acid derivative betaines[29,44] (71, 72) from *L. maculatum* and *L. galeobdolon* and two proline betaines[28,29,44] (73, 74) from *L. album, L. purpureum, L. maculatum*, and *L. galeobdolon*, as well as a different type of betaine, trigonellin[29,44] (75), were isolated and identified (Fig. 5, Table 1).

VIc. Miscellaneous

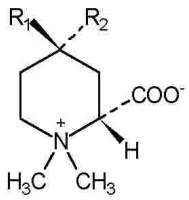
Two nitrogen-containing compounds with miscellaneous structure, allantoin (76) and uridine (77), were isolated and identified from *L. maculatum* var. *kansuense*[22,38].

VII. Essential oils

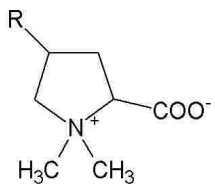
Although Lamiaceae family plants are known to contain a high rate of essential oils, the plants from the genus *Lamium* belonging to the subfamily Lamioideae[45] contain a small amount of essential oils.



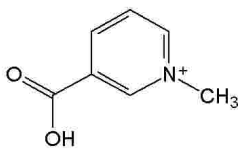
66	R_2= β-glucopyranosyl	R_4= H	R_6= H	R_7= H
67	R_2= β-glucopyranosyl	R_4= H	R_6= OH	R_7= H
68	R_2= β-glucopyranosyl	R_4= H	R_6= H	R_7= OH
69	R_2= β-glucopyranosyl	R_4= OH	R_6= H	R_7= H
70	R_2= H	R_4= OH	R_6= H	R_7 = H



71 R_1= H R_2= H
72 R_1= OH R_2= H



73 R= H
74 R= OH



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76

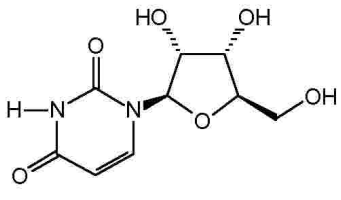

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Figure 5. Nitrogen-containing compounds from Lamium species.

The yields of the essential oils obtained from the fresh flowers of *Lamium* plants vary between 0.01-0.31% (9,30-32). The earliest study was realized on *L. purpureum* essential oil, which showed 1-octen-3-ol, hexen-1-ol, phenethyl alcohol, benzyl alcohol, phenol, o-, m- and p-cresols, guaiacol, eugenol, and fatty acids as main components[30]. In another study, *L. garganicum* subsp. *laevigatum* Arcangeli was examined by GC and GC / MS, and 1,8-cineole (47.5%), citronellal (25.1%) and isoeugenol (11.8%) were found to be the major compounds[9]. In a comparative study on the essential oils of four *Lamium* species from Bulgaria, the essential oils obtained from *L. album, L. purpureum, L. garganicum*, and *L. maculatum* flowers collected from nine populations were analyzed by GC / MS. A similarity of the volatile profile of all samples was shown. Qualitative and quantitative differences in the oil composition of plants collected at different locations were observed. However, all studied samples contained significant amounts of hydrocarbons with C_{12} to C_{31} carbon atoms exclusively with straight chains and fully saturated[31]. The essential oils of *L. purpureum, L. hybridum, L. bifidum* and *L. amplexicaule* were analyzed by GC-MS and SPME, respectively. All these essential oils were characterized by their high contents of germacrene D. In *L. purpureum* (35.4%), *L. hybridum* (39.0%) and *L. bifidum* (34.9%), it was the main compound, while in *L. amplexicaule* (28.9%), the main compound was trans-chrysanthenyl acetate (41.1%)[32].

CONCLUSION

Lamium species, commonly called dead nettles, have been used in folk medicine worldwide as remedy in the treatment of several disorders, such as trauma, fracture, paralysis, hypertension, menorrhagia, and uterine hemorrhage. The interest due to the medicinal properties of *Lamium* species has led to intensive phytochemical investigations on the plants. As a result of these phytochemical investigations, several iridoids and secoiridoids, phenylpropanoids, flavonoids, anthocyanins, phytoecdysteroids, betaines, benzoxazinoids, terpenes, and megastigmen compounds as well as essential oils have been recognized from different *Lamium* species. The most prominent compounds in *Lamium* species are the iridoid glucosides, which contain a C_{10} or C_9 skeleton. Moreover, the iridoid glucosides were consider ed as chemotaxonomic markers of the genus *Lamium*.

The collected data provides a means to understand the latest developments in the pharmacology and phytochemistry of the genus. The information summarized here is intended to serve as a tool to scientists in the fields of ethnopharmacology and natural products chemistry.

REFERENCES

1. Mill RR. *Lamium* L., Davis PH (ed.), Flora of Turkey and the East Aegean Islands, University Press, Edinburgh, Vol. 7, 126-148, 1982.
2. Willis A. Dictionary of Flowering Plants and Fern, 8th edition, Cambridge University Press, Cambridge, 624-626, 1973.
3. Weiss RF. Herbal Medicine, Beaconsfield, 313-314, 1988.
4. Bisset NG. Herbal Dr ugs and Phytopharmaceuticals: A Handbook for Practice on a Scientific Basis. Scientific Publishers, Stuttgart, 288-291, 1994.
5. Shuya C, Xingguo C, Zhide H. Identification and determination of ecdysone and phenylpropanoid glucoside and flavonoids in *Lamium maculatum* by capillary zone electrophoresis, *Biomed. Chromatogr.*, 17, 477-482, 2003.
6. Trouillas P, Calliste C-A, Allais D-P, Simon A, Marfak A, Delge C, Duroux J-L. Antioxidant, anti-inflammatory and anti-proliferative properties of sixteen water plant extracts used in the limousin countryside as herbal teas, *Food Chem.*, 80, 399-407, 2003.
7. Matkowsi A, Piotrowska M. Antioxidant and free radical scavenging activities of some medicinal plants from Lamiaceae, *Fitoterapia*, 77, 346-353, 2006.
8. Paduch R, Wójciak-Kosior M, Matysik G. Investigation of biological activity of Lamii albi flos extracts, *J. Ethnopharmacol*., 110(1), 69-75, 2007.
9. Roussis V, Chinou I, Perdetzoglou D, Loukis A. Identification and bacteriostatic activity of the

essential oil of *Lamium garganicum* L. subsp. *laevigatum* Arcangeli, *J. Essent. Oil*, 8(3), 291-293, 1996.

10. Duman H. *Lamium* L, Güner A, Özhatay N, Ekim T, Bafler KHC (eds.), Flora of Turkey and the East Aegean Islands, University Press, Edinburgh, Vol. 11 (Suppl. 2), 199-200, 2000.
11. Özayd›n S, Dirmenci T, Tümen G, Bafler KHC. Plants used as analgesic in the folk medicine of Turkey. In: Proceedings of the 4th International Congress of Ethnobotany (ICEB 2005), Ertu¤ F (ed.), Ege University Publications, 167-171, 2006.
12. Baytop T, Türkiye'de Bitkiler ile Tedavi (Geçmiflte ve Bugün), 2nd edition, Nobel T›p Kitabevi, ‹stanbul, 163, 1999.
13. Küpeli E, Yalç›n FN, Kaya D, Çal›fl ‹, Yeflilada E, Ersöz T. In vivo anti-inflammatory and antinociceptive activities of some Lamium species growing in Turkey, *J. Ethnopharm*. (submitted) 2007.
14. Yalç›n FN, Kaya D, K›l›ç E, Özalp M, Ersöz T, Çal›fl ‹. Antimicrobial and free radical scavenging activities of four *Lamium* species from Turkey: *L. eriocephalum* subsp. *eriocephalum*, *L. garganicum* subsp. garganicum, *L. garganicum* subsp. *pulchrum, L. purpureum* var. *purpureum*, *Hacettepe University, Journal of Faculty of Pharmacy* 27 (1), 11-22, 2007.
15. Scarpati ML, Guiso M. Lamioside from *Lamium amplessicaule, Tetrahedron*, 22, 4709-4718, 1967.
16. Alipieva KI, Kokubun T, Taskova R, Evstatieva L, Handjieva NV. LC-ESI-MS analysis of iridoid glucosides in *Lamium* species, *Biochem. Syst. Ecol.*, 35(1), 17-22, 2007.
17. Alipieva KI, Taskova RM, Evstatieva LN, Handjieva NV, Popov SS. Benzoxazinoids and iridoid glucosides from four *Lamium* species, *Phytochemistry*, 64(8), 1413-1417, 2003.
18. Ersöz T, Kaya D, Yalç›n FN, Çal›fl ‹, Jensen SR, Gotfredsen CH, Kazaz C, Palaska E. Iridoid glucosides from *Lamium garganicum* subsp. *laevigatum*, *Turk. J. Chem*., 31(2). 155-162, 2007.
19. Yalç›n FN, Ersöz T, Avc› K, Gotfredsen CH, Jensen SR, Çal›fl ‹. New iridoid glycosides from *Lamium eriocphalum* subsp. *eriocephalum*, *Helv. Chim. Acta*, 90(2), 332-336, 2007.
20. Damtoft S. Iridoid glucosides from *Lamium album*, *Phytochemistry*, 31(1), 175-178, 1992.
21. Budzianowski J, Skrzypczak L. Phenylpropanoid esters from *Lamium album* flowers, *Phytochemistry*, 38(4), 997-1001, 1995.
22. Deng YR, He L, Li WQ, Wang HQ. Studies on chemical constituents in herb of *Lamium maculatum* L. var. *kansuense*, *Zhongguo Zhong Yao Za Zhi.*, 28(8), 730-732, 2003; Ref: CA 142: 276784, 2005.
23. Shuya C, Xingguo C, Zhide H. Identification and determination of ecdysone and phenylpropanoid glucoside and flavonoids in *Lamium maculatum* by capillary zone electrophoresis, *Biomed. Chromatogr.*, 17, 477-482, 2003.
24. Ito N, Nihei T, Kakuda R, Yaoita Y, Kikuchi M. Five new phenylethanoid glycosides from the whole plants of *Lamium purpureum* L., *Chem. Pharm. Bull.*, 54(12), 1705-1708, 2006.
25. Saito N, Harborne JB. Correlations between anthocyanin type pollinator and flower colour in the Labiatae, *Phytochemistry*, 31(9), 3009-3015, 1992.
26. Savchenko T, Blackford M, Sarker SD, Dinan L. Phytoecdysteroids fr om Lamium spp: identification and distribution within plants, *Biochem. Syst. Ecol.*, 29(9), 891-900, 2001.
27. Sarker SD, Dinan L, šik V, Rees H. 9δ-*O*-β-D-Glucopyranosyloxy-5-megastigmen-4-one from *Lamium album*, *Phytochemistry*, 45(7), 1431-1433, 1997.
28. Wood KV, Bonham CC, Miles D, Rothwell AP, Peel G, Wood BC, Rhodes D. Characterization of betaines using electrospray MS / MS, Phytochemistry, 59(7), 759-765, 2002.
29. Yuan Z-X, Patel AV, Blunden G, Turner CH. Trans-4-hydroxypipecolic acid betaine from Lamium maculatum, *Phytochemistry*, 31(12), 4351-4352, 1992.
30. Abuzaina AES, Handjieva N, Popov S, Evstatieva L. Volatile constituents from *Lamium maculatum* leaves and *Nepeta mussini* roots, Dokladi na Bolgarskata Akademiya na Naukite 46, 37-39, 1993; Ref: CA 121: 276682, 1993.
31. Alipieva KI, Evstatieva L, Handjieva N, Popov S. Comparative analysis of the composition of flower volatiles from *Lamium* L. species and

Lamiastrum galeobdolon Heist. ex Febr., *Z. Naturforsch.*, 58c, 779-782, 2003.

32. Flamini G, Cioni PL, Morelli I. Composition of the essential oils and in vivo emission of volatiles of four Lamium species from Italy: *L. purpureum, L. hybridum, L. bifidum* and *L. amplexicaule*, *Food Chem.*, 91, 63-68, 2005.
33. Bianco A, Guiso M, Iavarone C, Marini-Bettolo R, Trogolo C. Iridoids XXI. The stereochemistry of ipolamiide and the structure of its natural 8-O-acetyl derivative, ipolamiidoside, *Gazz. Chim. Ital.*, 106, 947-953, 1976.
34. Alipieva KI, Taskova RM, Jensen SR, Handjieva NV. Iridoid glucosides from *Lamium album* and *Lamium maculatum* (Lamiaceae), *Biochem. Syst. Ecol.*, 34(1), 88-91, 2006.
35. Brieskorn CH, Ahlborn R. Lamalbid, ein neues iridoid aus Flores Lamii Albi, *Tetrahedron Lett.*, 41, 4037-4038, 1973.
36. Eigtved P, Jensen SR, Nielsen BJ. A novel iridoid glucoside isolated from *Lamium album* L., *Acta Chem. Scand.* B, 28, 85-91, 1974.
37. Kobayashi S, Mima A, Kihara M, Imakura Y. Iridoid glucosides from *Lamium amplexicaule*, *Chem. Pharm. Bull.*, 34(2), 876-880, 1986.
38. Deng YR, Ding L, Wu SX, Wang HQ. Studies on chemical constituents in herb of *Lamium maculatum* var. *kansuense* (II), *Zhongguo Zhong Yao Za Zhi.*, 30(4), 272-274, 2005; Ref: SciFinder AN: 2006 725494.
39. Bianco A, Melchioni C, Ramunno A, Serafini M. Iridoid glucosides from Lamium garganicum flowers, *Nat. Prod. Res.*, 17(4), 225-227, 2003.
40. Guiso M, Martino C. 6-Deoxylamioside, a new iridoid glucoside from *Lamium amplexicaule, J. Nat. Prod.*, 46(2), 157-160, 1983.
41. Scarpati ML, Guiso M. Lamioside from *Lamium amplessicaule, Tetrahedron*, 22, 4709-4718, 1967.
42. Agostini A, Guiso M, Marini-Bettolo R, Martinazzo G. 5-Deoxylamioside, a new iridoid glucoside from *Lamium amplexicaule* L. and reassignment of OH-6 configuration of ajugol, *Gazz. Chim. Ital.*, 112, 9-12, 1982.
43. Damtoft S, Jensen SR. Hemialboside, a hemiterpene glucoside from *Lamium album, Phytochemistry*, 39(4), 923-924, 1995.
44. Blunden G, Yang M-H, Yuan Z-X, Smith BE, Patel A, Cegarra JA, Mathe JRI, Janicsak G. Betaine distribution in the Labiatae, *Biochem. Syst. Ecol.*, 24(1), 711-81, 1996.
45. Cantino PD, Harley RM, Wagstaff SJ. Genera of Labiatae: status and classification, Harley RM, Reynolds T (eds.), Advances in Labiatae Science, Royal Botanic Gardens, Kew, 511-513, 1992.