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A review on various classes of secondary metabolites and biological activities of Lamiaceae (Labiatae) (2002-2018)

Nousiba A. Abdelaty, Eman Z. Attia, Ashraf N. E. Hamed*, Samar Y. Desoukey.

Department of Pharmacognosy, Faculty of Pharmacy, Minia University, 61519 Minia, Egypt

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Abstract

Lamiaceae (Labiatae) or the mint family is one of the most important families containing volatile oil. It is one of the largest plant families including 236 genera and more than 7,000 species. By reviewing the current available literature (2002-2018), many classes of secondary metabolites of this family were determined, *viz*., flavonoids (113 compounds), fatty derivatives (26 compounds) and sterols (15 compounds). Moreover, plants belonging to this family have been shown many biological activities such as antioxidant, cytotoxic, anti-inflammatory, antibacterial, antifungal, antiviral, analgesic, cardiovascular, hypoglycemic, hypolipidemic, antispasmodic, antiepileptic, anti-anxiety and anti-angiogenic. The most chemically investigated genus is Leonurus, while, *Lavandula latifolia*, *Lamium garganicum*, *Lamium purpureum*, *Melissa officinalis* and *Moluccella laevis* need more phytochemical attention. Regarding the biological investigation, *Melissa officinalis* was the most investigated species. Due to limited phytochemical and biological studies on many genera of this family, we were encouraged to perform this review to help the researchers and orient them to carry out extensive studies on these plants.

Key words

Lamiaceae, Labiatae, phytochemistry, biological activity.

1. Introduction

Lamiaceae is one of the most important families containing volatile oils and was previously called Labiatae, or the mint family. It is one of the largest plant families including 236 genera and more than 7,000 species. Due to ease of cultivation, several plants of Lamiaceae are cultivated for their aromatic characters and are used in perfume, food and medicine industries [1]. Most species of this family are shrubby or herbaceous, whereas trees are extremely rare [2]. The original family name is Labiatae, so given because the flowers typically have petals fused into an upper lip and a lower lip [3]. Although this is still considered an acceptable alternative name, most botanists now use the name "Lamiaceae" in referring to this family.

Various active secondary metabolites with important biological and economical values found in the above mentioned family are volatile oils with (monoterpenes and sesquiterpenes), diterpenes, triterpenes, phenolic acids and flavonoids,…etc [4].

This review potentiates the scientific researchers to carrying out more studies on this family to isolate and develop new natural products with high relative safety and investigate their biological activities and possible mechanisms of action. The literature was collected from 2002 to 2018 using various databases including Google Scholar, PubMed, Science Direct, ChemWeb and Dictionary of Natural Products.

2. Taxonomy

It belongs to Kingdom: Plantae; Subkingdom: Tracheobionta; Superdivision: Spermatophyta; Division: Magnoliophyta; Class: Magnoliopsida; Subclass: Asteranae; Order: Lamiales; Family: Lamiaceae [5].

3. Results and discussion

3.1 Phytochemistry

This review displayed 154 compounds. They are classified into various classes viz., flavonoids flavonoids 113 (flavones 65, flavonols 32, flavanonols 2, flavanols 1, flavanones 12 and isoflavone 1), fatty acids (unsaturated 7 and saturated 9), fatty alcohols 10 and sterols 15. The isolated compounds as well as their chemical structures are shown in Table 1 and Figure 1.

**** Correspondence: Ashraf N. E. Hamed***
***Tel.:** +2086-234-77-59**; Fax:** +2086-236-90-75.*
***Email Address:** ashrafnag@mu.edu.eg*

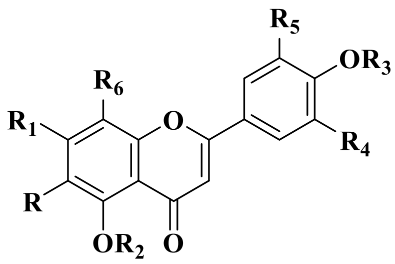
Table 1: A list of some previously reported compounds belonging to various species of family Lamiaceae (2002-2018).

No	Compound	Source	Plant part	Ref.
	I-Flavonoids			
	IA-Flavones			
1	Acacetin	*Leucas aspera*	Whole plant	[6]
		Satureja khuzistanica	Aerial parts	[7]
2	Acacetin-7-*O*-[2'-*O*-*α*-L-rhamnopyranosyl-6"-*O*-*β*-D-glucopyranosyl]-*β*-D-glucopyranoside	*Origanum syriacum*	Aerial parts	[8]
3	Acacetin-7-*O*-rutinoside			
4	Acacetin-7-*O*-glucoside			
5	Apigenin	*Leucas aspera*	Whole plant	[6]
		Stachys tmolea	Aerial parts	[9]
6	Apigenin-7-*O*-glucoside	*Mentha longifolia*	Aerial parts	[10]
7	Apigenin-7-*O*-glucuronide	*Scutellaria adenostegia*	Aerial parts and roots	[11]
8	Apigenin-4',7-dimethylether	*Teucrium polium*	Aerial parts	[12,13]
9	Apigenin-5-galloylglucoside	*Teucrium polium*	Aerial parts	[12]
10	3',6-Dimethoxy apigenin	*Teucrium polium*	Aerial parts	[13]
11	Apigenin-4'-*O*-*α*-D-glucopyranoside	*Elsholtzia rugulosa*	Aerial parts	[14]
12	Apigenin-7-methylether-6-C-glucoside	*Origanum syriacum*	Aerial parts	[8]
13	Chrysoeriol	*Leucas aspera*	Whole plant	[6]
14	Chrysoeriol-7-*O*-*β*-allopyranosyl (1'"→2") 6"-*O*-acetyl-*β*-glucopyranoside	*Stachys spinosa*	Aerial parts	[15]
15	*O*-(6"-O-Acetyl-)-*β*-glucopyranosyl chrysoeriol	*Sideritis lanata.*	Aerial parts	[16]
16	7-*O*-*β*-D-glucopyranosyl chrysoeriol			
17	Cirsilineol	*Satureja khuzistanica*	Aerial parts	[7]
18	Cirsiliol	*Teucrium polium*	Aerial parts	[12]
19	Cirsimaritin	*Salvia officinalis*	Aerial parts	[17]
20	Diosmetin	*Satureja khuzistanica*	Aerial parts	[7]
21	Diosmetin-7-*O*-glucoside	*Origanum syriacum*	Aerial parts	[8]
22	Eupatorin	*Orthosiphon stamineus*	Leaves	[18]
23	3'-*O*-Methyl eupatorin	*Otostegia limbata*	Roots	[19]
24	Ginkwanin	*Salvia officinalis*	Aerial parts	[17]
25	Hispidulin	*Orthosiphon aristatus*	Aerial parts	[20]
26	7-*O*-[(6'"-*O*-acetyl)-*β*-D-allopyranosyl (1→2)-*β*-D-glucopyranosyl] hypolaetin	*Sideritis lanata.*	Aerial parts	[16]
27	7-*O*-[(6'"-*O*-acetyl)-*β*-D-allopyranosyl(1→2)-*β*-D-glucopyranosyl] hypolaetin-3'-methylether			
28	7-*O*-[(6'"-*O*-acetyl)-*β*-D-allopyranosyl (1→2)-*β*-D-glucopyranosyl] isoscutellarein			
29	Isovitexin	*Leonurus japonicus, L. persicus and L. cardiaca*	Aerial parts	[21]
30	Luteolin	*Vitex negundo*	Aerial parts	[22]
31	7-Methoxy luteolin	*Satureja khuzistanica*	Aerial parts	[7]
32	Luteolin-7-*O*-glucuronide	*Scutellaria adenostegia*	Aerial parts and roots	[11]
33	Luteolin-7-*O*-*β*-D-glucopyranoside	*Salvia officinalis*	Aerial parts	[23]
34	6-Hydroxyluteolin-7,3'-dimethyl ether	*Satureja khuzistanica*	Aerial parts	[7]
35	6-Hydroxyluteolin	*Teucrium polium*	Aerial parts	[12]
36	Luteolin-7,4'-dimethyether-6-C-glucoside	*Origanum syriacum*	Aerial parts	[8]
37	Luteolin-3'-methylether-6-C-glucoside	*Elsholtzia rugulosa*	Aerial parts	[14]
38	Luteolin-6-C-glucoside	*Origanum syriacum*	Aerial parts	[8]
39	Luteolin-3'-*O*-*β*-D-glucuronide-6"-methyl ester	*Elsholtzia rugulosa*	Aerial parts	[14]

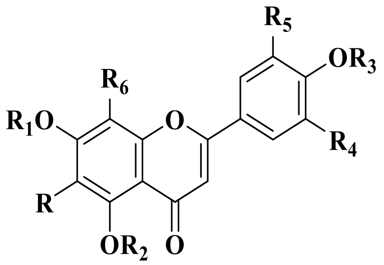
40	Pectolinarigenin	*Orthosiphon aristatus*	Aerial parts	[20]
41	Salvigenin	*Orthosiphon stamineus*	Leaves	[18]
42	Scutellarein	*Scutellaria adenostegia*	Aerial parts and roots	[11]
43	Scutellarin			
44	Sinensetin	*Orthosiphon stamineus*	Leaves	[18]
45	5-Desmethylsinensetin	*Orthosiphon aristatus*	Whole plant	[20]
46	Vicenin-2	*Salvia officinalis*	Aerial parts	[23]
47	Vitexin	*Leonurus japonicus, L. persicus and L. cardiaca*	Aerial parts	[21]
48	Xanthomicrol	*Satureja khuzistanica*	Aerial parts	[7]
49	5-Hydroxy-6,7,3',4'-tetramethoxyflavone	*Orthosiphon stamineus*	Leaves	[18]
50	3',5,6,7-Tetramethoxy-4'-hydroxy-8-C-prenylflavone			
51	5,7,3',4',5'-Pentamethoxy flavone	*Leonurus japonicus, L. persicus and L. cardiaca*	Aerial parts	[21]
52	5,7,3',4'-Tetrahydroxy-5'-C-prenylflavone-7-*O*-*β*-D-glucopyranoside	*Elsholtzia rugulosa*	Aerial parts	[14]
53	3',4',5,7-Tetrahydroxy-8-prenyl flavone			
54	4',5,7-Trihydroxy-3'-*O*-*β*-D-glucuronic acid-6''-methylester	*Vitex negundo*	Leaves	[24]
55	Baicalein	*Scutellaria adenostegia*	Aerial parts and roots	[11]
56	Baicalin			
57	Chrysin	*Elsholtzia bodinieri*	Whole plant	[25]
58	Wogonin	*Leonurus japonicus, L. persicus and L. cardiaca*	Aerial parts	[21]
59	6-Hydroxy-5,7,3'-trimethoxyflavone	*Orthosiphon stamineus*	Leaves	[18]
60	Luteolin-7-*O*-[6-(3-hydroxy-4-methoxy cinnamoyl)]-*β*-D-glucopyranoside	*Elsholtzia bodinieri*	Whole plants	[25]
61	Luteolin-7-*O*-(6-feruloyl)-*β*-D-glucopyranoside			
62	Saturejin (3'-(2,5-dihydroxy-p-cymene) 5,7,4'-trihydroxyflavone	*Satureja khuzistanica*	Aerial parts	[7]
63	Peregrinumin A	*Dracocephalum peregrinum*	Whole plant	[26]
64	Peregrinumin B			
65	Peregrinumin C			
	IB-Flavonols			
66	3-Acetoxy-7-methoxyflavone	*Salvia elegans*	Leaves and flowers	[27]
67	Artemetin	*Vitex negundo*	Aerial parts	[22]
68	Astragalin	*Leonurus japonicus, L. persicus and L. cardiaca*	Aerial parts	[21]
69	Chrysosplenetin	*Vitex negundo*	Aerial parts	[22]
70	Chrysosplenol-D			
71	Hyperoside	*Leonurus japonicus*, L. *persicus* and L. *cardiaca*	Aerial parts	[21]
72	Isoquercetin (syn.: Quercetin-3-*O*-glucoside)	*Leonurus japonicus, L. persicus and L. cardiaca*	Aerial parts	[21]
73	Isorhamnetin-3-*O*-rutinoside			
74	Isorhamnetin 3-*O*-rutinoside-7-*O*-rutinoside-4'-*O*-*β*-glucoside	*Ajuga remota*	Aerial parts	[28]

75	Kaempferol	*Leonurus japonicus, L. persicus and L. cardiaca*	Aerial parts	[21]
76	7,4'-Dimethyl kaempferol	*Elsholtzia rugulosa*	Aerial parts	[14]
77	Kaempferol-3-*O*-[β-D-glucopyranosyl-(1→2)-[β-D-glucopyranosyl (1→3)]-[β-D-glucopyranosyl-(1→4)]-α-L-rhamnopyranoside]-7-*O*-[α-L-rhamnopyranoside]	*Otostegia limbata*	Roots	[19]
78	Kaempferol-3-*O*-[β-D-glucopyranosyl-(1→4)-β-D-6-[4-hydroxy (*E*)-cinnamoyl] glucopyranosyl-(1→3)-[β-D-glucopyranosyl-(1→2)]-α-L-rhamnopyranoside]-7-*O*-[α-L-rhamnopyranoside]			
79	Kaempferol-3-*O*-[β-D-glucopyranosyl (1→4)-[α-L-rhamnopyranosyl-(1→6)]-β-D-glucopyranoside	*Lamium amplexicaule*	Aerial parts	[29]
80	Myricetin	*Leonurus japonicus, L. persicus and L. cardiaca*	Aerial parts	[21]
81	Myricetin-3-*O*-rutinoside-4'-*O*-rutinoside	*Ajuga remota*	Aerial parts	[28]
82	Myricetin-3-*O*-rutinoside-3'-*O*-rutinoside			
83	Penduletin	*Vitex negundo*	Aerial parts	[22]
84	Quercetin	*Salvia officinalis*	Aerial parts	[17]
85	Quercetin-3-*O*-[β-D-glucopyranosyl-(1→4)][α-L-rhamnopyranosyl-(1→6)]-β-D-glucopyranoside	*Micromeria dalmatica*	Aerial parts	[30]
86	Quercetin-3-*O*-β-D-glucuronide-6''-methyl ester	*Elsholtzia rugulosa*	Aerial parts	[14]
87	Quercetagein-3,6,7-trimethyl ether	*Micromeria dalmatica*	Aerial parts	[30]
88	Rutin	*Micromeria juliana*	Aerial parts	[9]
89	Vitexicarpin (syn.: Casticin)	*Vitex rotundifolia*	Aerial parts	[22]
90	Tiliroside	*Leonurus japonicus, L. persicus and L. cardiaca*	Aerial parts	[21]
91	5'-Hydroxy-3',4',3,6,7-pentamethoxyflavone	*Vitex negundo*	Leaves	[24]
92	Leonurusoide A	*Leonurus japonicus*	Aerial parts	[21]
93	Leonurusoide B			
94	Leonurusoide C			
95	Leonurusoide D			
96	Leonurusoide E			
97	2'''-Syringylrutin			
	IC-Flavanonols			
98	Aromadendrin	*Satureja khuzistanica*	Aerial parts	[7]
99	Taxifolin			
	ID-Flavanols			
100	Catechin	*Leucas aspera*	Whole plant	[6]
	IE-Flavanones			
101	Carthamidin	*Scutellaria adenostegia*	Aerial parts and roots	[11]
102	Carthamidin-7-*O*-glucuronide			
103	Eriodictyol	*Elsholtzia bodinieri*	Whole plant	[25]
104	Hesperidin	*Micromeria juliana*	Aerial parts	[9]
105	Miscanthoside	*Elsholtzia bodinieri*	Whole plant	[25]
106	Naringenin	*Satureja aintabensis*	Aerial parts	[9]
107	Naringin			
108	Persicogenin	*Vitex negundo*	Aerial parts	[22]

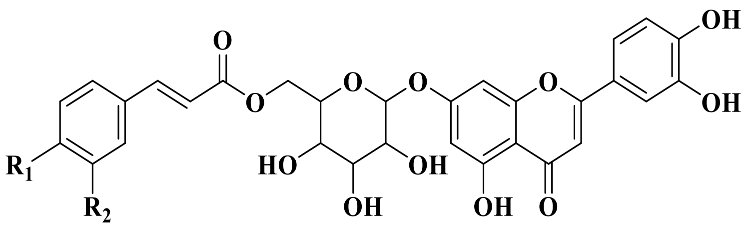
109	5,7,3',5'-Tetrahydroxy flavanone	*Satureja khuzistanica*		[7]
110	5,7,2',4'-Tetrahydroxyflavanone7-*O*-*β*-glucopyranoside (syn.: Steppogenin-7-*O*-*β*-D-glucopyranoside)	*Salvia plebeia*	Whole plant	[27]
111	Eriodictyol-7-*O*-(6''-feruloyl)-*β*-D-glucopyranoside	*Elsholtzia bodinieri*	Whole plant	[25]
112	Eriodictyol-7-*O*-[6''-(3'''-hydroxy-4'''-methoxy cinnamoyl)]-*β*-D-glucopyranoside			
	IF-Isoflavone			
113	Daidzein	*Leonurus japonicus, L. persicus and L. cardia*ca	Aerial parts	[21]
	II-Fatty acids			
	IIA-Unsaturated fatty acids			
114	Linoleic acid	*Micromeria* dalmatica	Aerial parts	[30]
115	α-linolenic acid			
116	Palmitoleic acid			
117	Hexadecadienoic acid			
118	Pentadecadienoic acid	*Sideritis taurica*	Aerial parts	[31]
119	Pentadecenoic acid			
120	Hexadecadienoic acid			
	IIB-Saturated fatty acids			
121	Tetradecanoic acid (Myristic acid)	*Micromeria dalmatica*	Aerial parts	[30]
122	Octadecanoic acid (Stearic acid)			
123	Octanoic acid			
124	Capric acid	*Sideritis taurica*	Aerial parts	[31]
125	Lauric acid			
126	Pentadecanoic acid			
127	Arachidic acid			
128	Lignoceric acid			
129	Behenic acid			
	III-Fatty alcohols			
130	1-Dodecanol	*Micromeria dalmatica*	Aerial parts	[30]
131	1-Tetradecanol			
132	1-Hexadecanol			
133	1-Octadecanol			
134	1-Eicosanol			
135	1-Docosanol			
136	1-Tetracosanol			
137	1-Hexacosanol			
138	1-Octacosanol			
139	Dotriacontanol	*Leucas aspera*	Whole plant	[6]
	IV-Sterols			
140	*β*-Sitosterol	*Leonurus japonicus*	Aerial parts	[21]
141	*β*-Sitosterol-3-*O*-*β*-D-glucopyranoside	*Mentha pulegium and Mentha longifolia*	Aerial parts	[1]
142	Stigmasterol	*Leonurus japonicus*	Aerial parts	[21]
143	Stigmasterol-3-*O*-*β*-D-glucopyranoside	*Plectranthus montanus*	Aerial parts	[32]
144	(22*E*)-Stigmasta-4,22,25-trien-3-one			
145	Stigmasta-4,25-dien-3-one			
146	Stigmasta-4,22-dien-3-one			
147	Clerosterol			
148	Clerosterol-3-*O*-*β*-D-glucopyranoside			
149	22-Dehydroclerostero			
150	22-Dehydroclerosterol-3-*O*-*β*-D-glucopyranoside			
151	Campesterol	*Teucrium polium*	Aerial parts	[12]
152	Brassicasterol			
153	Cholest-5-en-3-*O*-*β*-D-glucopyranoside	*Plectranthus montanus*	Aerial parts	[32]
154	Sitosteryl ferulate			



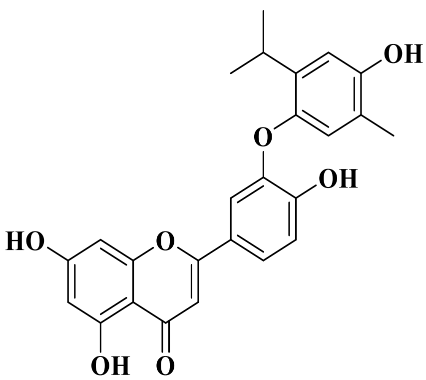
	R	R1	R2	R3	R4	R5	R6
1	H	H	H	Me	H	H	H
2	H	Rha.(2→6)Glc-*β*-Glc	H	Me	H	H	H
3	H	Rutinoside	H	Me	H	H	H
4	H	Glc	H	Me	H	H	H
5	H	H	H	H	H	H	H
6	H	Glc	H	H	H	H	H
7	H	Gluc	H	H	H	H	H
8	H	Me	H	Me	H	H	H
9	H	Galloyl Glc	H	H	H	H	H
10	OMe	H	H	H	OMe	H	H
11	H	H	*α*-Glc	H	H	H	H
12	Glc.	Me	H	H	H	H	H
13	H	H	H	H	OMe	H	H
14	H	All(2→1)Ac *β*-Glc.	H	H	OMe	H	H
15	H	Ac.Glc	H	H	OMe	H	H
16	H	Glc	H	H	OMe	H	H
17	OMe	Me	H	H	OMe	H	H
18	OMe	H	H	H	H	H	H
19	H	Me	H	H	H	H	H
20	H	H	Me	H	H	H	H
21	H	Glc	H	Me	H	H	H
22	OMe	Me	H	Me	H	H	H
23	OMe	H	Me	Me	H	H	H
24	H	Me	H	H	H	H	H
25	OMe	H	H	H	H	H	H
26	H	Ac.All(1→2)Glc	H	H	OH	H	OH
27	H	Ac.All(1→2)Glc	H	H	OMe	H	OH
28	H	Ac.All(1→2)Glc	H	H	H	H	OH
29	O-Glc	H	H	H	H	H	H
30	H	H	H	H	OH	H	H
31	H	Me	H	H	OH	H	H
32	H	Gluc	H	H	OH	H	H
33	H	Glc	H	H	OH	H	H
34	OH	Me	H	H	OMe	H	H
35	OH	H	H	H	OH	H	H
36	Glc	Me	H	Me	OH	H	H
37	Glc	H	H	H	OMe	H	H
38	Glc	H	H	H	OH	H	H
39	H	H	H	H	Gluc (6→Me ester)	H	H
40	OMe	H	H	Me	H	H	H
41	OMe	Me	H	Me	H	H	H
42	OH	H	H	H	H	H	H
43	OH	Gluc	H	H	H	H	H
44	OMe	Me	Me	Me	OMe	H	H
45	OMe	Me	H	Me	OMe	H	H
46	Glc	H	H	H	H	H	Glc
47	H	H	H	H	H	H	Glc
48	OMe	Me	H	H	H	H	OMe
49	OMe	Me	H	Me	OMe	H	H
50	OMe	Me	Me	H	OMe	H	Prenyl
51	H	Me	Me	Me	OMe	OMe	H
52	H	Glc.	H	H	OH	Prenyl	H
53	H	H	H	H	OH	H	Prenyl
54	H	H	H	H	Gluc(6 ester)	H	H



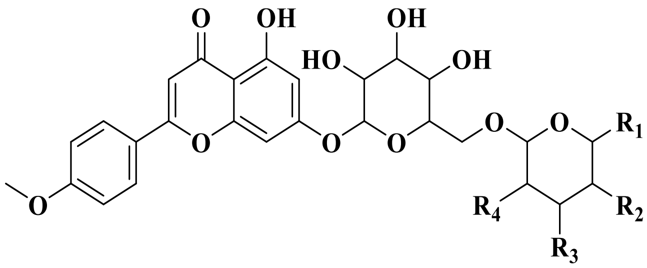
	R	R_1	R_2	R_3	R_4	R_5	R_6
55	**OH**	**H**	**H**	**H**	**H**	**H**	**H**
56	**Gluc**	**H**	**H**	**H**	**H**	**H**	**H**
57	**H**	**H**	**H**	**H**	**H**	**H**	**H**
58	**H**	**H**	**H**	**H**	**H**	**H**	**OMe**
59	**OH**	**Me**	**Me**	**H**	**OMe**	**H**	**H**



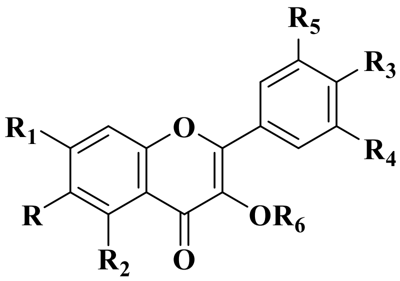
	R_1	R_2
60	**OMe**	**OH**
61	**OH**	**OMe**



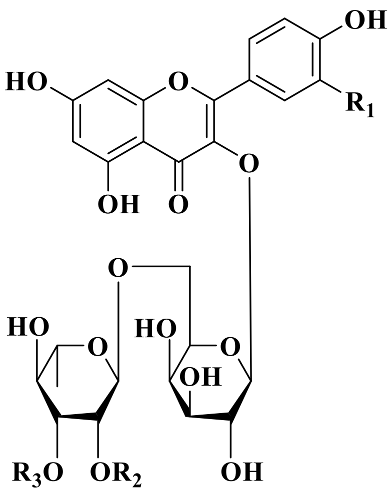
62

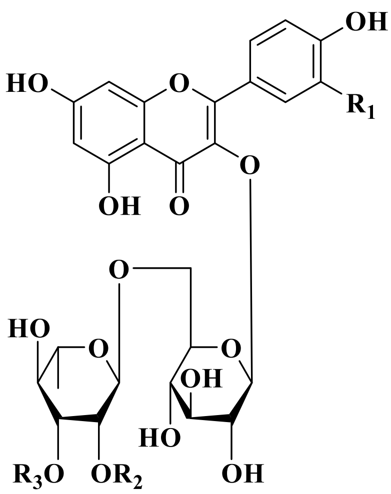


	R_1	R_2	R_3	R_4
63	**Me**	**OH**	**OAc**	**OAc**
64	**Me**	**OAc**	**OH**	**OAc**
65	**Me**	**OAc**	**OAc**	**OH**



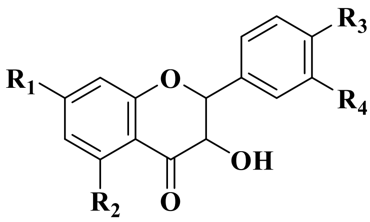
	R	R_1	R_2	R_3	R_4	R_5	R_6
66	H	OMe	H	H	H	H	AC
67	OMe	OMe	OH	OMe	OMe	H	OMe
68	H	OH	OH	OH	H	H	Glc
69	OMe	OMe	OH	OH	OMe	H	OMe
70	OMe	OMe	OH	OH	OH	H	OMe
71	H	OH	OH	OH	OH	H	Gal
72	H	OH	OH	OH	OH	H	Glc
73	H	OH	OH	OH	OMe	H	Rutinoside
74	H	Rutinoside	OH	OGlc.	OMe	H	Rutinoside
75	H	OH	OH	OH	H	H	OH
76	H	OMe	OH	OMe	H	H	OH
77	H	O-α-L-Rha	OH	OMe	H	H	β-Glc(1→2)βGlc(1→3) βGlc(1→4)α-L-Rha
78	H	O-α-L-Rha	OH	OMe	H	H	β-Glc(1→4)-β-6-[4-hydroxy (*E*)-cinnamoyl]Glc-(1→3)-[β-Glc-(1→2)]-α-L-Rha
79	H	H	OH	OMe	H	H	β-Glc(1→4)α-L-Rha(1→6)β-Glc
80	H	OH	OH	OH	OH	OH	H
81	H	OH	OH	Rutinoside	OH	OH	Rutinoside
82	H	OH	OH	OH	Rutinoside	OH	Rutinoside
83	OMe	OMe	OH	OH	H	H	Me
84	H	OH	OH	OH	H	H	OH
85	H	OH	OH	OH	H	H	β-Glc(1→4)α-L-Rha(1→6)β-Glc
86	H	OH	OH	OH	H	H	Gluc.Me.ester
87	H	OH	OH	OH	OH	H	Rutinoside
88	OMe	OMe	OH	OH	OH	H	OMe
89	OMe	OMe	OH	OH	OMe	H	Me
90	H	OH	OH	OH	H	H	(6'-*P*-coumaroyl)Glc
91	OMe	OMe	OH	OMe	OMe	H	OMe

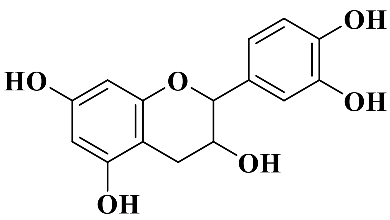




	R_1	R_2	R_3
92	H	syringyl	H
94	H	H	syringyl
96	OH	syringyl	H

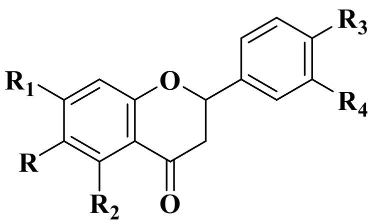
	R_1	R_2	R_3
93	H	syringyl	H
95	H	H	syringyl
97	OH	syringyl	H



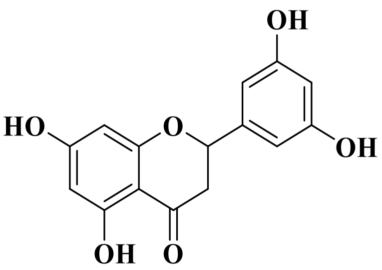


	R_1	R_2	R_3	R_4
98	OH	OH	OH	H
99	OH	OH	OH	OH

100



	R	R_1	R_2	R_3	R_4
101	OH	OH	OH	OH	H
102	OH	Gluc	OH	OH	H
103	OH	OH	OH	OH	OH
104	H	Rutinoside	OH	OMe	OH
105	H	O-Glc	OH	OH	OH
106	H	OH	OH	OH	H
107	H	Glc(2 $\rightarrow$ 1)Rha	OH	OH	H
108	H	OMe	OH	OMe	H



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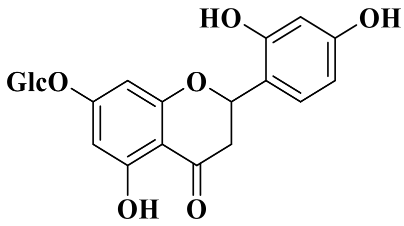

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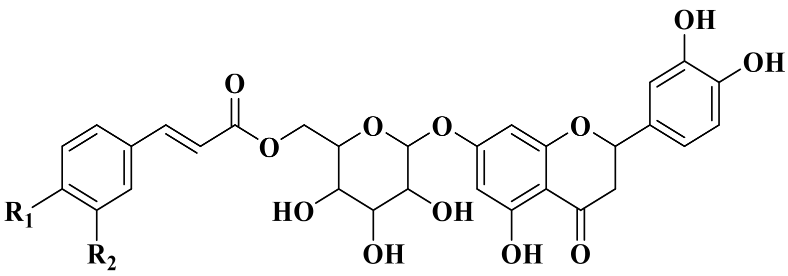
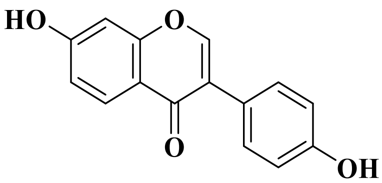


	R_1	R_2
111	OH	OMe
112	OMe	OH



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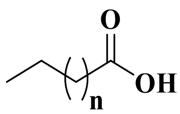
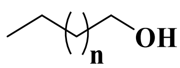
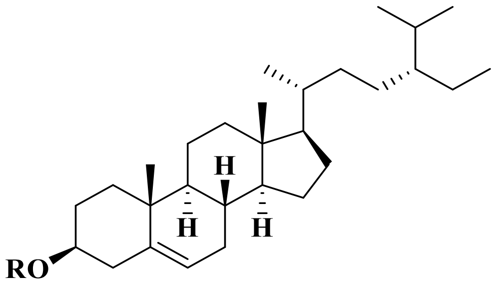


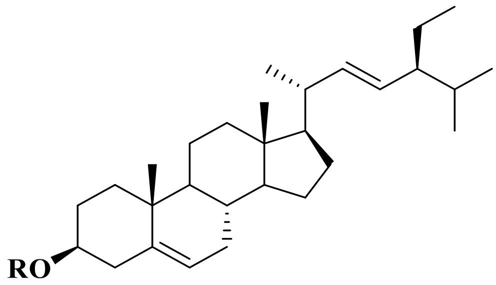
114-n=15& $\Delta^{9,12}$
115-n=15& $\Delta^{9,12,15}$
116-n=13& Δ^{9}
117-n=13& $\Delta^{2,4}$
118-n=12& $\Delta^{2,4}$
119-n=12& Δ^{2}
120- n=12& Δ^{9}
121-n=11
122-n=15
123-n=5
124-n=7
125-n=9
126-n=12
127-n=17
128-n=21
129-n=19



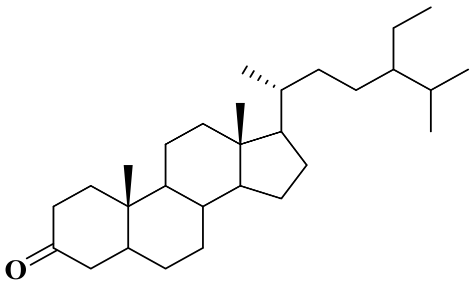
130-n=9
131-n=11
132-n=13
133-n=15
134-n=17
135-n=19
136-n=21
137-n=23
138-n=25
139-n=29



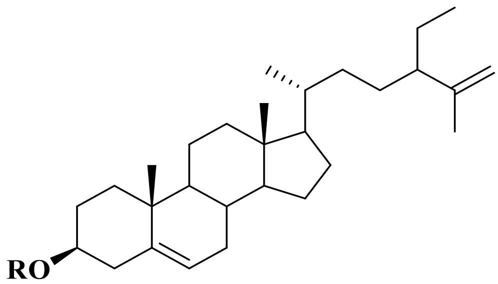
140-R=H
141-R=β-Glc



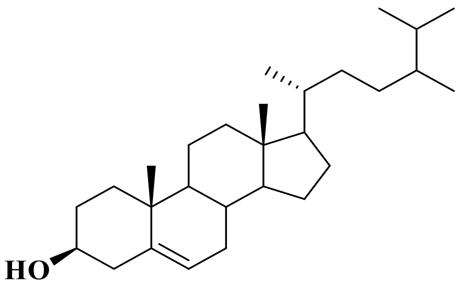
142-R=H
143-R=β-Glc.



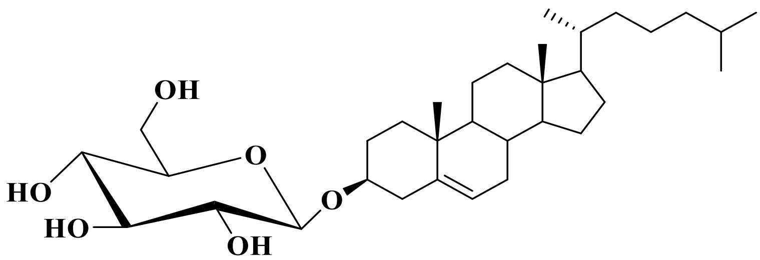
144-$\Delta^{4,22,25}$
145-$\Delta^{4,25}$
146-$\Delta^{4,22}$



147-R=H
148-R=β-Glc
149-Δ^{22}
150-R= β-Glc.Δ^{22}



151
152- Δ^{22}



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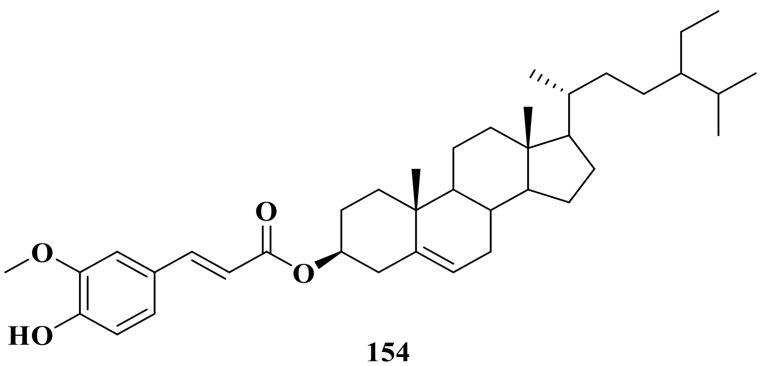

154

Figure 1: Structures of some previously reported compounds belonging to various species of family Lamiaceae (2002-2018).

3.2 Biological activities

Table 2: Biological activities of some plants belonging to family Lamiaceae (2002-2018).

Plant name	Extract, fraction or compound	Method/Result	Ref.
		I-Antioxidant activity	
Ocimum basilicum	Ethanol and aqueous extracts	Anti-lipid peroxidation: both ethanol and aqueous extracts showed an inhibitory effect on peroxidation of linoleic acid emulsion of 97.5% and 94.8%, respectively at the concentration of 50 μg/mL. In DPPH method: the DPPH radical decreased in the order: *α*-tocopherol > butylated hydroxyanisole (BHA) > ethanol extract > butylated hydroxytoluene (BHT) > aqueous extract with scavenging effect of 69%, 67%, 65%, 62% and 55%, respectively at the same above mentioned concentration.	[33]
Teucrium polium	EtOAc extract	DPPH with IC_{50} (10 mg/mL).	[12]
Melissa officinalis	Aqueous extract	In Mn-induced neurotoxicity in a long-term mouse intoxication model: Co-treatment with aqueous extract (100 mg/Kg/day) significantly (p<0.05) attenuated the increase in Mn-induced TBARS levels in the hippocampus and striatum to levels indistinguishable from controls.	[34]
Lavandula latifolia	Lyophilized aqueous extract	In DPPH method, antioxidant capacity was 294.8l g trolox mg/lyophilized extract. In ABTS method, 839.1l g trolox/mg lyophilized extract.	[35]
Micromeria dalmatica	Hydromethanolic extract	DPPH with IC_{50} (21.36 μg/mL).	[30]
		II-Cytotoxic activity	
Melissa officinalis	Volatile oil	*In-vitro* cytotoxicity assay using MTT method: IC_{50} 93.9±0.6% for K562 and 73.9±16.4% for B16F10, at 1:2000 dilution (0.5×10^3). While, IC_{50} 95.2±1.2% for K562 and 45.1±5.8% for MCF-7, at 1:10000 dilution (0.1×10^3).	[36]
	Ethanolic extract	In NR and MTT cytotoxicity assays on HCT-116 cells: the ethanolic extract reduced cell proliferation to 40% at the lowest dose (5 μg /mL).	[37]
Teucrium polium	Essential oil	Highest anti-proliferative effect on CACO-2 cell lines (IC_{50} = 52.7 μg/mL).	[12]
Melissa officinalis	Dichloromethane (DCM) fraction	Induction of apoptosis by DCM fraction at concentration of 50 μg/mL on Jurkat cell line was (85.66 ± 4.9%) and on K562 cell line was (65.04 ± 0.93%) at 24 h after treatment (p<0.002).	[38]
	Hydroethanolic extract (Rosmarinic acid, caffeic acid and luteolin)	Rosmarinic acid, caffeic acid and luteolin had potent cytotoxic activity (IC_{50} values of; 34.6, 41.1 and 62.4 μg/mL, respectively).	[39]
	Hydroethanolic extract	Inhibition of the proliferation of HT-29 and T84 cells with IC_{50} of 346 and 120 μg/mL, respectively as well as apoptosis induction.	[40]
	Aqueous extract	Growth inhibition against HepG-2 and MCF-7 with GI_{50} values of 67 and 51 μg/mL, respectively.	[41]
Orthosiphon aristatus	5-Desmethylsinensetin	Anti-proliferative activity on MDA-MB-435, MCF-7, DU-145, HT-29, DMS-114 and SK-MEL5. (IC_{50}=0.06, 0.03, 2.2, 5.0, 0.11 and 1.1 μg/mL), respectively.	[20]
Moluccella laevis	Methanolic extract	No cytotoxic activity on HT-29 and DLD-1 cell lines at a concentration 100 μg/mL using MTT assay. No anti-angiogenic activity at concentrations 25, 50 and 100 μg/mL in rat aortic ring assay.	[42]
		III-Anti-inflammatory activity	
Sideritis taurica	Dichloromethane (DCM) fraction	In carrageenan induced paw edema method: DCM fraction decreased edema in the rats' paw in a dose dependent manner and at a dose of 300 mg/Kg also, it showed 69.5% of protection compared with indomethacin (5 mg/Kg) that was 81.4%.	[31]
Lamium eriocephalum subsp. eriocephalum, L. garganicum subsp. laevigatum, L. garganicum subsp. pulchrum and L. purpureum var. purpureum	*n*-Butanol	Carrageenan-induced hind paw edema model. *n*-Butanol extracts (200 mg/Kg) of *L. garganicum* subsp. *Laevigatum* (LGLB), *L. garganicum* subsp. *Pulchrum* (LGPB) and *L. purpureum var. purpureum* (LPPB) exhibited notable inhibition (16.5-28.9%, 14.5-26.9%, 12.3-21.5%, respectively). The LGLB (7.1-30.4%) and LGPB (5.9-24.1%) extracts also demonstrated potent anti-inflammatory activity against PGE2-induced hind paw edema model. LGLB and LGPB were also found to show remarkable anti-nociceptive activity in *p*-benzoquinone-induced abdominal constriction test at the same dose (25.0% and 24.3%, respectively).	[43]
Melissa officinalis	Volatile oil	In carrageenan induced paw edema method: essential oil at the doses of 200 and 400 mg/Kg p.o, showed significant inhibition of edema with 61.76% and 70.58%, respectively.	[44]

		IV-Antibacterial activity	
Teucrium polium	Aqueous extract	In a disc diffusion method: (2.5, 10 and 20 g/L), the aqueous extract inhibited the growth of *Saccharomyces cerevisiae* and *Yarrowia lipolytica*. In hole-plate diffusion method: one g/mL was active against both Gram-positive and Gram-negative bacteria.	[12]
Melissa officinalis	Volatile oil	The highest sensitivity to essential oil was observed with *E. coli* with inhibition zones (30.2 and 39.8 mm) and the multiresistant strain of *Shigella sonei* (37.4 and 38.4 mm) at concentration of (20% and 50%), respectively.	[45]
	Petroleum ether, chloroform, ethyl acetate, *n*-butanol and water extracts	Petroleum ether and ethyl acetate extracts were the most effective antibacterial extracts on *Sarcina lutea*.	[46]
	Aqueous extract	The most sensitive bacteria to the aqueous extract were *P. aeruginosa* and *S. typhimurium*, which showed the same MBC as ampicillin (0.40 mg/mL) against *S. aureus* and the same MIC as streptomycin (0.20 mg/mL) against *P. aeruginosa*.	[41]
		V-Antifungal activity	
Melissa officinalis	Volatile oil	The volatile oil exhibited antifungal activity with MFC (15 µL/mL) against *Trichophyton tonsurans* (both 15 µL/mL) as compared with the synthetic antimycotic bifonazole (10 µL/mL).	[45]
		VI-Antiviral activity	
Melissa officinalis	Hydroalcoholic extract	Anti-HSV-2 activity with the maximum inhibiting effect (60%) of 0.5 mg/mL.	[47]
	Volatile oil (Balm oil)	*In vitro* plaque reduction assay on monkey kidney cells: the plaque formation was significantly reduced by using balm oil with 98.8% for HSV-1 and 97.2% for HSV-2.	[48]
	Volatile oil	Inhibition of replication of HSV-2 at a dose of 100 µg/mL.	[49]
		VII-Analgesic activity	
Stachys spinosa	Petroleum ether fraction	At a dose of 400 mg/Kg: the analgesic activity produced by pet. ether is similar to that produced by acetylsalicylic acid (200 mg/Kg) after 45 and 60 min from extract administration.	[31]
Lamium garganicum subsp. *laevigatum* (LGLB) *and L. garganicum* subsp. *pulchrum* (LGPB)	*n*-Butanol	*P*-Benzoquinone-induced abdominal constriction test: LGL-BuOH and LGP-BuOH exhibited remarkable anti-nociceptive activity at a dose of 200 mg/Kg (25.0 and 24.3%, respectively).	[43]
Melissa officinalis	Ethanolic extract	Glutamate-induced nociception: Ethanolic extract given by p.o. route, produced inhibition of glutamate-induced pain of 62.5±5% at a dose of 1000 mg/Kg with ID_{50} values of 198.5 mg/Kg.	[50]
		VIII-Cardiovascular activity	
Melissa officinalis	Ethanolic extract	In $CaCl_2$-induced arrhythmias in rats: ethanolic extract decreased heart rates and percentages of incidence of VPB, VT and VF with the highest activity at (200 mg/Kg) in comparison with the negative control group.	[51]
	Aqueous extract	Using rats' isolated heart The aqueous extract administered at dose level (0.38, 3.8 and 38 mg/Kg) promoted significantly a decrease in cardiac rate (P<0.05).	[52]
	Aqueous extract	In reperfusion-induced lethal ventricular arrhythmias in rats: the aqueous extract produced a decrease in VF at doses of (50, 100 and 200 mg/Kg) compared with control group (treated with amiodarone 30 mg/Kg).	[53]
	Aqueous extract	The aqueous extract (1-1000 mg/mL) produced concentration-dependent relaxation in phenylephrine-precontracted endothelium intact thoracic aorta rings with maximal decrease intension (Emax) 9171.5%.	[54]
		IX-Hypoglycemic activity	
Melissa officinalis	Ethanolic extract	Strong anti-diabetic effects of ethanolic extract in HFD-fed mice was detected, where treated mice revealed significantly reduced concentrations of fasting blood glucose, equally potent to the anti-diabetic drug rosiglitazone (RGZ) with no significant effects on fasting plasma insulin levels. It also significantly decreased the HFD-induced insulin resistance by 35% (P = 0.03), which is approximately half as potent as RGZ (71% decrease).	[55]
	Volatile oil	Effect of long term administration of volatile oil (0.01, 0.02 and 0.04 mg/day) on plasma glucose level: doses of 0.02 or 0.04 mg/day, in diabetic animals significantly (p<0.001 and p<0.001, respectively) decreased levels of plasma glucose as compared with untreated diabetic animals.	[56]
		X-Hypolipidemic activity	
Melissa officinalis	Ethanolic extract	Treatment of insulin-resistant high fat diet-fed mice with ethanolic extract (200 mg/Kg/day) for 6 weeks considerably reduced plasma triacylglycerol, non-esterified fatty acids and LDL/VLDL cholesterol levels.	[55]
	Aqueous extract	The administration of aqueous extract (2 g/Kg/day for 28 days) reduced total	[57]

		cholesterol, total lipid, ALT, AST and ALP levels in serum and LPO levels in liver tissue, but increased glutathione levels in the tissue.	
	Volatile oil	Treatment with volatile oil at 800 mg/L for 24 h reduced cellular TG and total cholesterol concentrations in hepatocytes by 32 and 27%, respectively (p<0.05).	[58]
		XI-Antispasmodic activity	
Melissa officinalis	Volatile oil	The effect of volatile oils on rat isolated ileum contractions: inhibited ileum contraction induced by KCl with an IC_{50} value of 19±2.1 ng/mL, reduced significantly the effect of ACh response with an IC_{50} of 20±2.1 ng/mL and reduced the response to 5-HT with an IC_{50} value of 20±4.1 ng/mL.	[59]
		XII-Antiepileptic activity	
Melissa officinalis	Methanol and aqueous extracts	In the model of PTZ induced seizures, it was observed that methanol extract showed 12.22% and 25.53% protection from seizures at the dose of 250 and 500 mg/Kg, respectively, while the aqueous extract showed 29.59% and 62.24% protection from seizures at the same dose level where, diazepam showed 85% protection from seizures. Antiepileptic activity using MES: the methanol extract 250 and 500 (mg/Kg b.wt.) showed 66.75% and 80.56% inhibition of convulsion, respectively, while the aqueous extract at the same dose levels exhibited 46.59% and 64.61% inhibition of convulsion, respectively, where diazepam inhibited 91.25% of convulsion.	[60]
	Hydroalcoholic extract	Mortality rate was 100% in negative control group, 37.5% in the group injected with 50 mg/Kg b.wt hydroalcoholic extract, 12.5% for the group injected with 100 mg/Kg b.wt of the same extract and 12.5% for the positive control group (treated with Phenytoin).	[61]
		XIII-Anti-anxiety activity	
Melissa officinalis	Hydroethanolic extract	Inhibition of GABA-T resulted in an increase in the availability of GABA in the brain. The results demonstrate that the extract has anxiolytic-like effects under moderate stress conditions and does not alter activity levels.	[62]
		XIV-Anti-angiogenic activity	
Melissa officinalis	Aqueous extract	A polyherbal anti-angiogenic formulation containing aqueous extract has been shown to reduce mRNA levels of angiogenic factors VEGF-A,-B,-C,-D, fibroblast growth factor-2 (FGF-2) and MMPs (MMP-2 and MMP-9).	[63]
		The anti-angiogenic effect of aqueous extract on the sprouting of micro vessels from rat aorta was dose dependent and micro vessel growth was significantly inhibited in the presence of 200 µg/mL aqueous extract.	[64]

Table 3: Biological activities of some plants belonging to family Lamiaceae (2002-2018).

Activity	*Lamium eriocephalum, L. garganicum, L. purpureum*	*Lamium garganicum*	*Lavandula latifolia*	*Melissa officinalis*	*Micromeria dalmatica*	*Moluccella laevis*	*Ocimum basilicum*	*Orthosiphon aristatus*	*Sideritis taurica*	*Teucrium polium*
Antioxidant			+	+	+		+			+
Cytotoxic				+		+		+		+
Anti-Inflammatory	+			+					+	
Antibacterial				+						+
Antifungal				+						
Antiviral				+						
Analgesic		+		+					+	
Cardiovascular				+						
Hypoglycemic				+						
Hypolipidemic				+						
Antispasmodic				+						
Antiepileptic				+						
Anti-Anxiety				+						
Anti-Angiogenic				+						

The aerial parts were the main parts used in 23 genera and 37 species. Moreover, other parts were used as *Scutellaria adenostegia* (aerial parts and roots), *Orthosiphon stamineus* (roots) and *Lamium purpureum* (seeds).

The main secondary metabolites in this review (2002-2018) are flavonoids (113). They are classified into (flavones 65, flavonols 32, flavanonols 2, flavanols 1, flavanones 12 and isoflavone 1). Additionally, 26 fatty compounds were isolated *viz.*, fatty acids (unsaturated fatty acids 7 and saturated fatty acids 9) and fatty alcohols 10. Finally, fifteen sterols were also reported. The most chemically investigated genus is Leonurus, while, *Lavandula latifolia*, *Lamium garganicum*, *Lamium purpureum*, *Melissa officinalis* and *Moluccella laevis* need more phytochemical attention. Regarding the biological investigation, *Melissa officinalis* was the most investigated species as illustrated in Tables 2 and 3.

Conclusion

This review affords valuable information about the different phytoconstituents and biological activities of family "Lamiaceae" including 23 genera and 37 species from 64 references. It is reported that "Lamiaceae" plants contain different classes of chemical constituents including flavonoids, fatty compounds (acid and alcohol) and sterols, together with several medicinal benefits such as; antioxidant, cytotoxic, anti-inflammatory, antimicrobial (antibacterial, antifungal and antiviral), analgesic, cardiovascular, hypoglycemic, hypolipidemic, antispasmodic, antiepileptic, anti-anxiety and anti-angiogenic. According to the present review, many genera of family "Lamiaceae" are considered to be good points of interest that need more studies to explore the mechanisms of action of their pharmacological activities assisting the development and discovering of new or novel natural products.

Declarations of interest

The authors declare that they have no conflict of interest.

Orcid

Ashraf N. E. Hamed orcid.org/0000-0003-2230-9909

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