Solidarité avec la Tunisie
Contre le Coronavirus

JICHA 2-2020

Tunis, le 24 Juin 2020

ATTESTATION

Décernée à:

Hamdi BENDIF

Qui a présenté **un Article Review** aux "**Deuxièmes Journées Internationales sur la Chimie Hétérocyclique et ses Applications**: **JICHA 2-2020**", organisées par l'Association Tunisienne de Chimie Hétérocyclique et ses Applications **STCHA** les 22 et 23 Juin 2020 au Technopole Borj Cedria - Tunisie.

Intitulé:

PHYTOCHEMICAL CONSTITUENTS OF LAMIACEAE FAMILY

Co-auteurs: *Yamina BEN MIRI, Nabila SOUILAH, Amina BENABDALLAH, Mohamed DJAMEL MIARA*

Néji BESBES
Président de la **STCHA**
Président des **JICHA 2-2020**

Taha GUERFEL
Trésorier de la **STCHA**
Président du Comité Scientifique
des **JICHA 2-2020**

Green and Applied Chemistry

RHAZES

CNRSM
Centre National des Recherches en Sciences des Matériaux

RHAZES Green and Applied Chemistry

CiteFactor
Academic Scientific Journals

ISSN: 2605-6895

Indexing and abstracting

- CAS Source Index (CASSI)
- BIBILOTECA
- Citefactor

PHYTOCHIMIE & SUBSTANCES NATURELLES

Rhazes: Green and Applied Chemistry,

Volume 11, 2021, N°2, 71-88

RHAZES: Green and Applied Chemistry

RHAZES: Green and Applied Chemistry, Vol. 11, 2021, 2, 71~88

Phytochemical constituents of *Lamiaceae* family

Hamdi Bendif[a,b*], Yamina Ben Miri[c], Nabila Souilah[d], Amina Benabdallah[e] & Mohamed Djamel Miara[f]

[a] Laboratoire d'Ethnobotanique et des Substances Naturelles, Département des Sciences Naturelles, Ecole Normale Supérieure (ENS), Kouba, BP 92 Kouba, Algiers 16308, Algeria.
[b] Natural and Life Sciences Department, Faculty of Sciences, University of M'sila, BP 166 Msila 28000, Msila, Algeria.
[c] Microbiology and Biochemistry Department, Faculty of Sciences, University of M'sila, M'sila 28000, Algeria.
[d] Natural Sciences and Life Department, Faculty of Sciences, University of Skikda, Skikda 21 000, Algeria.
[e] Laboratory on Biodiversity and Ecosystem Pollution, Faculty of Life and Nature Sciences. University Chadli Bendjedid, El-Tarf, 36000, Algeria.
[f] Department of Biology, Faculty SNV, University Ibn Khaldoun, Tiaret 14000, Algeria.

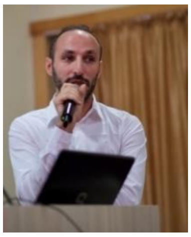
E-mail: hamdi.bendif@univ-msila.dz, sys_yamina@yahoo.com, nabilasouilah21@yahoo.fr, benabdallahamina@hotmail.fr, miara14130@yahoo.fr

Hamdi Bendif[ab] : is an algerian-born (1981), Working at Faculty of Sciences, University of M'sila, Algeria. He involved in reaserch and teaching in biotechnological sciences. He is working on Ethnobotanic, bioactive constituents obtained from Algerian medicinal and aromatic plants and the *in vitro* culture. He has published many papers in these fields (https://www.researchgate.net/profile/Bendif_Hamdi3), in addition, he participated in many conferences in Algeria and out of Algeria.

Yamina Benmiri[c] : is currently a lecturer-researcher in Microbiology and Biochemistry Department at Mouhamed Boudiaf University, M'sila, Algeria. After undergraduation at University of Mouhamed Bougura, Boumerdes, she completed her PhD in Biochimestry, Microbiology and Food science in 2019 at Mouloud Mammri University, Tizi-Ouzou, where her research has focused on the application of plant extracts to reduce mycotoxin in food system.

Nabila Souilah[d] : is originally from Skikda (Algeria). Graduated and holder of a Ph.D. degree in Phytochemistry (Univ Constantine 1). Assistant Professor in Department of Pharmacy (Univ of Constantine 3). Afterwards, she worked in the Univ of Skikda. A member of Laboratory for Valorization of Natural Resources, Bioactive Molecules and Physicochemical and Biological Analyzes.She is Interested inphytochemistry, medicinal plants and ethnobotany.

Amina Benabdallah[e] : is an Algerian lecturer at Chadli Bendjedid University, El tarf, Algeria. She is a part of the laboratory of biodiversity and pollution of ecosystems. Her research expertise field is focused on the valorization of wild Algerian aromatic and medicinal plants, including the extraction and identification of phytochemical substances, such as essential oils and polyphenols. Besides, the evaluation of their biological activities, like antioxidant, antibacterial, antifungal, anti-Alzheimer and antidiabetic propertie.



Mohamed Djamel Miara[f] : holds a PhD in plant ecology from Oran university-Algeria since 2017. He currently works as lecturer-researcher at the faculty of natural and life sciences at the University of Tiaret-Algeria. He is working on several fields related to botany such as: plant ecology, plant taxonomy and ethnobotany. He is also interested in research on endemic taxa and orchids in North Africa. He participates in some research related to ethnobotany such as: ethnopharmacology and phytochemistry.

Abstract

Lamiaceae is a family comprising 236 genera, and more than 7000 species. It is one of the most widely used and phytochemically studied families, because of their various compounds.Lamiaceae can be divided into two major categories, the first one includes all those species that mainly produce volatile terpenoids, found in the volatile compounds, such as *Salvia* sp., *Mentha* sp., Thymus sp. and *Rosmarinus* sp. While the second one comprises species that mainly biosynthesize constituents of the polar fraction, as Ajuga sp., Origanum sp., *Teucrium* sp., *Melittis* sp., and *Stachys* sp. Numerous researches on phytochemicals have led to the identification of many compounds, such as α- and β-pinene, menthol, thymol, eucalyptol, and limonene among the volatile constituents, and mono- and sesquiterpenes. From the other hand, Terpenes phenolic acids (rosmarinic, caffeic acids) and Alkaloids (apigenin, hesperidin), were detected. Therefore, the purpose of this article is to produce a comprehensive review by summarizing the results from the literature on phytochemical constituents of the Lamiaceae family.

Keywords : alkaloids, Lamiaceae, phenolics, phytochemicals, terpenes volatile.

Introduction

In the plant world, naturally synthesized molecules can be classified into two main categories: Primary metabolites and secondary metabolites. Specific enzymes participate in the formation of small molecules which will constitute the basic elements of macromolecules: proteins, nucleic acids, polysaccharides and lipids. These compounds are produced in all cells and play a central role in the metabolism and reproduction of these cells. Their synthesis characterizes growing cells or organisms and constitutes the primary metabolism. In addition, plants have the particularity of having an important secondary metabolism: they synthesize a large number of chemical substances, called secondary metabolites, which are substances that derive from primary metabolites [1]; and which do not participate directly in the development of the plant [2]. Unlike primary metabolites, the products of secondary metabolism are not essential to the survival of the individual but to the survival of the plant population as a whole within its biotope. Their role is not well established, but it would seem that some of these molecules have specific functions as pigment or signal substance (attraction of pollinating insects), phytohormone, defense substance (insects, herbivores, oxidative stress) or precursor synthesis [3]. From a chemical point of view, Lamiaceae family has been the subject of intense investigations in order to isolate different types of compounds such as sterols, flavonoids, iridoids, sesquiterpenes, diterpenes and triterpenes [4]. The aim of this article is to summarize the results from the literature on phytochemistry of different species of Lamiaceae by using various search engines such as Google Scholar, Scopus, PubMed and Science Direct.

Lamiaceae : An overview

The Lamiaceae are a family of flowering plants and one of themost distinctive families, comprising about 236 genera and more than 7,000 species worldwild. Salvia (900 sp.), Scutellaria (360 sp.), Stachys (300 sp.), Plectranthus (300 sp.), *Hyptis* (280 sp.), Teucrium (250 sp.), Vitex (250 sp.), *Thymus* (220 sp.), and Nepeta (200 sp.) are the largest genera [5]. Many of the plants from the Lamiaceae are commonly aromatic and incorporate a wide variety of plants with biological and medical applications after confirmation by researches [6,7] (Table 1). The most known members of this family are a variety of aromatic spices like thyme, mint, oregano, basil, sage, savory, rosemary [8].
The Lamiaceae family alternatively called Labiatae refers to the fact that the flowers typically have petals fused into an upper lip and a lower lip. The flowers are bilaterally symmetrical with five united petals and five united sepals. They are usually bisexual and verticillastrate. Although this is still considered an acceptable alternative name, most botanists now use the name Lamiaceae in referring to this family. The leaves emerge oppositely, each pair at right angles to the previous one or whorled. The stems are frequently square in cross section [9] but this is not found in all members of the family, and is sometimes found in other plant families.

Table 1. Some Lamiaceae species with biological and medical application.

Species	**Medicinal properties due to biological activity**	**References**
Elsholtzia splendens	Antibacterial, anti-inflammatory, antioxidant	[10]
Hyptis suaveolens (L.) Poit.	Carminative, stomachic, and stimulant	[11]
Leucas aspera Willd	Hepatoprotective, antioxidant	[12]
Melissa officinalis L.	Digestive, tranquiliser, antimicrobial, antioxidant	[13]
Mentha arvensis L.	Analgesic, antiseptic, antispasmodic, carminative, antimicrobial	[14]
Micromeria fruticosa (L.) Druce	Anti-inflammatory and gastroprotective	[15]
Ocimum americanum L.	Antiviral	[16]

Ocimum basilicum L.	Antioxidant	[17]
Origanum majorana L.	Antioxidant, antibacterial, expectorant, sedative, carminative, and stimulant	[18]
Perilla frutescens (L.) Britton	Antibacterial and antitumour	[19]
Rosmarinus officinalis L.	Antiseptic, anti-inflammatory, antispasmodic, hepatoprotective, anti-diabetic, anti-ulcerogenic, antidepressant, and antioxidant	[20]
Salvia officinalis L	Antibacterial, allelopathic, and antioxidant	[21]
Satureja hortensis L.	Antibacterial	[22]
Satureja montana L.	Cytotoxic, antioxidant, and antimicrobial	[23]
Scutellaria baicalensis	Cardiovascular, kidney, and liver diseases	[24]
Teucrium chamaedrys L.	Antioxidant	[25]
Thymbra spicata L.	Antioxidant	[26]
Thymus serpyllum L.	Antibacterial, antioxidant, antimalarial, and antiproliferative	[27]
Thymus vulgaris L.	Antioxidant and antibacterial	[28]
Ziziphora clinopodioides Lam.	Antioxidant and antibacterial	[28]
Ziziphora tenuior L.	Anti-diarrhea, febrifuge, and pectoral effects	[29]

Phytochemistry of Lamiaceae

Phytochemicals are chemical compounds synthesized during the plants' metabolic processes [30]. Based on their chemical structurescharacteristics, phytochemicals can be classified into major categories, carbohydrate, lipids, phenolics, terpenoids and alkaloids, and other nitrogen-containing compounds (Figure 1), and each category can be further divided to different subcategories based on biosynthetic origins and similar chemical structures [31].

Various investigations on the chemistry of Lamiaceae are well documented and recent researches are attended to isolate individual components to understand their mechanism. This family contains a vast range ofphytochemicals such as, monoterpenoids, triterpenoids, sesquiterpenoids, phytosterols, flavonoids, organic acids, lignins, glycosides, alcohols and aldehydes.

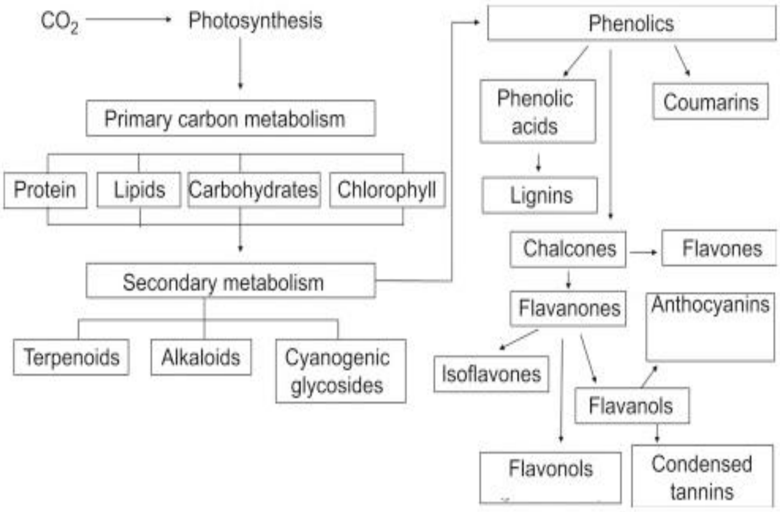


Figure 1. Phytochemical categories [32].

Volatile chemical composition

The main chemical constituents of selected Lamiaceae family plants are presented in Table 2, while the structures of some major and important compounds are described in table 3 and figure 2.

Table 2. The main chemical constituents of selected *Lamiaceae* family plants.

Species	Main Components	References
Dracocephalum heterophyllum Benth.	Citronellol (74.2%), Geraniol (2.8%), cis-Rose oxide (2.2%), Citronellyl acetate (1.7%).	[33]
Hymenocrater longiflorus Benth.	δ-Cadinol (18.49%), α-Pinene (10.16%), p-Menth-1-en-8-ol (9.82%), Hedycaryol (6.42%), β-Eudesmol (4.56%), Spathulenol (4.14%), δ-Cadenene (3.02%), Linalool (2.98%), Caryophyllene oxide (2.81%), β-Bourbonene (2.72%), β-Caryophyllene (2.29%).	[34]
Lavandula multifida L.	Carvacrol (41.5%-42.8%), β-Ocimene (27.0%-27.4%), Myrcene (5.5%-5.7%), β-Bisabolene (5.0%-5.6%), Terpinolene (2.1%-3.1%), α-Farnesene (2.6%-2.8%).	[35]
Lavandula viridis L'Her.	1,8-Cineole (34.5%-42.2%), Camphor (13.4%), α-Pinene, (9.0%), Linalool (6.7%-7.9%).	[36]
Marrubium vulgare L.	γ-Eudesmol (11.93%), β-Citronellol (9.9%), Citronellyl formate (9.5%), Germacrene-D (9.37%), Geranyl formate (6.25%), Geranyl tiglate (5.53%), Ledene (5.35%), 1,8-	[37]

	Cineole (3.72%), Neryl acetate (3.41%), δ-Cadinene (3.3%), Cyclononasiloxane octadecamethyl (3.08%), Geraniol (2.74%), N-trimethylsilyl trifluoroacetamide (2.35%), Eicosamethyl cyclodecasiloxane (2.29%), α-Thujone (2.29%), trans-Caryophyllene (2.15%).	
Mentha requienii Benth.	Pulegone (77.6%), Isomenthone (18.2%), Limonene (1.76%).	[38]
Moluccella spinosa L.	α-Pinene (26.6%), Caryophyllene oxide (16.8%), β-Caryophyllene (8.6%), α-Thujene (5.9%), Nonacosane (5.5%), Heptacosane (5.3%), Ethylbenzaldehyde (3.4%), Pentacosane (2.5%), Tetracosane (2.3%), Sabinene (2.2%).	[39]
Nepeta clarkei Hook. f.	β-Sesquiphellandrene (22.0%), Actinidine (10.0%), Germacrene D (8.0%).	[40]
Ocimum forskolei Benth.	endo-Fenchol (31.1%), τ-Cadinol (12.2%), Fenchone (12.2%), Camphor (6.2%), Linalool (5.7%), Methyl(E)-cinnamate (5.1%), α-Bergamotene (3.1%), γ-Cadinene (2.9%), endo-Fenchyl acetate (2.8%), Limonene (2.5%).	[41]
Origanum majorana L.	Terpinen-4-ol (6.66%-33.84%), Sabinene hydrate (2.31%-28.33%), 1,8-Cineole (0.0%-20.9%), Carvacrol (0.0%-20.8%), γ-Terpinene (7.59%-19.5%), Thymol (0.0%-12.18%), α-Terpinene (3.03%-10.08%), β-Phellandrene (1.96%-8.0%), p-Cymene (2.45%-7.84%), Sabinene (3.2%-6.7%), Limonene (0.0%-5.3%), α-Terpineol (2.7%-4.7%), Linalool (0.0%-4.4%), Terpinolene (0.98%-3.76%), Linalool acetate (1.82%-3.2%), Geraniol (2.7%), β-Caryophyllene (1.7%-2.38%), α-Pinene (0.0%-2.0%).	[42-46]
Pogostemon cablin (Blanco) Benth.	Patchouli alcohol (38.3%-44.52%), α-Bulnesene (0.0%-13.3%), δ-Guaiene (12.64%), α-Guaiene (8.89%-9.6%), Pogostol (0.0%-6.2%), Seychellene (5.8%), α-Bergamotene (5.76%), Eremophilene (4.34%), β-Guaiene (3.54%), β-Caryophyllene (1.93%-3.0%), β-Patchoulene (1.8%-2.77%).	[47,48]
Pogostemon heyneanus Benth.	Acetophenone (51.0%), Patchouli alcohol (14.0%), Nerolidol (5.4%), β-Pinene (5.3%), Limonene (4.0%), Benzoyl acetone (3.1%), α-Pinene (2.4%), β-Caryophyllene (2.0%).	[48]
Premna Microphylla Turcz.	Blumenol C (49.7%), β-Cedrene (6.1%), Limonene (3.8%), α-Guaiene (3.3%), Cryptone (3.1%), α-Cyperone (2.7%), cis-14-nor-Muurol-5-en-4-one (2.4%).	[49]

Salvia mirzayanii Rech. f. and Esfand	1,8-Cineole (41.2%), Linalool acetate (10.7%), α-Terpinyl acetate (5.7%), Myrcene (4.7%), Geranyl acetate (3.7%), γ-Cadinene (3.3%), Linalool (2.5%), Neryl acetate (2.3%).	[50]
Satureja Montana L.	Carvacrol (47.1%), p-Cymene (9.0%), γ-Terpinene (6.1%), β-Caryophyllene (3.6%), Linalool (3.1%), Thymol (2.6%), Borneol (2.1%).	[43]
Stachys pubescens Ten.	Germacrene (22.4%), δ-Cadinene (19.7%), 2,6-Octadien (11.5%), Linalool (9.7%), Limonene (6.3%), δ-Elemene (5.4%), β-Ocimene (2.8%), α-Terpinene (2.7%), 2,6-Octadienal (2.1%).	[43]
Thymus serpyllum L.	Thymol (52.6%), p-Cymene (15.3%), β-Caryophyllene (6.8%), Sabinene hydrate (3.8%), γ-Terpinene (2.9%), Terpinen-4-ol (2.4%).	[43]
Vitex agnus-castus L.	Bicyclogermacrene (0.0%-16.2%), β-Farnesene (0.0%-16.1%), Sabinene (0.0%-14.57%), Sclarene (0.0%-10.9%), α-Pinene (0.9%-9.76%), Manool (0.0%-8.2%), β-Caryophyllene (3.0%-6.6%), β-Caryophyllene oxide (0.0%-5.83%), Limonene (0.0%-4.89%), Vulgarol B (0.0%-4.7%), β-Pinene (0.4%-4.4%), α-Terpinyl acetate (1.2%-4.21%), β-Sitosterol (3.13%), p-Cymene (0.0%-3.11%), Geranyl linalool (0.0%-3.1%), β-Phellandrene (0.0%-3.0%), Cembrene A (0.7%-2.8%), Beyrene (0.0%-2.6%),β-Myrcene (trace-2.12%), γ-Elemene (2.11%), s-Cadinol (2.01%).	[51,52]
Zataria multiflora Boiss.	Thymol (25.8%-48.4%), Carvacrol (1.5%-34.36%), Carvacrol methyl ether (0.0%-28.32%), p-Cymene (2.27%-13.2%), γ-Terpinene (0.92%-10.6%), Linalool (0.9%-6.52%), α-Terpinenyl acetate (5.4%), α-Terpineol (0.5%-3.69%), α-Pinene (0.02%-3.13%),β-Caryophyllene (2.24%-3.12%), Carvacrol acetate (0.0%-2.26%), Terpinen-4-ol (0.0%-2.21%)	[53,54]

The chemical composition of the essential oils from inflorescences and vegetative parts of *Thymus munbyanus* subsp. *coloratus* showed that the essential oils were dominated by oxygenated monoterpenes (68.2% in flowers and 59.4% in vegetative parts), monoterpene hydrocarbons (12.1% and 24.4%, respectively), sesquiterpene hydrocarbons (11.0% and 8.5%, respectively) and oxygenated sesquiterpenes (6.7% and 4.9%, respectively) [55a].

A study was conducted on the chemical composition of essential oils, pressurized liquid extracts (PLE) and supercritical fluid extracts (SFE-CO_2) obtained from *Thymus munbyanus* subsp. coloratus (TMC) and subsp. *munbyanus* (TMM). Essential oils and SFECO_2 extracts were analyzed by GC-FID and Gas chromatography-time-of-flight mass spectrometry (GC×GC-TOFMS). The essential oils of TMC and TMM were characterized by a high content of oxygenated monoterpenes (63.5 and 53.8%, respectively), oxygenated sesquiterpenes (17.4 and 24.6%, respectively) and monoterpene hydrocarbons (6.8 and 13.1%, respectively). On the other hand, TMC and TMM SFE-CO_2 extract were rich in long chain hydrocarbons such as squalene (10.8 and 11.4%, respectively) and n-triacontane (6.5 and 8.9%, respectively) [56a].

The volatile chemical composition of hydrodistilledessential oils from the three parts of *Rosmarinus eriocalyx*growing in Algeria were analyzed by GC/MS. The investigation revealed that the main volatile constituents in the three parts were monoterpenoids such as camphor (29.7% in flowers, 36.9% in leaves and 41.2% in stems), α-pinene (7.8% in stems, 15.1% in flowers and 17.8% in leaves), camphene (10.0% in stems, 13.1% in flowers and15.6% in leaves) and 1,8-cineole (3.5% in flowers, 5.8% in stems and 10.2% in leaves [57b]. In the same year, Bendif et *al*. [58c], developed a more sensitive, precise and accurate headspace solid phase microextraction (HS-SPME) coupled with gas chromatography mass spectrometry (GC/MS) technique to identify and qualify the volatile compounds from different parts of *Rosmarinus eriocalyx*such as camphor (68.2% in stems, 45.8% in flowers, and 20.3% in leaves), camphene (37.4% in leaves and 15.5% in flowers), α-pinene (9.8% in flowers and 23.1% in leaves) and 1,8-cineole (7.9% in flowers and 10.8% in leaves). These main compounds were higher amounts compared with that previously reported for essential oils of the same plant. The authors attributed the difference to the absence of heat- and water-dependent oxidative and hydrolytic reactions that can occur during hydrodistillation yielding artifact products, and that, on the contrary, do not occur during SPME procedure. Contrary, in the SFE-CO_2 extracts these compounds were at poor (camphor 3.2%) or trace (α-pinene and 1,8-cineole) levels [59b].

GC×GC-TOFMS was used for studying the chemical composition obtained from vegetative parts and flowers of *Teucrium polium* L by two methods hydrodistillation and SFE-CO_2. In hydrodistillation, Germacrene D (13.8%), β-eudesmol (8.7%), bicyclogermacrene (4.9%), and (E)-caryophyllene (4.2%) were introduced as the principal components of vegetative partsessential oil, while germacrene D (12.5%), shyobunol (5.6%), δ-cadinene (4.7%), and bicyclogermacrene (4.6%) were the major components in flowers. The chemical composition of *Teucrium polium* SFE-CO_2 extracts was different. Shyobunol (3.9%), β-eudesmol (6.3%), germacrene D (2.7%), and elemol (2.7%) were the major compounds in extract from the vegetative parts; while the flowers extracts were dominated by germacrene D (7.8%), δ-cadinene (7.7%), and α-cadinol (4.2%) in the flowers extract [60c].

In the study performedby Giatropoulos et *al*. [61], 14 EOs derived from12 Lamiaceae plant speciessuch as *Thymusvulgaris*, *Ocimum basilicum*, *Origanum dictamnus*, *Origanum majorana*, *Origanumvulgare*, *Mellisaofficinalis*, *Mentha spicata* and *Satureja thymbra* were characterized by the presence of a high number of terpenes in the EOs. In results presented by Piras et al. [62], the main compounds were methyl eugenol (84.7%) and β-caryophyllene (7.4%) for *Ocimum tenuiflorum* and linalool (35.1%), eugenol (20.7%) and 1,8-cineole (9.9%) for *Ocimum basilicum*, while in Mehalaine et al. [63], GC–MS analysis of essential oils extracted from three aromatic plants *Thymus algeriensis* Boiss & Reut, *Rosmarinus officinalis* L., and *Salvia officinalis* L. indicated the dominance of camphor (17.09% and 13.62%, respectively) for *Rosmarinus officinalis* L and *Thymus algeriensis*,and β-thujone (16.44%) for *Salvia officinalis* L.

The essential oils from *Cantinoa althaeifolia*, *Cantinoa heterodon*, *Cantinoa mutabilis*, *Cantinoa stricta* and *Cantinoa sylvularum* collected from Rio Grande do Sul, South Brazil and its volatile chemical compositions were analyzed by GC/MS. The study revealed the essential oils of these species, demonstrated the presence of β-pinene, δ-3-carene, β-caryophyllene, bicyclogermacrene, caryophyllene oxide and globulol in higher amounts. Besides monoterpenes and sesquiterpenes, three species presented diterpenes. Kaurenoic acid was isolated from *C. heterodon* exudate and detected by gas chromatography in *Cantinoa stricta* and *Cantinoa mutabilis.* Although kaurane diterpenes are widely found in nature, their occurrence in Lamiaceae seems to be restricted to few genera [64]. The GC/MS profile of the *Phlomis kurdica* Rech. Fil. Essential oil showed the dominance of germacrene D (55.4%), (*Z*)-β-farnesene (11.2%), and hexadecanoic acid (8.4%) [65]. Two *Thymus* species were investigated by Küçükaydın et *al*. [66], the major compounds of essential oil of *Thymus cariensis* were germacrene D (33.59%) and carvacrol (14.86%), whereas the main compounds of essential oil of *Thymus cilicicus* were borneol (16.97%), 1,8-cineol (16.78%), and camphor (12.54%). Some authors have described that the content of active substances varies depending on the geographical origin of the plant, the extraction technique, the time of harvest and climatic factors. The essential oil of *Thymus capitatus* from western Algeria were composed mainly of thymol (51.22%), carvacrol (12.59%) and γ-terpinene (10.3%) [67]. However, *Thymus capitatus* essential oil from Tizi Ouzou, Algeria comprised of thymol (25.82%), linalool (23.40%), and geraniol (14.22%) [68]. *T. capitatus* EO of Morocco were composed mainly of carvacrol (55.59%) and *p*-cymene (11.23%) [69].

Table 3. Classification of some main volatile constituents in the *Lamiaceae* family.

Components	Formula	Classification
1,8-Cineole	$C_{10}H_{18}O$	Bicyclic monoterpenoid
Camphene	$C_{10}H_{16}$	Bicyclic monoterpene
Camphor	$C_{10}H_{16}O$	Bicyclic monoterpenoid
Carvacrol	$C_{10}H_{14}O$	Cyclic monoterpenoid
Carvone	$C_{10}H_{14}O$	Cyclic monoterpenoid
Caryophyllene	$C_{15}H_{24}$	Bicyclic sesquiterpene
Caryophyllene oxide	$C_{15}H_{24}O$	Bicyclic sesquiterpene
Estragole	$C_{10}H_{12}O$	Cyclic phenylpropanoid
Germacrene D	$C_{15}H_{24}$	Cyclic sesquiterpene
Limonene	$C_{10}H_{16}$	Cyclic monoterpene
Linalool	$C_{10}H_{18}O$	Acyclic monoterpenoid
Menthol	$C_{10}H_{20}O$	Cyclic monoterpenoid

Ocimene	$C_{10}H_{16}$	Acyclic monoterpenoid
Perillaldehyde	$C_{10}H_{14}O$	Cyclic monoterpenoid
Thymol	$C_{10}H_{14}O$	Cyclic monoterpenoid
α-Pinene	$C_{10}H_{16}$	Bicyclic monoterpene
α-Terpinene	$C_{10}H_{16}$	Cyclic monoterpene
α-Terpineol	$C_{10}H_{18}O$	Cyclic monoterpenoid
β-Pinene	$C_{10}H_{16}$	Bicyclic monoterpene
γ -Terpinene	$C_{10}H_{16}$	Cyclic monoterpene

In the work of [71], GC–MS analysis of extracted by hydrodistillation from *Thymus capitatus*collected at different growth times extracted from *Thymus capitatus*, identified 55 components while carvacrol (81.2-14.2%), γ-terpinene (34.4-2.6%) and *p*-cymene (22.8-5.0%) were the major compounds. Singh and Pandey [72] in their review on chemical composition of essential oils of some Mentha species from different geographical regions reported that most of the oils being rich in pulegone, menthon, menthol, carvone, 1,8-cineole, limonene and β-caryophyllene. According to Scalas et al. [73], the major compounds in *Thymus vulgaris* essential oil were thymol and its precursor p-cymene (26.52%, and 16.26%, respectively), limonene (13.20%), α-pinene (11.50%), carvacrol (7.85%), and γ-terpinene (4.02%), while *Origanum vulgare* essential oil was found to be rich in carvacrol (62.61%), p-cymene (12.36%), and in γ-terpinene (7.60%). *Thymus albicans* HOFFMANNSvolatiles were collected by SPME and analyzed by GC/MS and by GC for component identification and quantification, respectively. Of the 23 components identified, 1,8-cineole was the dominant volatile (57-93 %) in all *Thymus albicans* plant organs (leaves, bracts, calyx, corolla and inflorescences) [74].

The commercial essential oils of Tunisian *Rosmarinus officinalis*, *Thymus capitatus*, *Origanum majorana* and *Salvia officinalis* were dominated by carvacrol, 1,8-cineole, α-thujone, α-terpineol and α-pinene [75]. GC-MS/FID was used to identify and quantify the volatile constituents of three *Salvia* species, *Salvia africana-lutea*, *Salvia lanceolata* and *Salvia chamelaeagnea* from South Africa. The essential oils of *Salvia africana-lutea* consisted mainly of terpinene-4-ol + β-caryophyllene (1.4-29.0%), T-cadinol (1.2-20.0%), α-eudesmol (trace-23.0%) and β-eudesmol (trace-26.0%), those of *Salvia lanceolata* comprised mainly terpinene-4-ol + β-caryophyllene (4.3-31.0%), α-humulene (2.3-15.0%), bicyclogermacrene (trace-37.0%) and spathulenol (trace-25.0%), while the EOs of *Salvia chamelaeagnea* were found to be rich in δ-3-carene (trace-18.0%), limonene (1.6-36.0%), viridiflorol (9.8-61.0%) and 1,8-cineole (not detected-11.0%) [76]. Semerdjieva et al. [77] in their study assessed the variability of essential oil chemical composition of *Satureja pilosa* Velen. Senso lato collected at 33 areas across the Balkan and Rhodope Mountains in Bulgaria. Through the GC-MS analysis, thymol and carvacrol were the major constituents of the phenolic monoterpenoids. Thymol varied from 36.6% to 67.1% and carvacrol varied from 52.4% to 93.0% of the total oil. p-cymene also varied widely, from 9.6%-34.0%. The study identified many chemotypes such as (1) thymol and p-cymene; (2) thymol, p-cymene and

γ -terpinene; (3) carvacrol and p-cymene; (4) carvacrol, p-cymene and γ-terpinene; and (5) carvacrol.

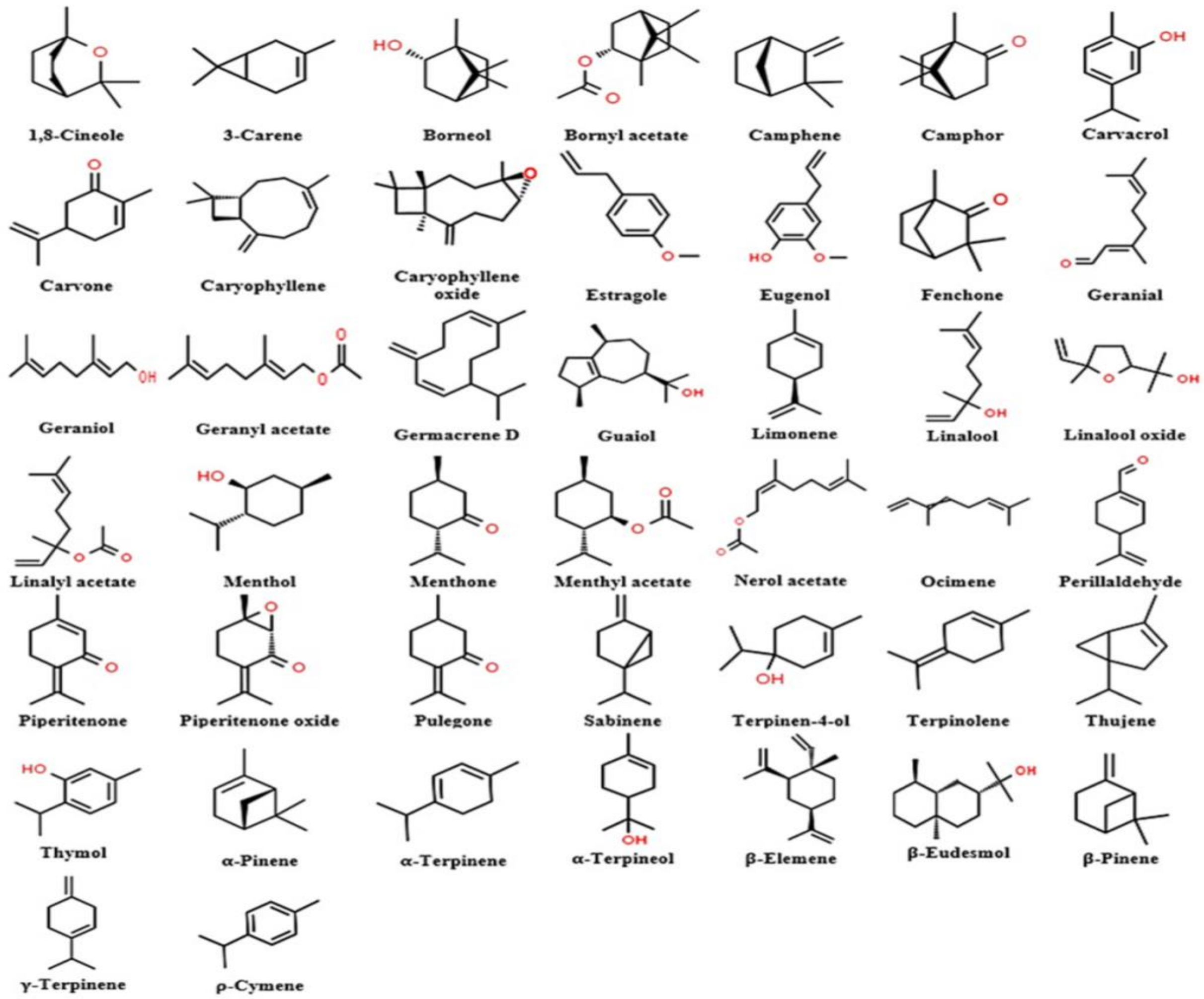


Figure 2. Chemical structure of main compounds of the *Lamiaceae* family [70].

Seven EOs from different species of *Ocimum*, an unknown sample, and a commercial sample were evaluated and compared to those from established and precise GC-MS and GC-FID methods. Chemometric evaluation from both ^{1}H NMR and GC-MS data revealed three chemotypes (Figure 3), eugenol for *Ocimum gratissimum*, *Ocimum micranthum*,and *Ocimum tenuiflorum*; estragole for *Ocimum basilicum*, *Ocimum basilicum* var.purpuracen, and *Ocimum selloi*; and methyl cinnamate for *Ocimum americanum*. The unknown and commercial species were cinnamate and eugenol chemotypes, respectively [78]. Mohammedi et al. [79] used GC-MS and ^{13}C-NMR to analyze the chemical composition, of EOs of Algerian *Ruta montana* from seven different regions. The major compounds identified were 2-undecanone (27.2-81.7%), 2-nonanone (1.9-39.5%) and 2-nonanyl acetate (tr -24.8%).

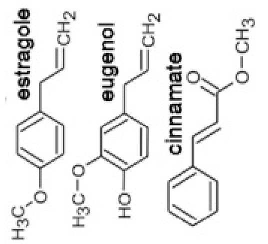


Figure 3. Chemotypes [78].

Non-Volatile chemical composition

Various phytochemicals belonging to phenolcarboxylic and cinnamic acids and their derivatives, flavonoids, among which areflavones,isoflavones, flavanols, flavanones, flavanones, flavans, flavans 3,4-diols, catechins, biflavonoids and proanthocyanidins.In addition to glycosides, triterpenes, lignins, aldehydes, and organic acids along with few other constituents were found as major and minor non-volatile components of Lamiaceae [80]. According to Wang et al. [81], more than 280 chemical compounds have been isolated and identified from different species of the genus *Clerodendrum* comprising 58 diterpenoids, 31 triterpenoids, 43 flavonoid and flavonoid glycosides, 40 phenylethanoid glycosides, 43 steroids and steroid glycosides, 13 cyclohexylethanoids, 4 anthraquinones, 2 cyanogenic glycosides. HPLC-DAD and LC-MS/MS analysis demonstrated that the composition of the infusion of *Salvia sclareoides* Brot were *luteolin diglucuronide, sagerinic acid,rosmarinic acid and luteolin-7-O-(6´´- O-acetylglucoside), while* rosmarinic acid was identified as the major component [82]. Aghakhani et al. [83] investigated the chemical constituents of *Phlomis* species including *Phlomis kurdia*, *Phlomis aucheri*, *Phlomis olivieri*, *Phlomis bruguieri*, *Phlomis persica, Phlomis anisodonta* and *Phlomis elliptica* using liquid chromatography tandem mass spectrometry (LC–MS/MS) technique on a triple quadrupole mass spectrometer (TQMS) isolating 35 chemical compounds from which 32 were identified as flavonoids through comparison with published literature and reference standards. These compounds were distributed in four flavonoid classes, Flavones (12), flavonols (11), flavanones (8) and flavane (1). The flavonoids such as naringenin, chrysoeriol, eriodictyol, dimethoxyflavanone, apigenin, luteolin, kaempferol and rhamnetin were in high proportions. Chen et al. [84] identified 14 compounds eight neo-clerodane diterpenes, two phytoecdysteroids, one stigmastane sterol and three iridoid glycosides of *Ajuga forrestii* Diels. Frezza et *al*. [85] isolated and identified eight constituents from *Teucrium chamaedrys* L. by means of classical column chromatography and spectroscopic techniques, such as NMR and MS, namely verbascoside, forsythoside b, samioside, alyssonoside, harpagide, 8-*O*-acetyl-harpagide, cirsiliol and β-arbutin. By HPLC, 1D and 2D NMR , and spectrometric ESI-HRMS analysis, Saidi et *al*.[86], characterized iridoid glycosides, tunispinosides A-D, phenylethanoid glycosides, verbascoside, leucosceptoside A, martynoside, isoverbascoside and plantainoside C, together with 4-hydroxy-2,6-dimethoxyphenyl 6′-*O*-vanilloyl-*β*-D-glucopyranoside, 8,3′-neolignan glycosides, plucheosides D_1-D_2, coniferyl aldehyde, vanillic acid, syringic acid, ferulic acid and tyrosol from the trunk bark ethyl acetate extract of *Citharexylum*. Delnavaziet al.[87] studied the chemical constituents of the aerial parts of *Stachys lavandulifolia* Vahl and isolated 9 compounds using ^{1}H-NMR, ^{13} C-NMR, UV and EIMS spectral analyses to identify; pachypodol, chrysosplenetin, kumatakenin, velutin, penduletin, viscosine, chrysoeriol, hydroxygenkwanin and apigenin (Figure 4).

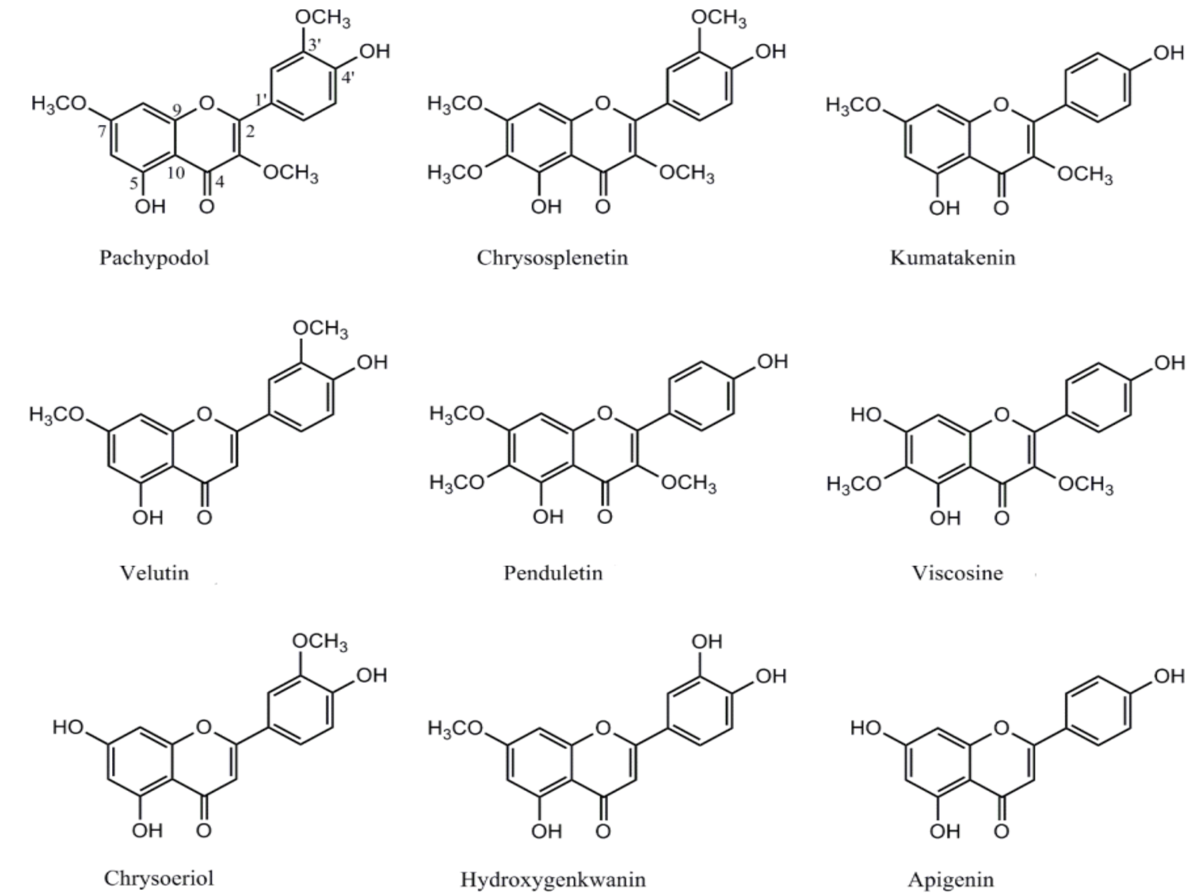


Figure 4. Structures of the isolated compounds.

From the aerial parts of *Stachys lavandulifolia* [87].On the basis of 1D and 2D NMR spectroscopy, UV, MS, Qiu et *al*. [88] identified a new diterpene,2β,14-dihydroxy−11-formyl-12-carboxy-13-des-isopropyl-13-hydroxymethyl-abieta-8,11,13-triene-16(17)-lactone, along with the known compounds12,18-dicarboxy-14-hydroxy-13-des-isopropyl-13-hydroxymethyl- abieta-8,11,13-triene-16(17)-lactone, 5-hydroxy-3′,4′,7-trimethoxyflavone, 5-hydroxy-4’,7-dimethoxyflavone, luteolin-7-O-β-glucoside, verbascoside, luteolin 7-O-(6″-O-β-D-apiofuranosyl)-β-D-glucopyranoside, chlorogenic acid, echinacoside, apigenin-7-O-β-D-glucoside, p-coumaric acid, vanillic acid, apigenin-7-O-(6″-*E*-p-coumaroyl)-β-D-glucopyranoside, apigenin-7-O-(3″,6″-*E*-p-dicoumaroyl)-β-glucoside, lamalbide, 6β-hydroxy-7-*epi*-loganin, phloyoside II from *Eremostachys moluccelloides* Bunge. TaoXu et *al*. [89] identified 12 undescribed phenylethanoid glycosides (nepetifosides A–L) and one undescribed phenylmethanoid glycoside (nepetifoside M) from the *n*-butanol fraction of *Schnabelia nepetifolia* (Benth.) P. D. Cantino by 2D-NMR and chemical-hydrolysis methods.Alexa et *al*. [90] reported that the main constituents of *Mentha* × *piperita* L. and *Lavandula angustifolia* Mill. were hydroxycinnamic acid content, in particular, caffeic, p-cumaric, ferulic, and rosmarinic acids using LC-MS. Four abietane-type diterpenoids (Figure 5), sahandone, sahandol, 12-deoxy-salvipisone and sahandinone were identified from Salvia sahendica Boiss. & Buhse by the mean of HR-ESIMS, 1D and 2D NMR spectroscopy [91].

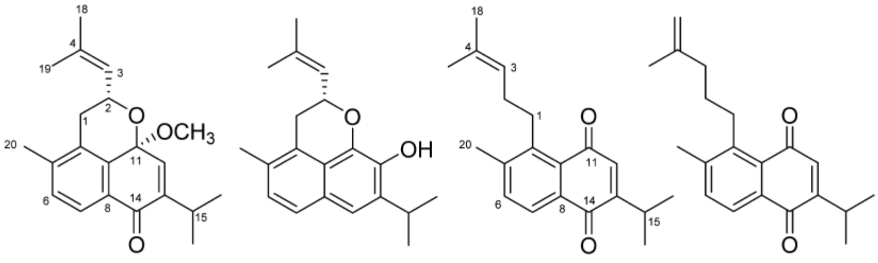


Figure 5. The fourabietane-type diterpenoids identified in *Schnabelia nepetifolia* [91].

Chemical compounds of *Salvia circinata* were determined and quantified using HPLC-DAD identified by comparison of the values of ^{1}H NMR, ^{13}C NMR and ESIMS reported in the literature. These compounds were terpenoids (Amarisolide A, ursolic acid, oleanolic acid, α-amyrin, and β- sitosterol) (Figure 6), phenolic acids (Ferulic acid, caffeic acid, and chlorogenic acid), and flavonoids **(**Quercetin, phloretin, were rutin, phlorizin, and pedalitin) [92].

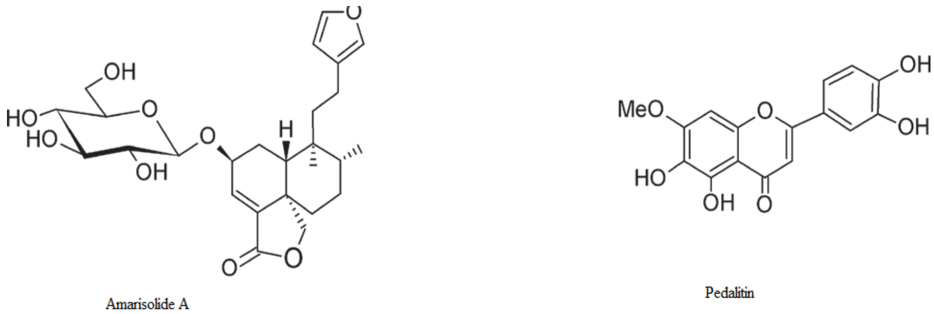


Figure 6. Structure of *amarisolide A and pedalitin* [92].

Chemical investigation of *Leucas zeylanica* (L.) B. Br. led to isolation of a new norditerpenoid isomer, with other compounds, including norditerpenoid, flavonoid glycosides, flavonoids, phytosterols, phenylpropanoids, phthalate esters, phenolic compounds, five terpenoids, aliphatic glycoside, nucleobase, amino acid, alkaloids, and cytochalasin. The structures of these compounds were identified using NMR spectroscopic methods [93]. Two new diterpenes, kunminolide A and rabdokunmin F were determined from the leaves of *Isodon interruptus* by spectroscopic means including analysis of 1D- and 2D-NMR spectral data [94]. The HPLC-DAD showed that the main phenolic acids were caffeic acid, sinapic acid, ferulic acid, and p-coumaric acid. As well, apigenin, luteolin, and quercetin were identified as the main flavonoid aglycones present in *Marrubium vulgare* [95]. Oxygenated diterpenoids were isolated from the aerial parts of *Leonurus japonicus* Houtt. 14,15-Dinor-labd-5,8-dien-3,13-dione and 7*β*,9*α*-Dihydroxy-6-oxo-labd-13-en-15,16-amide represented a rare example of labdane diterpenoid featuring an *α*,*β*-unsaturated-*γ*-lactam [96].

Conclusion

Lamiaceae family is being explored globally to obtain chemical constituets for making new drug molecules with great therapeutic potential as well as in the fragrance industry. This review summarizes the updated research reacherches on the phytochemisty of Lamiaceae. As chemical constituents of Lamiaceaevary depending on the origin and plant parts, a protocol needs to be standardized to isolate constituets.

References

[1] A. Aharoni, G. Galili, *Curr. Opin. Biotechnol*., **2011**, *22*, 239-244.
[2] D.J. Kliebenstein, A. Osbourn, *Curr. Opin. Plant Biol*., **2012**, *15(4)*, 415-423.
[3] A.P. Nacoulma. Thèse de Doctorat en Sciences Biomédicales et Pharmaceutiques, **2013**, 187p.
[4] C.M. Uritu, C.T. Mihai, G.D. Stanciu, G. Dodi, T. Alexa-Stratulat, A. Luca, M. M. Leon-Constantin, R. Stefanescu, V. Bild, S. Melnic, B.I. Tamba, *Pain. Res. Manag*., **2018**, doi.org/10.1155/2018/7801543.
[5] J. Tamokou, A. Mbaveng, V. Kuete, *Med. Spices.Veg. Africa*, **2017**, 207-37.
[6] H. Nasri, A. Baradaran, H. Shirzad, M. Rafieian-Kopaei, *Int. J. Prev. Med*., **2014**, *5*, 1487-1499.
[7] I. Tripathi, R. Tripathi, A. Tiwari, *Int. J. Multidiscip. Curr. Res*., **2017**, *5*, 31-7.
[8] Z. Sadeghi, M. Akaberi, J. Valizadeh, *Avicenna J. Phytomed*., **2014**, *4(2*), 79-88.
[9] J. Parnell, T. Curtis, Cork University Press, **2012**, 978-185918-4783.
[10] Z. Guo, Z. Liu, X. Wang, W. Liu, R. Jiang, G. Cheng, *Chem. Cent. J*., **2012**, *6*, 147.
[11] S. Arijit, B. Arpita, *Int. Res. J. Biol. Sci*., **2013**, *2*, 63-65.
[12] S. Banu, B. Bhaskar, *Pharm. Biol*., **2012**, *50*, 1592-1595.
[13] A.C.B. Sodré, J.M.Q. Luz, L.L. Haber, M.O.M. Marques, C.R. Rodrigues, A.F. Blank, *Br. Pharmacogn*., **2012**, *22*, 40-44.
[14] M. Akram, M. Uzair, N.S. Malik, A. Mahmood, N. Sarwer, A. Madni, H.M. Asif, *J. Med. Plant Res*., **2011**, *5*, 4499-4503.
[15] E. Abu-Gharbieh, N.G. Shehab, S.A. Khan, *Pak. J. Pharm. Sci*., **2013**, *26*, 799-803.
[16] R. Yucharoen, S. Anuchapreeda, Y. Tragoolpua, *Afr. J. Biotechnol*., **2011**, *10*, 860-866.
[17] G.Trakoontivakorn, P. Tangkanakul, K. Nakahara, *J. pn. Agric. Res. Q*., **2012**, *46*, 347-353.
[18] L. Chih-Chien, Y. Chao-Hsun, W. Pey-Shiuan, K. Chang-Chin, C. Yi-Shyan, *J. Med. Plant Res*., **2011**, *5*, 6203-6209.
[19] A.B. Yildirim, F.P. Karakas, A.U. Turker, *Asian Pac. J. Trop. Med*., **2013**, *6*, 616-624.
[20] Z .Yosr, C. Hnia, T. Rim, B. Mohamed, *Ind. Crop. Prod*., **2013**, *43*, 412-419.
[21] S. Bouajaj, A. Benyamna, H. Bouamama, A. Romane, D. Falconieri, A. Piras, B. Marongiu, *Nat. Prod. Res*., **2013**, *27*, 1673-1676.
[22] C. Dincer, I. Tontul, I.B. Cam, K.S.Ozdemir, A.Topuz, H.S. Nadeem, S. Tugrulay, R.S. Gokturk, *Turk. J. Agric. For*., **2013**, *37*, 561-567.
[23] H. Miladi, R. Ben Slama, D. Mili, S. Zouari, A. Bakhrouf, E. Ammar, *J. Chem*., **2013**.
[24] C.C. Lai, P.H. Huang, A.H. Yang, S.C. Chiang, C.Y. Tang, K.W. Tseng, C.H. Huang, *Planta.Med*., **2016**, *82*, 181-189.
[25] M.S. Stankovic, M. Topuzovic, S. Solujic, V. Mihailovic, *J. Med. Plant Res*., **2010**, *4*, 2092-2098.
[26] O. Yilmaz, H. Akkaya, *Ekoloji*., **2012**, *21*, 34-40.

[27] A.I. Hussain, F. Anwar, S.A.S. Chatha, S. Latif, S.T.H. Sherazi, A. Ahmad, J. Worthington, S.D. Sarker, *LWT-Food. Sci. Technol.*, **2013**, *50*, 185-192.
[28] J. Aliakbarlu, F. Shameli, *Turk. J. Biochem*., **2013**, *38*, 425-431.
[29] L. Joudi, G. H. Bibalani, H. Shadkami, *Curr. Res. J. Biol. Sci*., **2011**, *3*, 385-387.
[30] I. Süntar, Ö.F. Yakınc, *Phytonutrients in Food*, **2020**, 137-155.
[31] Y. Huang, I. Edirisinghe, D. Xiao, B.M. Burton-Freeman, *Reference Module in Food Science*, **2016**.
[32] R. Campos-Vega, B.D. Oomah. Chemistry and classification of phytochemicals., **2013**, https://doi.org/10.1002/9781118464717.*In:*Tiwari BK & Brunton N P. (editors). Handbook of Plant Food Phytochemicals: Sources, Stability and Extraction.
[33] I. Stappen, J. Wanner, N. Tabanca, D.E. Wedge, A. Ali, V.K. Kaul, B. Lal, V. Jaitak, V.K. Gochev, E. *Nat. Prod. Commun.*, **2015**, *10*,133-138.
[34] F. Ahmadi, S. Sadeghi, M. Modarresi, R. Abiri, A. Mikaeli, *Food. Chem. Toxicol*., **2010**, *48*, 1137-1144.
[35] M. Zuzarte, L. Vale-Silva, M.J. Gonçalves, C. Cavaleiro, S. Vaz, J. Canhoto, E. Pinto, L. Salgueiro, *Eur. J. Clin. Microbiol. Infect. Dis*., **2012**, *31*, 1359-1366.
[36] M. Zuzarte, M.J. Gonçalves, C. Cavaleiro, J. Canhoto, L. Vale-Silva, M.J. Silva, E. Pinto, L. Salgueiro, *J. Med. Microbiol*., **2011**, *60*, 612-618.
[37] Z. Zarai, A. Kadri, I. Ben Chobba, R. Ben Mansour, A. Bekir, H. Mejdoub, N. Gharsallah, *Lipids. Health. Dis*., **2011**, *10*, 161.
[38] M. Chessa, A. Sias, A. Piana, G.S. Mangano, G.L. Petretto, M.D. Masia, B. Tirillini, G. Pintore, *Nat. Prod. Res*., **2013**, 27, 93-99.
[39] S. Casiglia, M.B. Jemia, L. Riccobono, M. Bruno, E. Scandolera, F. Senatore, *Nat. Prod. Res*., **2015**, *29*, 1201-1206.
[40] V. Kumar, C.S. Mathela, A.K. Tewari, K.S. Bisht, *Pest. Biochem. Physiol*., **2014**, *114*, 67-71.
[41] N.A.A. Ali, B.K. Chhetri, N.S. Dosoky, K. Shari, A.J.A. Al-Fahad, L. Wessjohann, W. N.Setzer, *Medicines*, **2017**, *4*, doi:10.3390/medicines4020017.
[42] B.X. Camiletti, C.M. Asensio, M.L. Pecci, E.I. Lucini, *J. Food. Sci*., **2014**, *79*, M2499-M2506.
[43] S. Nardoni, S. Giovanelli, L. Pistelli, L. Mugnaini, G. Profili, F. Pisseri, F. Mancianti, *Nat. Prod. Commun.*, **2015**, *10*, 1473-1478.
[44] M. Homa, I.P. Fekete, A. Böszörményi, Y.R. Singh, K.P. Selvam, C.S. Shobana, P. Manikandan, L. Kredics, C. Vágvölgyi, L. Galgóczy, *Planta Med*., **2015**, *81*, 1277-1284.
[45] S.B. Waller, I.M. Madrid, V. Ferraz, T. Picoli, M.B.Cleff, R.O. de Faria, M.C. Meireles, J.R. de Mello, *Bra. J. Microbiol*., **2016**, *47*, 896-901.
[46] M. Nikkhah, M. Hashemi, M.B. Habibi Najafi, R. Farhoosh, *Inter. J. Food. Microbiol*., **2017**, *257*, 285-294.
[47] R. Murugan, G.R. Mallavarapu, K.V. Padmashree, R.R. Rao, C. Livingstone, *Nat. Prod. Commun*., **2010**, *5*,1961-1964.
[48] D. Kocevski, M. Du, J. Kan, C. Jing, I. Lačanin, H. Pavlović, *J. Food. Sci*., **2013**, *78*, M731-M737.
[49] H.Y. Zhang, Y. Gao, P.X. Lai, *Molecules*, **2017**, *22*, doi:10.3390/molecules22030381.
[50] K. Zomorodian, M. Moein, K. Pakshir, F. Karami, Z. Sabahi, *Evid Based Complement Alternat Med*., **2017**, *22*, 770-776.
[51] B. Marongiu, A. Piras, S. Porcedda, D. Falconieri, M.J. Goncalves, L. Salgueiro, A. Maxia, R. Lai, *Nat. Prod. Res*., **2010**, *24*, 569-579.

[52] A. Asdadi, A. Hamdouch, A. Oukacha, R. Moutaj, S. Gharby, H. Harhar, M. El Hadek, B. Chebli, L.M. Idrissi Hassani, *J. Mycol. Med.*, **2015**, *25*, e118-e127.
[53] A. Alizadeh, E. Zamani, R. Sharaifi, M. Javan-Nikkhah, S. Nazari, *Commun. Agric. Appl. Biol. Sci*., **2010**, *75*, 761-767.
[54] M. Mahboubi, R. Heidary Tabar, E. Mahdizadeh, *J. Mycol. Med.*, **2017**, *27*, 232-237.
[55] H. Bendif, M. Boudjenib, M.D. Miara, L. Biqiku, M. Bramucci, G. Lupidi, L. Quassinti, L.A. Vitali, F. Maggi, *Biochem. Biodivers*., **2017**, e1600299.
[56] H. Bendif, K. Adouni, M.D. Miara, R. Baranauskienė, P. Kraujalis, P.R. Venskutonis, S.M. Nabavi, F. Maggi, *Food. Chem*., **2018**, *260*, 289-298.
[57] H. Bendif, M. Boudjenib, M.D. Miara, L. Biqiku, M. Bramucci, G. Caprioli, G. Lupidi, L. Quassinti, G.A. Sagratini, L. Vitali, S. Vittori, F. Maggi, *Food. Chem*., **2017**, *218*, 78-88.
[58] H. Bendif, M.D. Miara, G. Peron, S. Sut, S. Dall'Acqua, G. Flamini, F. Maggie, *Biochem. Biodivers*., **2017**, e1700248.
[59] H. Bendif, M.D. Miara, Z. Kalboussic, D. Grauzdytėe, D. Povilaitise, P.R. Venskutonise, F. Maggie, *Ind. Crop. Prod*., **2018**, *111*, 768-774.
[60] H. Bendif, M. Lazali, N. Souilah, M.D. Miara, R. Kazernavičiūtė, R. Baranauskienė, P.R. Venskutonis, F. Maggie, *J. Essent. Oil Res*., **2018**, *30(6)*, 488-497.
[61] A. Giatropoulos, A. Kimbaris, A. Michaelakis, D.P. Papachristos, M.G. Polissiou Emmanouel, N. Parasitol. *Res*., **2018**, *117*, 1953-1964.
[62] A. Piras, M. JoseGonçalves, J. Alves, D. Falconieri, S. Porcedda, A. Maxia, L.Salgueiro, *Ind. Crop. Prod.*, **2018**, *113*, 89-97.
[63] S. Mehalaine, O. Belfadel, T. Menasria, A. Messaili, *Phytothérapie*, **2018**, *16*, S155-S163.
[64] H.B. Sérgio, A.L. Bordignon, M.A. Apel, G.L. Poser, *Biochem. Syst. Ecol.*, **2020**, *89*, 103992.
[65] A.E. Karadağ, B. Demirci, Ş. Kültür, F. Demirci, K.H.C. Başer, *J. Essent. Oil Res.*, **2020**, doi.org/10.1080/10412905.2020.1743786.
[66] S. Küçükaydın, G. Tel-Çayan, M.E. Duru, M. Kesdek, M. Öztürk, *Toxin Reviews*., **2020**, doi.org/10.1080/15569543.2020.1731552.
[67] M.B. Goudjil, S. Zighmi, D. Hamada, Z. Mahcene, S.E. Bencheikh, S. Ladjel, *Afr. J. Bot*., **2020**, *128*, 274-282.
[68] Y. Ben Miri, D. Djenane. *Phytotherapie*, **2019**, *17(6)*, 299-309.
[69] A.B. Aissaoui, A. El Amrani, S. Zantar, L. Toukour, *Eur. Sci. J*., **2018**, *14*, 118.
[70] A. Ebadollahi, M. Ziaee, F. Palla, *Molecules*, **2020**, *25*, 1556.
[71] S. Casiglia, M. Bruno, E. Scandolera, F. Senatore, F. Senatore, *Arab. J. Chem*., **2019**, *12*, 2704-2712.
[72] P. Singh, A.K. Pandey, *Front. Plant Sci*., **2018**, *4*, doi: 10.3389/fpls.2018.01295.
[73] D. Scalas, N. Mandras, J. Roana, R. Tardugno, A.M. Cuffini, V. Ghisetti, S. Benvenuti, V. Tullio, *BMC Complement. Altern. Med*., **2018**, *18*, 143.
[74] N.T. Marques, A. Filipe, P. Pinto, J. Barroso, H. Trindade, D.M. Power , A.C. Figueiredo *Biochem. Biodivers*., **2020**, *17(3)*, e1900669.
[75] S. Moumni, A. Elaissi, A. Trabelsi, A. Merghni, I. Chraief, B. Jelassi, R. Chemli, S. Ferchichi, *BMC Complement. Altern. Med.*, **2020**, *20*, 103.
[76] M.J. LAh Tock, G.P.P. Kamatou, S. Combrinck, M. Sandasi, A.M. Viljoen, *Phytochemistry***,** **2020**, *172*, 112249.
[77] I.B. Semerdjieva, V. Zheljazkov, C.L. Cantrell, T. Astatkie, A. Ali, *Molecules*, **2020**, *25*, 827.

[78] B.J.V. Freitas, A.G.F.E. Filho, A.M.L. Silva, J.G. Zocolo, S.E.S. de Brito, V.N. Gramosa, *Talanta*, **2018**, *180*, 329-336.
[79] H. Mohammedi, S. Mecherara-Idjeri , A. Hassani, *J. Essent. Oil Res.*, **2020**, *32*, 1.
[80] V.V. Milevskaya, S. Prasad, A.Z. Temerdashev, *Microchem. J.*, **2019**, *145*, 1036-1049.
[81] H.J. Wang, F. Luan, D.X. He, Y. Wang, M.X. Li, *J. Tradit. Complement. Med.*, **2018**, *8*, 24-38.
[82] D. Batista, P.L. Falé, M.L. Serralheiro, M. E. Araújo, C. Dias, I. Branco, C. Grosso, J. Coelho, A. Palavra, A.J.P. Madeira, A. Martins, P.A. Rauter, *Open Chem.*, **2017**, *15*, 82-91.
[83] F. Aghakhani, N. Kharazian, Z.L. Gooini, *Phytochem. Anal.*, **2018**, *29(2)*, 180-195.
[84] T. Chen, Q.Y. Diao, H.Z. Yu, C.L. Jiao, J. Ruan, *Nat. Prod. Res.*, **2018**, *32(8)*, 977-981.
[85] C. Frezza, A. Venditti, G. Matrone, I. Serafini, S. Foddai, A. Bianco, *Nat. Prod. Res.*, **2018**, *32(13)*, 1583-1589.
[86] I. Saidi, P. Waffo-Tégu, L.E.A. Ayeb-Zakhama, F. Harzallah-Skhiri, A. Marchal, H. Ben, *Phytochemistry*, **2018**, *146*, 47-55.
[87] R.M. Delnavazi, P. Saiyarsarai, S. Jafari-Nodooshan, M. Khanavi, S. Tavakoli, H. Hadavinia, N. Yassa, *Pharma. Sci.*, **2018**, *24*, 332-339.
[88] Qiu, F. Khutsishvili, M. Fayvush, G. Tamanyan, Kamilla, *Food Agr. Org.*, **2019**, *84(24)*, 17-20.
[89] H. TaoXu, C. GangZhang, Y. QiongHe, S. ShanShi, Y. Li Wang, G. XinChou. *Phytochemistry*, **2019**, *164*, 111-121.
[90] E. Alexa, C. Danciu, I. Radulov, D. Obistioiu, M.R. Sumalan, A. Morar, A.C. Dehelean, *Anal. Cell. Pathol.*, **2018**, ID 2678924, 7.
[91] A. Moradi-Afrapolia, M. Shokrzadeh, F. Barzegard, G. Gorji-Bahrie, N.S. Ebrahimig, *Rev. Bras. Farmacogn.*, **2018**, *28*, 27-33.
[92] F.G. Moreno-Pérez, E.V. González-Trujano, J.M. Martínez-Gordillo, S.R. Miguel-Chávez, A.F. Basurto-Peña, A. Dorazco-González, E. Aguirre-Hernández, *Bot. Sci.*, **2019**, *97 (3)*, 355-365.
[93] N. Nidhal, X. MingZhoua, G. Chen, Zhang, C. Han, X. Song, *Biochem. Syst. Ecol.*, **2020**, *89*, 104006.
[94] Q. JiLi, C. Liang Zhao, C. FaiKu, Y. Zhu, X. Jin Zhu, J. Jie Zhang, T.S. Deyrup, L. TaiPana, H. Jie Zhang, *Bioorg. Chem.*, **2020**, *95*, 103512.
[95] M. Rezgui, N. Majdoub, B. Mabrouk, A. Baldisserotto, A. Bino, B.L. Ben Kaab, S. Manfredini, *J. Mycol. Med.*, **2020**, *30*, 100927.
[96] Y.H. Li, L.Y. Wen, W.J. Kai, M.L. Jian, K.C.J. Jian, *Phytochemistry*, **2020**, *172*, 112280.