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The Chemotype Of The Algerian Daphne Gnidium Essential Oil: Chemical Diversity And Bioactive Potentials

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Abstract:
The essential oil of Daphne gnidium collected from many sites in Center, East, and West Algeria was obtained through the hydrodistillation of the aerial parts with a low yield (0.01%). Then, we analyzed the essential oils of 04 populations using GC/MS and identified 70 chemical components, with (95.42 % ± 1.09) of total oil on average. The main components of this essential oil are palmitic acid (9.98 ± 3.71 %), linoleic acid (8.34 ± 2.68 %), hexadecanoic acid (7.35 ± 4.35%), carvone (5.67 ± 5.67 %) and spathulenol (5.33 ± 3.90 %). Besides, Daphne gnidium essential oil is rich in fatty acids (25.69 ± 3.21 %), monoterpenes (14.42 ± 3.98 %), and sesquiterpenes (12.85 ± 5.50 %). The hydrocarbons and ketone represent rates of 10.99 ± 6.05 % and 9.14 ± 5. 30 %, respectively. This study allowed identifying many chemotypes in the study populations, namely naphthalene chemotype and nonanal <n-> in the populations of Ouanougha and Zariffet forest, limonene chemotype in the populations of Bibans, and dodecane <n-> chemotype in the populations of Djebel Megress.
Keywords: *Daphne gnidium, essential oil, chemotype, GC-MS, Algeria.*

INTRODUCTION:

Thymelaeaceae are a small family of dicotyledons that includes 1200 species in 67 genera (Amari, 2015; Mekhelfi, 2016). Its members are distributed in the tropical and temperate zones, mainly in Africa, and are not found in the cold climates. A *Daphne* genus covers 70 species, mainly *Daphne gnidium* (Meslay, 2007). It is a thymelaeaceae shrub that comes from the Iberian Peninsula, France, Apennine Peninsula, Balkan Peninsula, Canary Islands, and North Africa (Quezel & Santa, 1962-1963). It generally grows in the Mediterranean maquis, mainly in the mountainous regions of the North African Tell in Tunisia and Morocco. We often find it on the steep embankments that border the wadis (El Fennouni, 2012; Mohammedi, 2013).

In the past, it was used as an ointment with epispastic properties (Bellakhdher et *al*, 1991). In traditional pharmacology, it was used for antiseptic, insecticidal (González et *al*., 2011-2013), depurative, scar-reducing, sudorific, and abortive treatments. In addition, it treats skin issues (Bnouham et *al*., 2002; EL Hilah et *al*., 2016), diabetes, (Bnouham et *al*., 2002), and intoxications (Benali et *al*., 2017). In Algeria, it is used for hair treatments and nervous depression (Chermat & Gharzouli, 2015), sinusitis (Bellifa et *al*., 2020), rheumatic and muscular pains (Yaici et *al*, 2020).

Its leaves are used in painting traditional fabrics (Cardon et *al*., 2011). Besides, it is appreciated for its antioxidant and antibacterial effects (Didi, 2009). In traditional medicine, the leaf infusion served as a hypoglycemic agent (Ziyyat et *al*., 1997). Another study showed that its bark and leaves have a good antibacterial and antifungal activity (Rapisarda et *al*., 1998; Mohammedi et *al*., 2013). In addition, Cottigli et *al*. (2001) showed that its stems have antibacterial and antifungal activities. Moreover, studies showed that its leaves have anti-leukemic (Chaabane et *al*., 2014), antioxidant (Kosheleva et *al*., 1968; Didi, 2009), anti-inflammatory and antigenotoxic activities (Harizi et *al*., 2011; Boudjelal et *al*., 2013; Chaabane et *al*., 2014).

However, dichloromethane extract from its aerial parts has a significant anti-retroviral capacity with the absence of cytotoxicity (Vidal et *al*., 2012). In addition, ethyl acetate extracts from its roots showed an apoptotic and anti-proliferative effect on lung cancer and hepatoma cells in vitro, proving its anti-cancer activity (Wannes et *al*., 2007; Chaabane et *al*, 2013). Different studies on its chemical composition showed its richness in coumarins (Daphnetin, daphnin, acetylumbelliferone, and daphnoretin) and flavonoids (luteolin-3′,7-di-O-glucoside luteoline, orientine, isoorientine, quercetin, apigenin-7-O-

glucoside, genkwanine, 5-O-b-D-primeverosyl genkwanine, 2, 5, 7,4'-tetrahydroxyisoflavanol). The seeds and bark of different species of Daphne show toxic diterpenes, daphnetoxin (bark), and mezerein in the seeds (Deian et *al.*, 2003; Nowik, 2005; Marques et *al.*, 2009; Mohammedi, 2013).
Its essential oil is mainly made of palmitic acid, eicosene, linoleic acid, and dodecane (Ramdani et *al.*, 2015). The chemotypes are chemical, biological, and botanical classes that refer to the main molecules present in essential oils (Zhiri et *al.*, 2005). To the best of our knowledge, no study was conducted on *D. gnidium* essential oil. Thus, our study aims at identifying the chemical composition of *Daphne gnidium* L. and at evaluating the geographic distribution of chemotypes in Algeria.

MATERIALS AND METHODS:

1. Plant material

The aerial parts of *Daphne gnidium* were collected from 4 locations in Algeria (Figure 1). The geographic coordinates of the sample stations are grouped in Table 1.

Table 1: Location of the study stations

Wilaya	Location	Geographic coordinates	Altitude	Bioclimatic stage
M'sila	**Ouanougha**	35° 58′ 51″ N 4° 11′ 10 ″ E	1134 m	Upper semi-arid with cool winters
Bordj Bou-Arreridj	**Bibans**	36° 11' 55" N 4° 23' 50" E	1100 m	Semi-arid with cool winters
Setif	**DjebelMegress**	36° 19' 54" N 5° 21' 14" E	1736 m	Subhumid with cold winters
Tlemcen	**Zariffet forest**	34° 51' 1° 16'	1200 m	Upper semi-arid

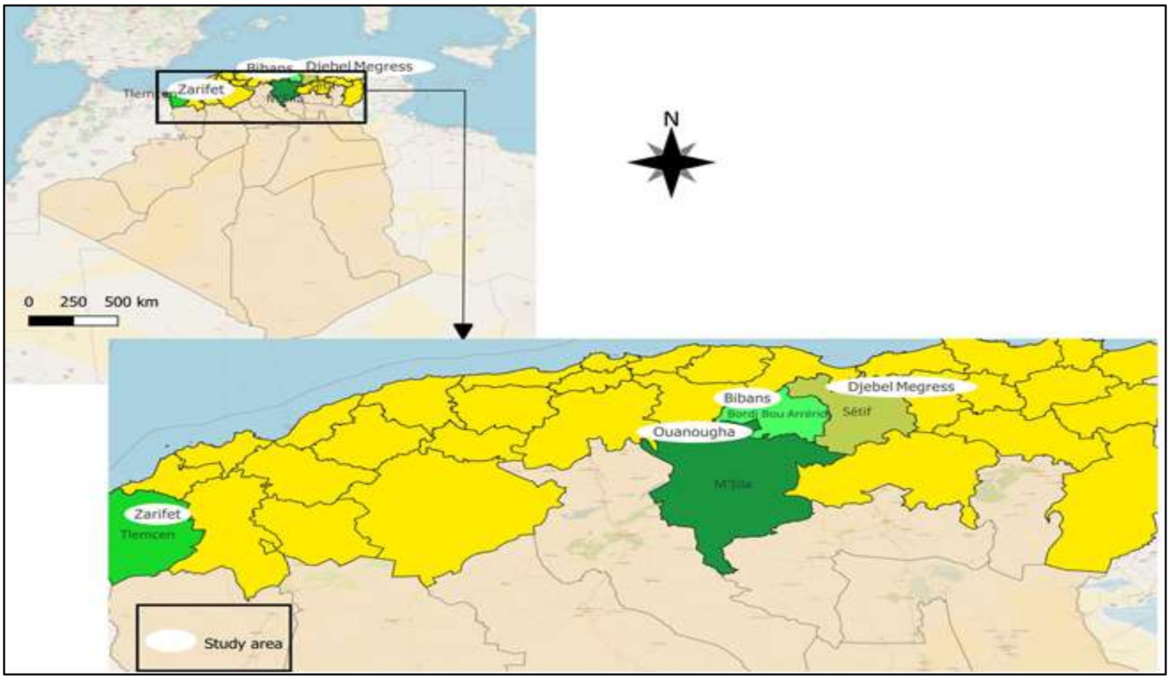

Figure 1. The sample populations of *Daphne gnidium*

2. Botanical description:

Garou is a perennial shrub of 60 cm to 02 m or more in height. It has an upright and ramified stem and persistent lanceolate-linear, cuspidate, very dense or oval-oblong, sharp, and glandulous leaves of 5-7 mm in width. Its biological type is nanophanerophytes (2 to 4 m) and the plant formation is nanophanerophytaie. Its branches are thin, very leafy, and puberulent in the top. It is a shrub of the Mediterranean garrigues and the Atlantic sands found in the entire Algerian Tell. Its flowering takes place from October to March. It is an entomogamous plant (Quezel et Santa, 1962-1963; Ladhari et *al.*, 2011; El Fennouni, 2012; Mohammedi, 2013).

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The leaves persist for a year and are sessile alternate with no stipules. They have a slightly glaucous color. They are shiny in the bottom and pale in the top, subcoriaceous, and glabrous. They leave an apparent scar after their fall. Besides, the stems are cylindrical and the branches are smooth, yellow, softly pubescent, upright, and ramified (Figure 02). The aerial parts were collected during the flowering period from 2023 to 2024. The plant material collected was dried in an aerated and shady place at an ambient temperature.

Figure 02: Different parts of *Daphne gnidium*

3. Extraction of the essential oil:

300g of the material dried in the air was subjected to hydrodistillation using Clevenger apparatus for 3 hours with 3000 ml of distilled water. The hydrodistillation was repeated until obtaining a sufficient amount of oil, which was collected and stored in glass vials in a refrigerator at 4-5°C until analysis (Bounab, 2020).

4. Analysis of the essential oils:

The essential oils were analyzed using a gas chromatograph Hewlett-Packard model 5890, coupled with Hewlett-Packard model 5971, equipped with a DB5 MS column (30 × 0,25 mm ; 0,25 µm), programming of 50°C (5 min) to 300°C at 5°C/min, with a hold of 5 min. The helium was used as a gas carrier (1.0 ml/min), the injection was fractioned (1:30), and the temperatures of the injector and the detector were 250 and 280°C, respectively. The mass spectrometry functioned in EI to 70 eV mode, the electron multiplier was at 2500 V, and the temperature of the ion source was 180 °C. Besides, MS data were acquired in the m/z 33-450 range. The identification of the components was based on the comparison of the mass spectra to NIST mass spectral library (NIST, 2002; Adams, 2005) and to those described by Adams on the site. Besides, we compared their retention indices to those of the authentic compounds or the values mentioned in other studies (Adams, 2005).

5. Statistical analysis:

The data were, first, subjected to PCA to examine the relations between the chemical compounds, identify the population's possible structure, and study the variations of *Daphne gnidium* essential oil composition. A hierarchical analysis of the chemical variables was conducted to test the effects and investigate the hierarchical associations between the populations. The statistical analyses were made using Minitab 19.

RESULTS:

The hydrodistillation of the dried aerial parts of the 04 populations gave yellow oil with a very strong aromatic odor. The average yield of essential oil is 0.01%. The analysis of the populations' essential oils with GC-MS allowed for the identification of 70 chemical components (Table 02), with an average of (95.42 % ± 1.09) of the total oil. The chemical composition of this species is dominated by palmitic acid (9.98 ± 3.71 %), linoleic acid (8.34 ± 2.68 %), hexadecanoic acid (7.35 ± 4.35%), carvone (5.67 ± 5.67 %), and spathulenol (5.33 ± 3.90 %).

Table 2: Chemical composition of essential oils of *Daphne gnidium*

Chemical components	KI	Ouanougha	Bibans	Djebel Megress	Zariffet Forest	Average	SD

Number of components		**42**	**39**	**36**	**40**		
Total %		**93,89**	**94,6**	**96,32**	**96,88**	**95,42**	**1,09**
Heptane	700	1,3	0	0,00	0	0,32	0,56
Pinene <α->	932	0,15	0,4	0,00	0	0,13	0,16
Benzaldehyde	952	0	0	0,00	0,19	0,04	0,08
Phellandrene <α->	1002	0	0	0,2	0,39	0,14	0,16
Terpinene <α->	1014	0,26	0	1,01	0	0,31	0,41
Cymene <ρ->	1020	0,47	0	0,00	0	0,11	0,20
Cymene <o->	1022	0	0,3	0,81	0	0,27	0,33
Limonene	1024	1,2	0	0,99	0	0,54	0,55
Terpinene <γ->	1054	3,3	1,26	0,86	0,11	1,38	1,18
Linalool	1095	2,01	1,48	0,65	1,23	1,34	0,48
Nonanal <n->	1100	4,3	2,8	1,86	2,11	2,76	0,94
Naphtalene	1178	0,78	0	0,2	1,35	0,58	0,52
Cryptone	1183	0	0	0	2,12	0,53	0,91
Methyl salicylate	1190	0	0,1	0,44	0	0,13	0,18
Dodecane <n->	1200	2,9	2,7	6,09	0	2,92	2,15
Decanal	1201	1,6	0,89	0	0,78	0,81	0,56
Cuminaldehyde	1238	0	0	0	0,93	0,23	0,40
Carvone	1239	11,19	0	0	11,51	**5,67**	5,67
Neryl formate	1280	0	0,6	2,4	0	0,75	0,98
Anethole <(E)->	1282	0	0	0	3,66	0,91	1,58
Thymol	1289	3,82	0,89	1,4	7,6	3,42	2,65
Tridecene <1->	1290	0,79	1,14	0,92	0	0,71	0,42
Carvacrol	1298	4,15	0	0,1	3,59	1,96	1,92
Undecanol <2->	1301	1,93	0	0	2,5	1,10	1,12
Hexenyl tiglate <(3E)->	1315	0	0,54	0,78	0,1	0,35	0,31
Eugenol	1356	0	0	0	0,23	0,05	0,09
Neryle acetate	1359	0	0	0,3	0,85	0,28	0,34
Piperitenone oxide	1366	0	0	0,00	3,62	0,90	1,56
Damascenone <(E)-β->	1383	0	0	0,88	1,09	0,49	0,49
Methyl decyl ketone	1388	0	0	0,00	0,8	0,2	0,34
Tetradecane <n->	1400	1,65	2,29	0,25	1,9	1,52	0,76
Decyl acetate	1407	0	1,07	0,00	0	0,26	0,46
Caryophyllene <(Z)->	1408	4,06	0	0,00	0	1,01	1,75
Caryophyllene <(E)->	1417	3,53	0	1,23	2,63	1,84	1,34
Copaene <β->	1430	0,24	0,82	0,00	0	0,26	0,33
Neryl acetone	1434	0	0	0,94	0,2	0,28	0,38
Guaiene <α->	1437	0	0,11	0,00	0	0,02	0,04
Aromadendrene <allo->	1458	0	0	0	1,53	0,38	0,66
Curcumene <ar->	1479	0,14	0	0	1,78	0,48	0,75
Germacrene-D	1484	0,18	0	0	0	0,04	0,07
Ionone <(E)-β->	1487	0	1,02	1,86	0	0,72	0,77
Tridecanone <2->	1495	1,56	8,1	0,00	0	2,41	3,34
Pentadecane <n->	1500	3,15	1,14	1,99	0,89	1,79	0,88
Tridecanal	1509	2,14	5,2	6,65	0	3,49	2,59

Cadinene <δ->	1522	0	0	0	0,81	0,20	0,35
Calamenene <cis->	1528	0	0	0	1,45	0,36	0,62
Nerolidol <(E)->	1561	0	0	2,44	0	0,61	1,05
Hexenyl benzoate <(3Z)->	1565	1,14	2,08	6,27	0	2,37	2,36
Spathulenol	1584	3,24	9,6	0,00	8,51	**5,33**	3,90
Hexenyl benzoate <(2E)->	1587	0,26	0	0	0,59	0,21	0,24
Caryophyllene oxide	1589	0,46	1,03	0,00	1,38	0,71	0,52
Tetradecanal	1611	0	0,7	1,09	0	0,44	0,46
Cadinol <α->	1652	0,23	0,19	0	0	0,10	0,10
Turmerone <ar->	1668	0	0	0	2,96	0,74	1,28
Pentadecanone <2->	1697	0,14	0	0	0	0,03	0,06
Heptadecane <n->	1700	0,29	0,16	1,64	0	0,52	0,65
Methyl hexadecanoate	1921	0	1,3	0	0	0,32	0,56
Phytol	1942	2,06	8,08	4,47	3,45	4,51	2,22
Hexadecanoic acid	1959	10,68	10,49	0	8,26	**7,35**	4,35
Palmitic acid	1966	8,56	7,42	16,37	7,6	**9,98**	3,71
Eicosene <n->	2000	0,3	4,12	9,59	0	3,50	3,87
Linoleic acid	2132	6,54	12,6	8,63	5,62	**8,34**	2,68
Tricosane <n->	2300	0	1,12	1,95	0	0,76	0,82
Tetracosane <n->	2400	1,04	0,97	0,88	0	0,72	0,42
Pentacosane <n->	2500	0,84	0,98	2,25	1,96	1,50	0,60
Hexacosane	2600	0,4	0,6	4,77	0,18	1,48	1,90
Octacosane	2800	0,79	0,21	3,16	0,23	1,09	1,21
Triacontane	3000	0,12	0	0	0,19	0,07	0,08
Dotriacontane	3200	0	0,04	0	0	0,01	0,017
Tritriacontane	3300	0	0,06	0	0	0,01	0,025

Note: KIc = calculated Kovats retention index

The chemical classes of D. gnidium essential oil are dominated by fatty acids (25.69 ± 3.21 %), monoterpenes (14.42 ± 3.98 %), and sesquiterpene (12.85 ± 5.50 %). Hydrocarbons and Ketone represent rates of 10.99 ± 6.05 % and 9.14 ± 5.30 %, respectively, of the total oil (Table 03; Figure 03).

Table 3: Chemical classes of essential oils of *Daphne gnidium*

Chemical classes	Ouanougha	Bibans	Djebel Megress	Zariffet Forest	Average	SD
Hydrocarbons	7,22	9,27	21,30	6,2	**10,99**	6,05
Monoterpenes	15,41	10,93	10,82	20,54	**14,42**	3,98
Alkane	7,13	6,26	12,59	0,89	6,71	4,14
Esters	0	0	3,07	0	0,76	1,32
Aldehydes	8,04	9,59	9,6	4,01	7,81	2,28
Sesquiterpene	12,08	12,77	5,53	21,05	**12,85**	5,50
Ketone	12,89	8,1	0,94	14,63	**9,14**	5,30
Acids	25,78	30,51	25	21,48	**25,69**	3,21
Alcohols	3,94	1,48	0,65	3,73	2,45	1,41
Others	1,4	2,62	7,05	4,35	3,85	2,12

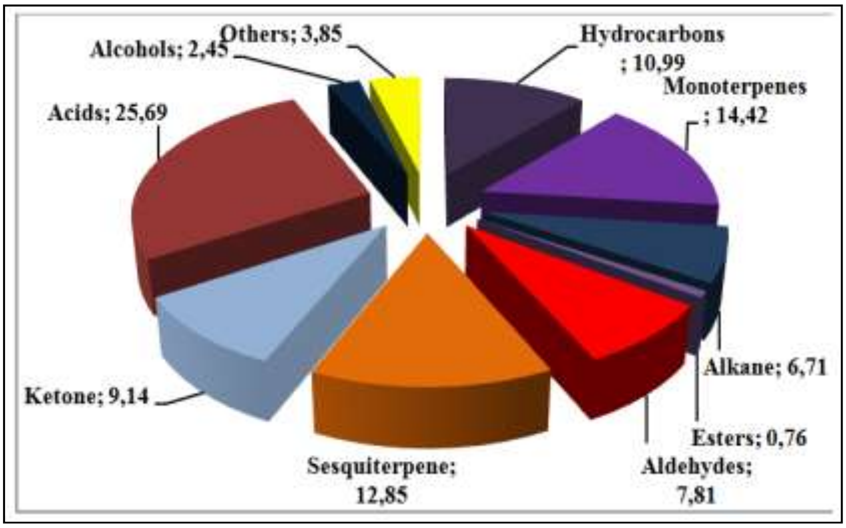

Figure 3. Chemical classes of *Daphne gnidium* oils.

The tridimensional spatial projection of 04 populations in figure 04 shows that the populations of Djebel Megress, Bibans and Ouanougha are separated from those of Zariffet forest.

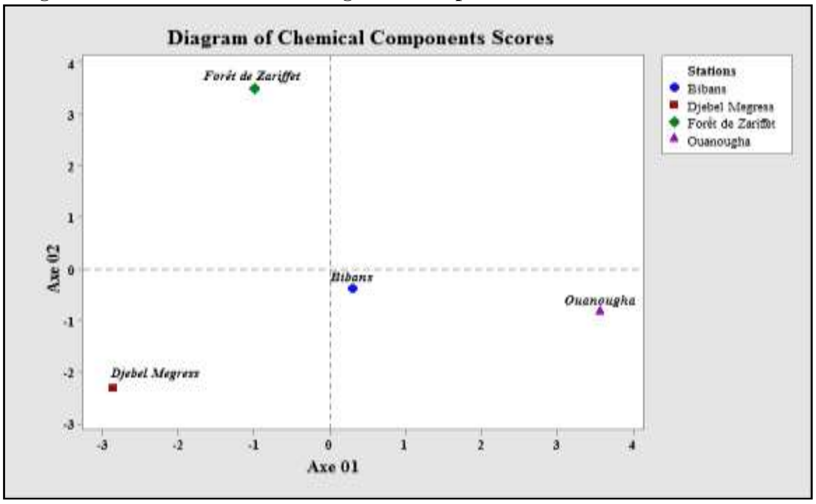

Figure 4. Spatial projection of *Daphne gnidium* populations

Daphne gnidium populations show a chemical composition that is very heterogeneous in essential oils with significant differences, and that the compounds' concentrations show a clear inter-population diversity (Figure 05).

Benzaldehyde, cryptone, naphtelene, and phellandrene <α-> are found in Zariffet populations, where naphthalene shows the biggest variation with an average of 0, 58 ± 0, 52 %.

Pinene <α-> and limonene are found in Bibans, and limonene is the dominant component with an average of 0.54 ± 0.55 %.

The populations of Ouanougha are represented by decanal, linalool, nonanal <n->, cymene <ρ->, heptane, and terpinene <γ->. Nonanal <n->, with an average of 2.76 ± 0.94 %, is the component that shows the biggest variation, followed by terpinene <γ-> (1.38 ± 1.18 %). Regarding the populations of Djebel Megress, we found out methyl salicylate, cymene <o->, terpinene <α->, and dodecane <n->, and that the latter shows the biggest variation with an average of 2.92± 2.15 %.

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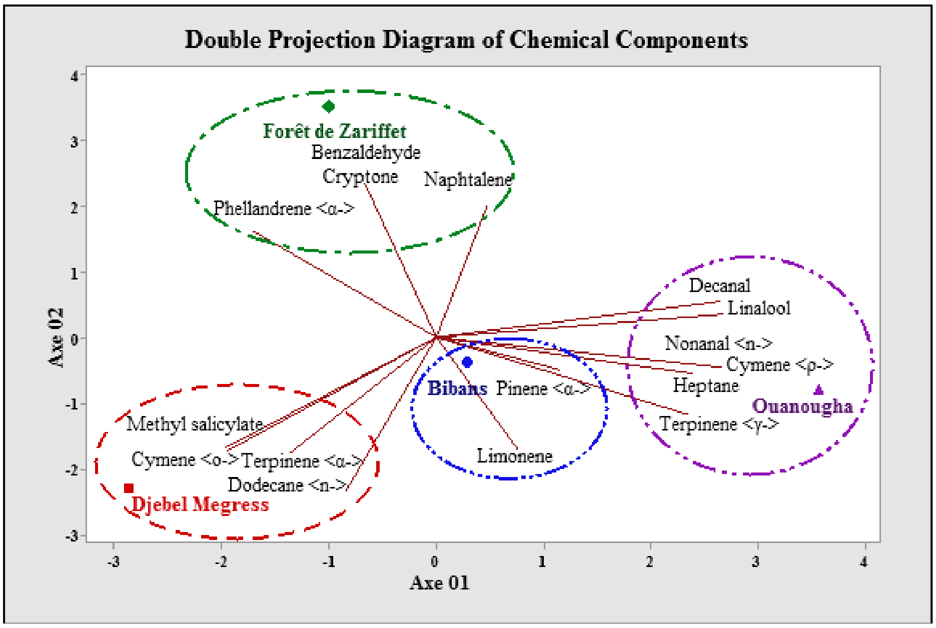

Figure 5. ACP of essential oils compounds of *Daphne gnidium* populations

The dendrogram analysis allows us to build a phylogenetic tree to prove the relations between *Daphne gnidium* populations. This analysis is based on the bond length and confirms the separation of populations into 03 groups and 03 clades (table 04; figure 06).

Table 4: Groups of chemical components liaisons according to populations

Groups	Variables	Similarity level
Group 1	Ouanougha, Zariffet Forest	89,2354
Group 2	Bibans	76,2930
Group 3	Djebel Megress	69,6538

The populations of Ouanougha and Zariffet forest are convergent and different than the 02nd and 03rd groups, as they include naphthalene and nonanal <n->, which dominate the superior semi-arid stage. On the other hand, the populations of Bibans and Djebel Megress are separated and predominate the semi-arid bioclimatic stages with fresh winters and the sub-humid stages with cold winters. These groups allowed us to identify different chemotypes.

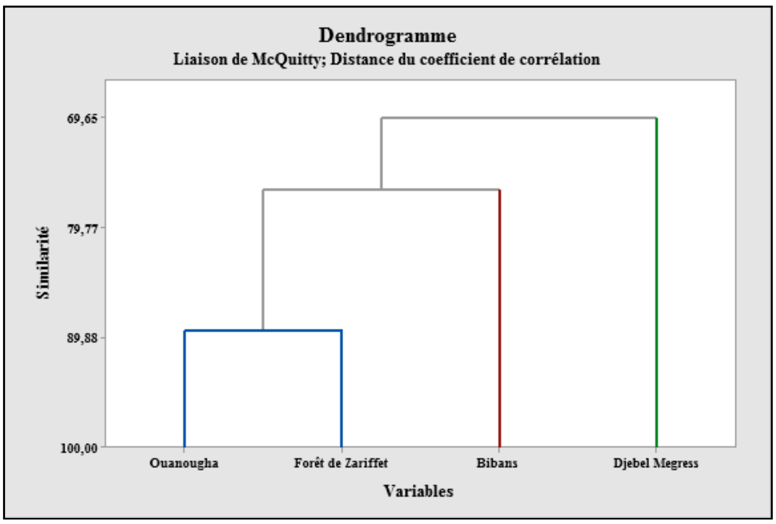

Figure 6. Dendrogram of essential oils compounds of *Daphne gnidium* populations.

The identification of *Daphne gnidium* chemotypes allows for a better understanding of the dominating bio-active compounds (Table 5).

Table 5: Chemotypes of *Daphne gnidium* populations in Algeria

Chemotypes	Populations (locations)
Naphthalene, nonanal <n->	Ouanougha, Zariffet forest
Limonene	Bibans
Dodecane <n->	Djebel Megress

Table 06 summarizes the results of the groups of different chemical compounds and their affinities according to the study site (Figure 07) where group 3 includes 15 chemical components received by group 9 which includes 9 chemical compounds compared to other groups which include 2 to 8 chemical components.

Table 6: Groups of different chemical components of *Daphne gnidium* populations

Groups	Chemical variables
Group 1	Heptane, Cymene <ρ-> , Terpinene <γ-> , Nonanal <n->, Caryophyllene <(Z)-> , Germacrene-D, Pentadecanone <2-> ;
Group 2	Pinene <α->, Decyl acetate, Copaene <β->, Guaiene <α->, Tridecanone <2->, Methyl hexadecanoate, Dotriacontane, Tritriacontane ;
Group 3	Benzaldehyde, Phellandrene <α->, Cryptone, Cuminaldehyde, Anethole <(E)->, Eugenol, Neryle acetate, Piperitenone oxide, Methyl decyl ketone, Aromadendrene <allo->, Curcumene <ar->, Cadinene <δ->, Calamenene <cis->, Turmerone <ar-> , Tetracosane <n-> ;
Group 4	Terpinene <α->, Tetradecane <n->, Neryl acetone, Nerolidol <(E)->, Heptadecane <n->, Hexadecanoic acid, Palmitic acid, Hexacosane, Octacosane ;
Group 5	Cymene <o-> Methyl salicylate Dodecane <n-> Neryl formate Hexenyl benzoate <(3Z)-> Eicosene <n->
Group 6	Limonene, Pentadecane <n-> ;
Group 7	Linalool, Decanal ;
Group 8	Naphtalene, Thymol, Tridecene <1->, Hexenyl benzoate <(2E)-> ;
Group 9	Carvone, Carvacrol, Undecanol <2->, Hexenyl tiglate <(3E)->, Ionone <(E)-β->, Tridecanal, Tetradecanal, Tricosane <n->, Triacontane ;
Group 10	Damascenone <(E)-β->, Cadinol <α->, Pentacosane <n-> ;
Group 11	Caryophyllene <(E)->, Phytol, Linoleic acid ;
Group 12	Spathulenol, Caryophyllene oxide ;

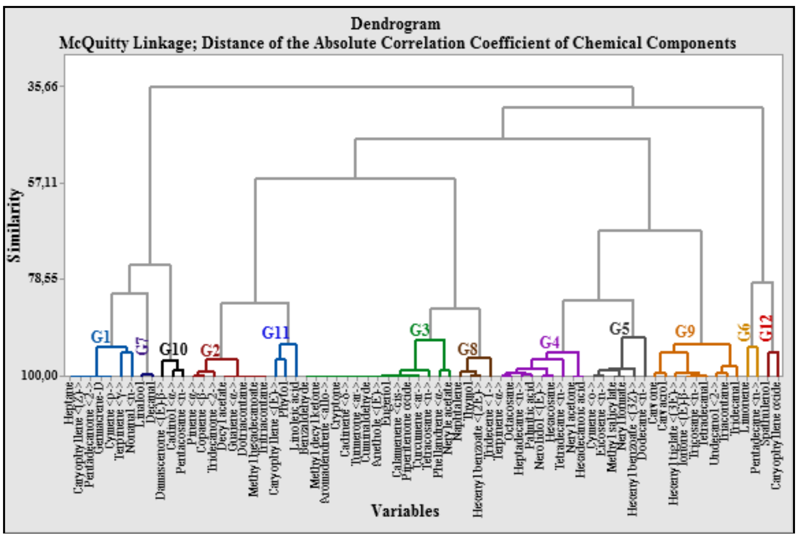

Figure 6: Dendrogram of *Daphne gnidium* essential oils

DISCUSSION

The chemical components of the study populations are completely different than those studied by other scholars in other regions. Our findings show that the main components are palmitic acid, linoleic acid, hexadecanoic acid, carvone and Spathulenol, which are similar to those reported by Ramdani et *al* (2015), where the major components of *Daphne gnidium* essential oil are palmitic acid, linoleic acid, carvone, and dodecane. It is clear that *Daphne gnidium* species are characterized with a significant intra-specific diversity in the chemical profile of its essential oils. This intra-specific polymorphism may be geographic, genetic (Karousou et *al.*, 2005; El Ajjouri et *al.*, 2008), or seasonal (Ghanmi et *al.*, 2010). Besides, these differences seem to be strongly influenced by the pedoclimatic conditions, including the altitude, exposition, and harvest period (Viljoen et *al.*, 2006; Sefidkon et *al.*, 2007).

CONCLUSION:

Daphne gnidium essential oils show a big chemical diversity. Our study showed the existence of many Daphne gnidium chemotypes in Algeria, reflecting the species' chemical plasticity. This diversity provides a significant potential for the phyto-therapeutic and industrial valorizations under a rigorous scientific supervision.

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