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Analysis of Volatile Organic Compounds from the Aerial Parts of Medicinal Plant, *Galium verum*

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Abstract*. The Galium verum herb, (Rubiaceae family) is well represented in the spontaneous Romanian flora. She is one of the most used plants in traditional medicine. Our research aimed to investigate the chemical volatile profile in fresh, dried and essential oil of Gallium verum using SPME and hydrodistillation techniques, followed by GC-MS analysis. Characterization of volatile compounds composition by SPME –GC-MS technique presented din this paper is the first study on fresh and dried of Galium verum plant to our knowledge. Galium verum fresh flower floral bouquet is given by monoterpenes (73,5%), sesquiterpenes (10,16%), esters (10,26%) and others(5.87%). The floral bouquet of Gallium verum dried flower, contains mainly: aldehydes (35.48%) monoterpenes (35.48%), alcohols (11.96%), sesquiterpenes, (3.71%), esters (3.14%) and others (10.11%). Sixty components were identified in the galium essential oil.*

Keywords: *Gallium verum, volatile organic compound, SPME, essential oil, GC-MS*

1.Introduction

In the last period, more and more people are choosing natural products to treat certain diseases. *Galium verum* L., (yellow bedstraw) is an herbaceous perennial, belonging to the *Rubiaceae* family, noted for their yellow-golden flowers, with think and rich inflorescences, and a very pleasant smell [1]. This plant spread throughout in all Europe, but also in North Africa and Asia. The genus *Galium* is well represented in the spontaneous Romanian flora, there are between twenty-eight and thirty-five species, with white and yellow flowers. [2]. She is one of the most used plants in traditional medicine from ancient times until now. Most of these species have been extensively investigated for antraquinones [3] and iridoids [4, 5] but little is known about other bioactive compounds classes. The plant contains flavonoids, small amounts of iridoid, glycosides, phenolics, [6-8] flavonoids, [9, 10] carbohydrates, tannins, enzymes which coagulate animal milk, amino acids and essential oil [11]. *Galium verum* possessed antioxidant, cytotoxic, antimicrobial, protective and endocrine effects. [12, 13] Today this plant is used in the treatment of many diseases, due to its sudorific and diuretic effects, choleretics, against diarrhea and in the treatment of some stomach complaints, respiratory and skin diseases, but also in cosmetics [14]. Can be used both internally, in the form of powder, tincture, macerate, tea, and externally, in the form of extract and ointment. [15]. Alleged medical benefits of the plant in folk medicine are numerous, but research nowadays focuses on cancer therapy [16].

Solid phase microextraction (SPME) technique was introduced the first time by Pawliszyn. [17] SPME technique is a more, rapid, sensitive, and solvent free compared to traditional methods for analyzing the fraction of volatile compounds in different matrices. SPME has been successfully utilized for a qualitative analysis of volatile components from various aromatic and medicinal plants. [18-21]. Studies on the chemical volatile profile in fresh and dried *Galium verum* plant have not been reported in the literature. There are few studies on *Gallium verum* oil composition. Extraction of essential oil was carried out by hydrodistillation, using a Clevenger-type apparatus. The main

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components previously identified in *Galium verum* oil are: caryophyllene, caryophyllene oxide, germacrene D [22], cis-3-hexenol, benzyl alcohol, squalene [23], phytol, tetradecane, hexadecane, 9,12,15-octadecatrienoic acid-methyl ester, hexadecanoic acid-methyl ester.[24] The volatiles composition influences the bioactivity of aromatic herbs and the essential oils produced from these.

There are comparative studies on different medicinal herbs between volatiles extracted from fresh living material and essential oil obtained from the same plant. [25-30].

Our research aimed to investigate the chemical volatile profile in *Gallium verum* fresh, dried and essential oil using SPME and hydrodistillation techniques (HD), followed by of gas-chromatography - mass spectrometry (GC-MS) analysis. Characterization of volatile organic compounds (VOCs) by SPME –GC-MS technique presented in this paper is the first study on *Galium verum* plant, fresh and dried to our knowledge.

2.Materials and methods

1. **Plant material**

The fresh of *Galium verum* plant (fam. *Rubiaceae)* were collected during full flowering stage from the wild Romanian flora (Cluj county), in June 2019. The vegetal herbal material was air dried at room temperature in shade, in thin layers, in a well-ventilated place until they reached a constant weight. From 3.5 kg fresh plant 1 kg of dry matter was obtained. The plant was identified in accordance with the specialized literature. [1, 2]

2. a. Solid phase microextraction (SPME)

In order to develop a SPME procedure for the isolation of *Galium verum* plant headspace volatiles, the optimisation of parameters influencing this process such as fibre coating, extraction time and temperature was carried out. The fresh and dried of *Galium verum* plant were subjected to chemoprofiling using by solid phase microextraction (SPME) coupled with gas-chromatograph-mass spectrometer (GC-MS). The sample (1g) together with distilled water (8 mL) was placed in a 20 mL vial and closed by a cap with a teflon septum. The vials were placed in a water bath with a temperature of 50-55°C for 15 minutes to disperse and release the volatiles from the matrix. The fiber used was Carboxen /PDMS 75µm. (Supelco). The preconditioned SPME fiber (270°C, 1h) in the GC-injector port was inserted into the head space of the vial containing the sample. Heating of the sample continue 20 min during collection/adsorption. The fiber was then retracted and inserted into the injector of GC-MS. Desorption was performed for 10 min with the injector at 240°C.

b.GC- MS analysis

Identification of the volatile compounds was performed using on instrument Model Agilent 7890 & 5975 Series MSD, equipped with a HP-5MS (5% phenyl)-methyl polysiloxane fused silica column Agilent (30 m x 0.25 mm x 0.25 µM). GC-MS data was obtained under the following conditions: carrier gas helium (He 6.0), flow rate 1ml/min, injector temperature was 260˚C, splitless mode. The temperature program was the following: Oven temperature was programmed as 40˚C for 1 min and an increase by 5 ˚C /min to 200 ˚C. From 200 ˚C to 240 ˚C, increase with 20 ˚C /min. It is maintained at 240 °C for 5 minutes. Mass spectra: electron impact (EI+) mode, 70 eV and ion source temperature, 230°C. Mass spectra were recorded over 50-500 a.m.u.range, scan mode. All analyses were carried out in duplicate. Data acquisition and processing were performed using MSD ChemStation software. NIST library was used for identification/ confirmation of the structure components In addition, a C_8-C_{20} standards alkanes (Alkane Standard Solution C_8-$C_{20,}$ Sigma Aldrich) was used for calculation of the linear retention index (RI), and matching the experimental values with those reported in the literature for similar chromatographic columns, in the same condition. For compounds with RT < 5.690 and RT > 29.978, KI was reported from Nist Library Spectra.

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3. a. Extraction of Essential Oil by Hydrodistillation Method (HD)

The aerial parts of *Galium verum* were dried in shadow at room temperature for one week, cut into pieces of size over the range 1-4 cm and grounded to a homogeneous powder. Extraction of essential oil was carried out by hydrodistillation, using a Clevenger-type apparatus.Two distillations were carried out by boiling 100 g of dried leaves of *Galium verum* in 1liter of distilled water during 3h, the yield of essential oil was determined in relation to the dry matter (1,1% w/w). The yellowish oil obtained was collected and dried over anhydrous MgSO4, and stored in dark glass bottles at 4 °C prior to use.

b. Analyses of Essential Oil by GC-MS.

The oils were analyzed by gas chromatography-mass spectrometry (GC-MS) using an instrument Model Agilent 7890 & 5975 Series MSD. The some chromatographic conditions and MS operating parameters were identical to those used for the analysis of fresh and dried plant volatiles. (2.b). The different temperature program was the following: oven temperature was programmed as 40˚C for 1 min and an increase by 5 ˚C /min to 200 ˚C. From 200 ˚C to 260 ˚C, increase with 20 ˚C /min. It is maintained at 260°C for 10 minutes. The constituents of the volatile oils were identified by calculation of their retention indices under temperature –programmed conditions for C8-C20 standards alkanes (Alkane Standard Solution C8-C20, Sigma Aldrich) and the oil on HP 5-MS column in the same conditions. For compounds with RT < 5.690 and RT > 29.978, KI was reported from Nist Library Spectra.

3.Results and discutions

A total of twenty-eight compounds were identified representing 99,86% of the fresh aerial parts of *Gallium verum* herb. The floral bouquet of fresh flowers, *Gallium verum* comprised mainly oxygenated monoterpenes representing 73.57%. The major components indentified were: 3-hexen-1-ol-acetate (9.27%); trans-β ocimene (6.73%), linalool (30.08%); linalyl acetate (12.07%); caryophyllene (6.89); A total of fifty compounds were identified representing 99.88% of the dried aerial parts of *Gallium verum* herb. The floral bouquet of dried flower, *Gallium verum* contains mainly: aldehydes, 35.48% monoterpenes 35.48%, alcohols 11.96%, sesquiterpenes, 3.71%, acetates 3.14% and others 10.11%. The major components indentified were, *Gallium verum* contains mainly: hexanal (4.98), *Z*-2-hexenal (12.75%), 1-hexanol (7.90%), eucalyptol (13.87%), linalool (5.29%), camphor (4.33). (Table 1).

Table 1. Volatile compounds identified in fresh and dried of *galium verum* plant

SPME- GC-MS					
	Compounds	RT	RI	Fresh %	Dried %
1	**Hexanal**	8.624	800	-	**4.98**
2	***Z*-2-Hexenal**	10.108	848	-	**12.75**
3	*Z*-3-Hexen-1-ol	10.129	849	1.80	-
4.	1-Hexanol	10.539	864	-	**7.90**
5	Heptanal	11.494	900	-	1.70
6	α-Pinene	12.583	938	-	1.47
7	Camphene	13.066	954	-	0.43
8	*E*-2-Heptenal	13.154	957	-	1.85
9	Benzaldehyde	13.372	965	-	2.17
10	3-Octen-1-ol	13.818	980	-	**3.23**
11	β-Pinene	13.912	983	-	2.66
12	3-Octanone	14.062	988	**3.12**	1.90
13	β-Myrcene	14.223	994	**5.45**	-
14	(*E,E*)-2,4-Heptadienal	14.373	999	-	1.55

15	Octanal	14.534	1004	-	0.81
16	**3-Hexen-1-ol-acetate**	14.659	1009	**9.27**	0.84
17	n-Hexylacetate	14.804	1014	-	1.55
18	o-Cymene	15.302	1031	0.26	0.77
19	d-Limonene	15.406	1034	1.33	0.83
20	**Eucalyptol**	15.520	1038	-	**13.87**
21	*Trans*-beta ocimene	15.598	1041	**6.73**	-
22	Benzenacetaldehyde	15.863	1050	-	2.41
23	*Cis*-beta - ocimene	15.920	1052	**4.23**	-
24	*E*-2-Octenal	16.200	1061	-	1.31
25	γ-Terpinene	16.304	1065	0.32	-
26	*Cis*-linalooloxide	16.714	1079	-	0.71
27	*Trans*-linalool oxide	17.170	1094	-	0.55
28	Terpinolene	17.201	1095	0.60	-
29	**Linalool**	17.456	1104	**30.08**	**5.29**
30	Nonanal	17.539	1107	-	**3.55**
31	1-Octen-3-yl acetate	17.710	1113	0.54	-
32	Phenylethyl alcohol	18.083	1126	-	0.55
33	(*E*,*Z*)-allo-ocimene	18.286	1134	1.80	0.42
34	(*E*,*E*)-allo-ocimene	18.654	1147	0.45	-
35	Lilac aldehyde A	18.720	1149	-	0.80
36	Cyclopentasiloxane,decamethyl	18.835	1153	-	1.57
37	**Camphor**	18.934	1157	-	**4.33**
38	*E*-2-Nonenal	19.131	1164	-	1.03
39	Lavandulol	19.391	1172	1.98	-
40	Pinocarvone	19.406	1173	-	1.14
41	Terpinen-4-ol	19.822	1188	**3.89**	0.39
42	Butanoic acid-hexyl ester	19.972	1193	0.45	-
43	Methyl salicylate	20.263	1204	-	0.75
44	Decanal	20.382	1193	-	0.69
45	3-p-Menthen-7-al	20.994	1231	-	0.49
46	**Linalyl acetate**	21.793	1261	**12.07**	0.34
47	*E*-2-Decenal	21.918	1266	-	0.14
48	Lavandulyl acetate	22.639	1293	1.22	-
49	Cyclopentasiloxane, dodecamethyl	23.494	1326	-	2.75
50	Eugenol	24.502	1366	-	0.77
51	Nerol acetate	24.538	1368	1.03	-
52	Geranyl acetate	25.015	1387	2.13	0.22
53	β-Bourbonene	25.384	1401	-	0.74
54	α-Santalene	26.157	1433	0.42	-
55	Caryophyllene	26.307	1440	**6.89**	1.89
56	Trans-α-Bergamotene	26.484	1447	0.32	0.11
57	Cis-β-Farnasene	26.852	1462	2.25	0.45
58	Humulene	27.096	1473	0.28	0.36
59	1,15-Pentadecanediol	27.719	1499	-	0.28
60	Squalene	29.656	1597	-	0.16
61	2,2,4-Trimethyl-1,3-pentanediol-diisobutyrate	30.137	1606	0.55	0.76
62	Tetradecanal	30.360	1616	-	0.54
63	Di-n-octyl-ether	31.167	1654	0.40	**3.13**
	Total			**99.86**	**99.88**

Extraction of essential oil from dried aerial part of *Galium verum* was carried out by hydrodistillation, using a Clevenger-type apparatus. Sixty components were identified in the essential oil of *Galium verum* representing to 26.84% aldehydes, 19.28% monoterpenes, 23.37% non-terpene-hidrocarbons, 9.06% heterocycles, 7.78% organic acids, 6.1% sesquiterpenes, 7.29% others (Table 2)

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Table 2. Composition of essential oils of aerial parts of *Galium verum*

HD-GC-MS				
	Compounds	RT	RI	*Galium verum* %
1	3-Hexanone	7.891	775	0.74
2	2-Hexenal	9.728	851	1.12
3	Benzene acetaldehyde	15.560	1048	0.84
4	Benzofuran	16.499	1079	1.33
5	**Linalool**	17.132	1101	**7.89**
6.	Nonanal	17.277	1106	2.52
7	2-Nonenal	18.901	1162	0.40
8	Cinnamaldehyde	19.456	1181	1.10
9	Alpha-terpineol	20.027	1201	1.61
10	Decanal	20.193	1207	0.98
11	Verbenone	20.437	1216	0.61
12	Trans-p-mentha-2,8-diol	20.733	1227	1.11
13	Linalyl acetate	21.340	1249	2.30
14	2-Decenal	21.754	1264	0.89
15	Lavandulyl acetate	22.227	1282	0.30
16	Tridecane	22.724	1300	1.66
17	Undecanal	22.959	1309	2.58
18	(*E*,*E*)-2,4-Decadienal	23.291	1322	0.98
19	Geranyl acetate	24.713	1377	1.72
20	Damascenone	24.920	1385	0.49
21	(*E*,*E*) -2,6-Dimethyl-1,3,5,7-octatetraene	25.067	1391	1.48
22	β-bourbonene	25.164	1395	0.63
23	Tetradecane	25.301	1400	1.26
24	Dodecanal	25.564	1411	1.38
25	Caryophyllene	26.098	1433	**2.15**
26	**Furane-2-methyl-5-(1,1,5-trimethyl-5-hexenyl)**	26.337	1443	**7.73**
27	β-Famesene	26.612	1454	0.74
28	2,6,10-Trimethyl-tridecane	26.752	1460	0.32
29	Humulene	26.980	1469	0.45
30	*Trans*-beta-ionone	27.369	1485	0.67
31	Pentadecane	27.738	1500	1.25
32	Tridecanal	28.028	1513	1.06
33	1,8-(2H,5H)-Naphthalenedione,hexahydro-8a-methyl,*cis*	28.275	1523	1.41
34	Lilial	28.526	1534	0.33
35	Caryophyllene oxide	29.995	1598	0.74
36	**Tetradecanal**	30.368	1615	**6.00**
37	Tau-cadinol	31.219	1654	2.87
38	Heptadecane	32.233	1700	0.71
39	Pentadecanal	32.579	1719	2.96
40	Tetradecanoic acid	33.372	1761	0.76
41	Hexadecanal	34.358	1821	**3.33**
42	2-Pentadecanone,6,10,14-trimethyl	34.654	1845	1.27
43	Nonadecane	35.333	1900	0.48
44	Heptadecanal	35.541	1922	0.46
45	**n-Hexadecanoic acid**	35.904	1961	**6.49**

46	Hexadecanoic acid, ethyl ester	36.190	1992	0.43
47	Eicosane	36.267	2000	0.56
48	Octadecanal	36.470	2037	1.01
49	*Z*-10-Heneicosene	36.911	2060	0.34
50	Heneicosane	37.129	2100	1.46
51	Phytol	37.285	2128	**3.44**
52	(*Z,Z*)-9,12-octadecadienoic acid	37.762	2147	0.53
53	Docosane	38.037	2200	1.23
54	*Z*-9-Tricosene	38.789	2274	**3.11**
55	**Tricosane**	39.044	2300	**5.94**
56	Tetracosane	40.221	2400	0.51
57	Hexacosane	41.088	2600	0.40
58	Heptacos-1-ene	41.233	2673	0.59
59	Heptacosane	41.654	2700	1.40
60	Ocatacosane	45.695	2800	0.67
	Total			**99.72**

The major components are: linalool (7.89%), Furane-2-methyl-5-(1,1,5-trimethyl-5-hexenyl) (7.73%), tetradecanal (6.00%), caryophyllene (2,15%), hexadecanal (3.33%), n-hexadecanoic acid (6.49%), phytol (3.44), 9-tricosene (3.11%), tricosane (5.94%).

From the study of the profile of the volatiles, we observed the considerable differences between the volatiles extracted from the fresh, dried plant and the essential oil obtained from the same plant. (Fig. 1.)

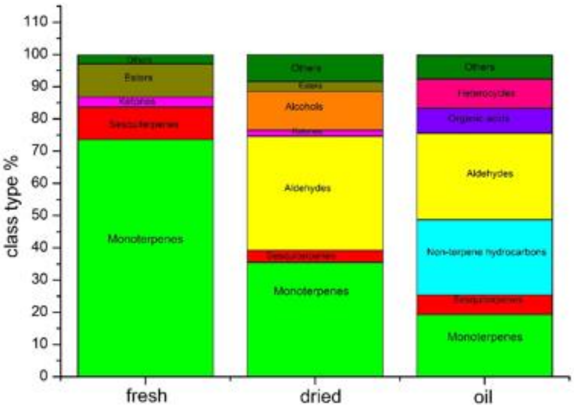

Figure 1. Class type found in the aerial part fresh, dried and oil in *Galium verum* by SPME and HD methods

From Figure 1 we observe in the oil a decrease of the content of monoterpenes (19.28%) compared to the content in monoterpenes from fresh (73.57%) and dry (35.48%).The gallium fresh flower has a scented odor, due to the presence of monoterpenic compounds in percentage of 73,75%. **Linalool and linalyl acetate** are common floral volatiles widely used in pharmaceutical industry due to bioactive properties demonstrated (anti-inflammatory, anticancer, anti-hyperlipidemic, antimicrobial, antinoceptive, analgesic, anxiolytic, antidepressive and neuroprotective), [31, 32], in cosmetical industry (perfumes, shampoos, among others) due to pleasant aroma [33], are involved in communication and protection through plant–pollinator interactions [34]. Numerous therapeutic uses of **β-caryophyllene** have been discovered, with the molecule displaying analgesic, antibacterial, antidepressant, anti-inflammatory, antiproliferative, antioxidant, anxiolytic, and neuroprotective actions. [35]. **β -Ocimene** is one of the most present volatile in floral scents and can play very relevant roles in the attraction of several types of pollinators to the flowers of a diverse array of plants. [36] Because the fresh plant contains many terpenes including linalool, linalyl acetate, caryophylene, b-ocimene, with demonstrated bioactive properties, a pharmaceutical or cosmetic formula for using the plant in fresh form may be found. The literature suggests the use of glycerin as an embedding matrix for fresh plants because it preserves them very well. [15, 37]

After drying the plant, the content of monoterpenic compounds that give off the fresh odor decreases, which are very volatile. The dried gallium flower has a grassy smell, due to the presence of **green leaf volatiles** (aldehydes, alcohols, acetates) specific to green plants and slightly mentholated due to camphor and eucalyptol. [38]. The dried material has a smaller sample of mass variation compared to the fresh plant and therefore contains a more predictable amount of stable active principles. So, on the market are found medicinal products from the dried gallium herb such as: teas, macerates, tinctures, creams with anti-inflammatory, anti-tumor, emollient, healing and antibacterial properties. [39]

There are few studies on the composition of the composition of *Gallium verum* oil. [22-24]. The oil isolated by hydro-distillation from the aerial parts of *Galium verum* contain: non-terpene hydrocarbons, organic acid and heterocycles, which are not present in the fresh and dried plant. These compounds are formed after distillation due to reactions caused by light, heat and oxygen when some terpenes, alcohols and aldehydes are converted to organic acids by hydrolysis and oxidation. [39] The new compounds were found in oil, which were not reported in the literature: furane-2-methyl-5-(1,1,5-trimethyl-5-hexenyl) (7.73%), tetradecanal (6%), hexadecanal (3.33%), tricosane (5.94), 9Z-tricosene (3.11%), etc. Essential oils have wide variety of bioactivities and play an important role as ideal natural sources of antimicrobial, antioxidant and chemopreventive agents. [41, 42].

This diversity of content gives the plants multiple healing, beauty and even immunization properties to different diseases, which justifies its reputation as a magic plant.

4.Conclusions

In the present study, VOC_s profile in *Gallium verum* fresh, dried and essential oil, were extracted using SPME and HD techniques, followed by GC-MS analysis. The *Gallium verum* herb was harvested from spontaneous Romanian flora.

- From the study of the *Galium verum* VOCs, we observed the considerable differences between the volatiles extracted from the fresh, dried plant and the essential oil obtained from the same plant.
- The differences in the extraction techniques applied resulted in differences in the extracted essential oil, such as considerably higher quantity of the monoterpenes adsorbed on SPME than in the HD oil.
- A literature search did not show any reference to previous work on the characterization of volatile profile from fresh and dried *Galium verum* by SPME-GC-MS technique.
- The new compounds were found in essential gallium oil, which were not reported in the literature: furane-2-methyl-5-(1,1,5-trimethyl-5-hexenyl) (7.73%), tetradecanal (6%), hexadecanal (3.33%), tricosane (5.94), 9Z-tricosene (3.11%), etc.
- Because the fresh plant contains many terpenes including linalool, linalyl acetate, caryophylene, β-ocimene, with demonstrated bioactive properties could be proposed, a pharmaceutical or cosmetic formula that uses fresh plant.

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