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 *Galium verum* using SPME and hydrodistillation techniques, followed by GC-MS analysis. Characterization of volatile compounds composition by SPME–GC-MS technique presented in 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 *Galium 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: *Galium 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 anthraquinones [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, choleric, 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 *Galium verum* oil composition. Extraction of essential oil was carried out by hydrodistillation, using a Clevenger-type apparatus. The main
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 *Galium 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 C₈-C₂₀ standards alkanes (Alkane Standard Solution C₈-C₂₀, 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.
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 1 liter of distilled water during 3 h, 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 same 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 *Galium verum* herb. The floral bouquet of fresh flowers, *Galium 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 *Galium verum* herb. The floral bouquet of dried flower, *Galium 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, *Galium 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).

| 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 | 984 | -       | 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    |
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-hydrocarbons, 9.06% heterocycles, 7.78% organic acids, 6.1% sesquiterpenes, 7.29% others (Table 2).

| No. | Component                              | Percentage (%) |
|-----|----------------------------------------|----------------|
| 15  | Octanal                                | 14.534         |
| 16  | 3-Hexen-1-ol-acetate                   | 14.659         |
| 17  | n-Hexylacetate                         | 14.804         |
| 18  | α-Cymene                               | 15.302         |
| 19  | δ-Limonene                             | 15.406         |
| 20  | Eucalyptol                             | 15.520         |
| 21  | Trans-beta ocimene                    | 15.598         |
| 22  | Benzenacetaldehyde                     | 15.863         |
| 23  | cis-beta - ocimene                     | 15.920         |
| 24  | E-2-Octenal                            | 16.200         |
| 25  | γ-Terpinene                            | 16.304         |
| 26  | cis-linalooloxide                      | 16.714         |
| 27  | trans-linalool oxide                   | 17.170         |
| 28  | Terpinelene                            | 17.201         |
| 29  | Linalool                               | 17.456         |
| 30  | Nonanal                                | 17.539         |
| 31  | 1-Octen-3-yl acetate                  | 17.710         |
| 32  | Phenylethyl alcohol                    | 18.083         |
| 33  | (E,Z)-allo-ocimene                     | 18.286         |
| 34  | (E,E)-allo-ocimene                     | 18.654         |
| 35  | Lilac aldehyde A                       | 18.720         |
| 36  | Cyclopentasiloxane, decamethyl         | 18.835         |
| 37  | Camphor                                | 18.934         |
| 38  | E-2-Nonenal                            | 19.131         |
| 39  | Lavandulol                             | 19.391         |
| 40  | Pinocarvone                            | 19.406         |
| 41  | Terpinen-4-ol                          | 19.822         |
| 42  | Butanoic acid-hexyl ester             | 19.972         |
| 43  | Methyl salicylate                      | 20.263         |
| 44  | Decanal                                | 20.382         |
| 45  | 3-p-Menthen-7-al                      | 20.994         |
| 46  | Linalyl acetate                        | 21.793         |
| 47  | E-2-Decenal                            | 21.918         |
| 48  | Lavandulyl acetate                     | 22.639         |
| 49  | Cyclopentasiloxane, decamethyl         | 23.494         |
| 50  | Eugenol                                | 24.502         |
| 51  | Nerol acetate                          | 24.538         |
| 52  | Geranyl acetate                        | 25.015         |
| 53  | β-Bourbonene                           | 25.384         |
| 54  | α-Santalene                            | 26.157         |
| 55  | Caryophyllene                          | 26.307         |
| 56  | Trans-α-Bergamotene                    | 26.484         |
| 57  | Cis-β-Farnasene                        | 26.852         |
| 58  | Humulene                               | 27.096         |
| 59  | 1,15-Pentadecanediol                  | 27.719         |
| 60  | Squalene                               | 29.656         |
| 61  | 2,2,4-Trimethyl-1,3-pentanediol-diisobutyrate | 30.137     |
| 62  | Tetradecanal                           | 30.360         |
| 63  | Di-n-octyl-ether                       | 31.167         |
| **Total** |                                      | **99.86**     | **99.88**   |
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 Benzo furan                               | 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 Tridecane                               | 28.028| 1513 | 1.06           |
| 33 1,8-(2H,5H)-Naphthalenedione,hexahydro-8a-methylLeis | 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           |
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.)

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, caryophyllene, 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 Gallium 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, VOCs 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 Gallium 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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