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Multivariate analysis (PCA) in Compositae biocompounds class

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Abstract

The paper presents a multivariate analysis (principal component analysis, PCA) study on the chromatographic (GC-MS) data of the main biocompounds from Compositae family plants. The samples were flower, leaf, stem, and root from *Matricaria chamomilla* L. – chamomile, *Achillea millefolim* L. - yarrow, *Cynara scolymus* L. - artichoke, and *Tussilago farfara* L. – coltsfoot, and the extracts were obtained by SDE (steam-distillation/extraction) with yield up to 0.5%. The main biocompounds identified especially in flower samples were α-bisabolol, bisabolol-oxides A and B, and camazulene, with the exception of artichoke samples, where the main compounds were sesquiterpenes like β-cubebene. PCA analysis revealed the best similarity of the chamomile, yarrow, and coltsfoot samples, by using the chromatographic data of the sesquiterpenoids.

Keywords: Compositae family, gas chromatography-mass spectrometry, essential oils, bisabolol, bisabolol-oxid, camazulene, principal component analysis

1. Introduction

The Compositae family contains very useful species from the pharmaceutical point of view: *Matricaria*, *Achillea*, *Artemisia*, *Tussilago*, *Arnica*, *Calendula*, *Arctium*, *Cynara*, *Silybum*, *Taraxacum* species. The chemical composition is very different, many compounds being identified in all species (like triterpenic saponosides, alantolactones, terpenoids), but some of them being specific (like silybin – a flavonolignan from *Silybum* species). These compounds are mainly responsible for the therapeutic properties of extracts from Compositae family plants (anti-inflammatory, antiseptic, antihemorrhagic, antispastic, hepatoprotective properties) [1,2]. Although few Compositae crops currently play a major role in global agriculture, many species hold unexploited potential, especially as novel crops for food and industrial applications [3].

Various species of chamomile (*Matricaria recutita* L., *Chamomilla recutita* L., *Matricaria chamomilla* L. etc.) are the most popular ingredient herbal teas, or tisanes and are traditionally used for medicinal purposes. The biological activity is mainly due to the phenolic compounds, primarily the flavonoids apigenin, quercetin, patuletin, luteolin and their glucosides, but also to the principal components of the essential oil extracted from the flowers: α-bisabolol and its oxides and azulenes, including camazulene. Chamomile has moderate antioxidant and antimicrobial activities, and significant antiplatelet activity *in vitro*. Animal model studies indicate potent anti-inflammatory action, some antimutagenic and cholesterol-lowering activities, as well as

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antispasmodic and anxiolytic effects. Adverse reactions to chamomile, consumed as a tisane or applied topically, have been reported among those with allergies to other plants in the daisy family, *i.e.* Asteraceae or Compositae [4-7]. The chamomile essential oils were investigated among the biocompounds distribution during the ontogenesis and flowering period. It can be see that the harvest-timing results as a compromise between increasing flower yield, decreasing oil content and changing composition of the essential oil [8].

The inhibitory effect of chamomile essential oils and its major constituents on four human cytochrome P450 enzymes was studied. Crude essential oil demonstrated inhibition of all enzymes, and camazulene, *cis*-spiroether, and *trans*-spiroether showed to be potent inhibitors of these enzymes (especially CYP 1A2). Other enzymes were inhibited by α-bisabolol [9]. The Arcaricidal properties of decoctions, infusions and macerates of dried flower heads of chamomile, *Matricaria chamomilla* L. were tested *in vitro* against the mite *Psoroptes cuniculi* Delafond. This mite species is responsible for otoacariasis in domestic animals [10]. Different preparations of chamomile (*i.e.* essential oils) were used to determine the inhibitory effect on the sister chromatid exchanges produced by some drugs in mouse marrow cells. The main biocompounds identified to having these activities were bisabolol and its oxides, camazulene, farnesene, germacrene, and other sesquiterpenes [11].

Another important species from Compositae family is *Achillea*. The composition of various essential oils from *Achillea* species was determined. The major constituents in leaves essential oils were germacrene-D, bicyclogermacrene, camphor, borneol, 1,8-cineole, spathulenol, and bornyl acetate [12]. *Achillea milefolium* L. (yarrow) extracts were traditionally used in cures and remedies, particularly for the treat of infections and infectious diseases, as spasmolytic, haemostatic and for its digestive effects [13]. The gentotoxicity of *Achillea milefolium* L. essential oils against *Aspergillus nidulans* was investigated. The major biocompounds identified in these oils were: camazulene, sabinene, terpinen-4-ol, β-caryophyllene, and eucalyptol (75% of the total) [14]. The volatile components from *Achillea ligustica* species from Italy by using headspace (HS) analysis and solid-phase microextraction (SPME) were especially camphor, artemisia ketone, santolina alcohol, camphene, and *trans*-sabinyl acetate [15]. The hydroalcohol extracts of *Achillea millefolium* L. and *Artemisia vulgaris* L. were evaluated by the hot plate, writhing, formalin and intestinal transit tests in an attempt to confirm their folk use as analgesic, anti-inflammatory and antispasmodic agents. Both species significantly inhibited abdominal contortions. The hydroalcohol extracts showed the same flavonoid glycoside as a principal constituent, which was identified as rutin. A high content of caffeic acid derivatives were also found in both extracts [16].

The ethanolic extracts and aqueous suspensions of *Cynara cardunculus* L. plant were evaluated for their antioxidant and antimicrobial properties (on *Salmonella*, *Escherichia*, *Bacillus*, *Staphylococcus* bacteria and some micromycetes), and these bioactivities were comparable with standard antibiotics [17]. Among other medicinal plants, *Cynara scolymus* L. has significantly effective in reduction of blood glucose. This antihyperlipidaemic property suggests the use of these plants as supplements in diabetes [18]. Artichoke leaf extracts have been reported to reduce plasma lipids levels, including total cholesterol [19].

Tussilago farfara L. (coltsfoot) are used as food and folk medicine. The root and leaves are used in chronic bronchitis, asthma, chest complaints, and inflammations. The leaves are smoked like tobacco, as a domestic remedy for asthma [20,21]. Among common bioactive compounds from Compositae family, coltsfoot also contain triterpenes like bauerane, friedelane, lanostane, lupane, oleanane, ursane [22].

In this study the composition of the *Matricaria chamomilla* L., *Achillea millefolium* L., *Cynara scolymus* L., and *Tussilago farfara* L. SPE extracts were evaluated by using the GC-MS analysis and the similarity of these species was pointed out by using the most powerful statistical multivariate analysis, PCA, as a continuation of the team activity in this field [23-24].

2. Materials and Method

Materials. Four plants (different parts) from the Compositae family were used for extraction: *Matricaria chamomilla* L. – chamomile, *Achillea millefolium* L. - yarrow, *Cynara scolymus* L. - artichoke, and *Tussilago farfara* L. – coltsfoot. These plants were colected in 2007 from the North-West of Romania (Apuseni mountains). C_8-C_{20} alkane standard solution was obtained from Fluka. *n*-Hexane used in separation and chromatographyc analysis was purchased from Merck and was GC grade solvent.

Steam-distillation/extraction (SDE). All significative parts (flower, leaf, stem, and root) of the selected plants from Compositae family were subjected to the steam-distillation/extraction; 50 g finelly grounded sample and 250 ml distilled water were added to a 500 ml three neck flask (steam distillation flask) and 20 ml hexane in the pear like flask (extraction flask) with boiling regulator. The flasks were connected to the SDE apparatus (with an efficient reflux condenser), the distillation flask was put in a oil bath, and the extraction flask in a water bath at 70-75ºC. The distilation-extraction was realized in 3 hours, the hexane extract was concentrated, dried over anhydrous $CaCl_2$, filtered and analyzed by GC-MS.

GC-MS analysis. For gas chromatography-mass spectrometry analysis of extracts a Hewlett Packard HP 6890 Series gas chromatograph coupled with a Hewlett Packard 5973 Mass Selective Detector was used. GC conditions were: HP-5 MS capillary column with a length of 30 m, inner diameter of 0.25 mm, and film thickness of 0.25 μm was used for separation; the program temperature was 50ºC to 250ºC with a rate of 6ºC/min, both injector and detector temperature 280ºC, injection volume 2μl; He was used as gas carrier. The MS detector has a EI energy of 70 eV, with a source temperature of 150ºC, scanning range of 50-300 amu, scanning rate 1 s^{-1}, and the obtained spectra were compared with the NIST/EPA/NIH Mass Spectral Library 2.0, 2002, in order to identify the biocompounds separed from the Compositae family plants. For some biocompounds (like common mono- and sesquiterpenoids) the Kovats indices (KI, calculated on the basis of retention times obtained by GC-MS analysis of the C_8-C_{20} alkane standard mixture in the same conditions as for the Compositae extract samples) were used as extraparameter for the identification of biocompounds. For all extracts the relative concentration (evaluated as biocompound area percent of the total area of peaks separed by GC) of biocompounds were calculated and these values were used for the statistical multivariate analysis (PCA).

Principal Component Analysis (PCA). The multivariate analysis of the GC data was achieved using the PCA analysis of the relative concentration of the main identified biocompounds from the Compositae family plants.

Principal component analysis (PCA) is the basis of the multivariate analysis of the data. PCA presumes an approximation of the *X* matrix (data) as a product of two reduced matrices, *T* and *P*, which retain only the useful information from *X*. The graphical representation of *T* columns conduct to the "object shape" images of *X*, and the graphical representation of *P* rows conduct to the "variable shape". Thus, the first direction (first principal component, PC_1) in the properties space, for which the data have maximum variance, conduct to the monodimensional representation of the data as projections on this PC_1; the second direction (named PC_2) has the same particularities, but it is perpendicular to PC_1. Other directions can be obtained in the

same way, but only some of them will be PCs. The *X* matrix can be described as a sum of a useful matrix (**X*), which is a product of score matrix (**T*) and loadings matrix (**P*), and an error matrix (*E*). Representation of the *t* vectors (one to another) can conduct to information about similarities and possible grouping of the studied objects; the same representation of the *p* vectors can furnish the similarities between properties and the importance of these properties for the model.

3. Results and Discussion

The yields of volatile oil separation in the case of *Matricaria chamomilla* L. were in the range of 0.1-0.5% for all plant parts (flower, leaf, stem, and root), with a maximum for flowers. The GC-MS analysis of extracts (Figure 1) revealed that the α-bisabolol (Figure 2) is the range of 26-31% (at RT 22.6 min), followed by bisabolol-oxid A and B (Figures 3 and 4) (12-14% and 16-26% at RT of 23.8 and 22.1 min, respectively) and camazulene (Figure 5) (3-3.6% at 23.5 min) for flowers. For the case of leaves, the concentration of α-bisabolol was lower (2.4-3.3%), as well as bisabolol-oxides (0.4-2.4%), but camazulene was more concentrated (18.7%); in this case, sesquiterpenes were more concentrated. A reduced number of compounds were identified in the stem and root extracts. The concentrations of main compounds from *Matricaria chamomilla* L. extracts are presented in Table 1.

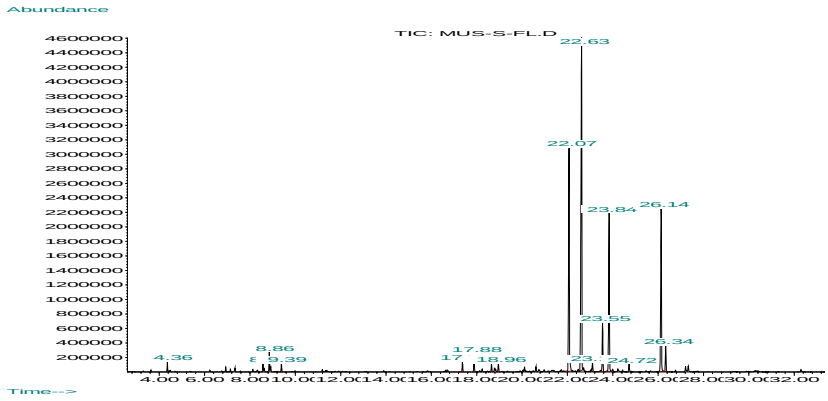

Figure 1. GC-MS chromatogram for the *Matricaria chamomilla* L. flowers extract

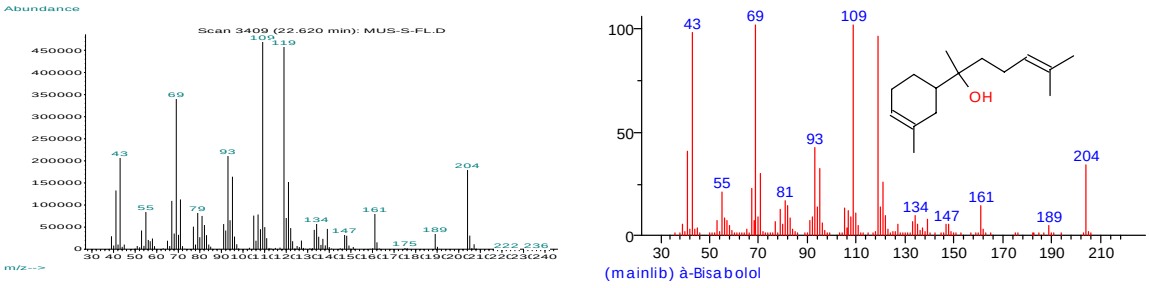

Figure 2. Experimental (left) and from the NIST database (right) MS spectrum for α-bisabolol

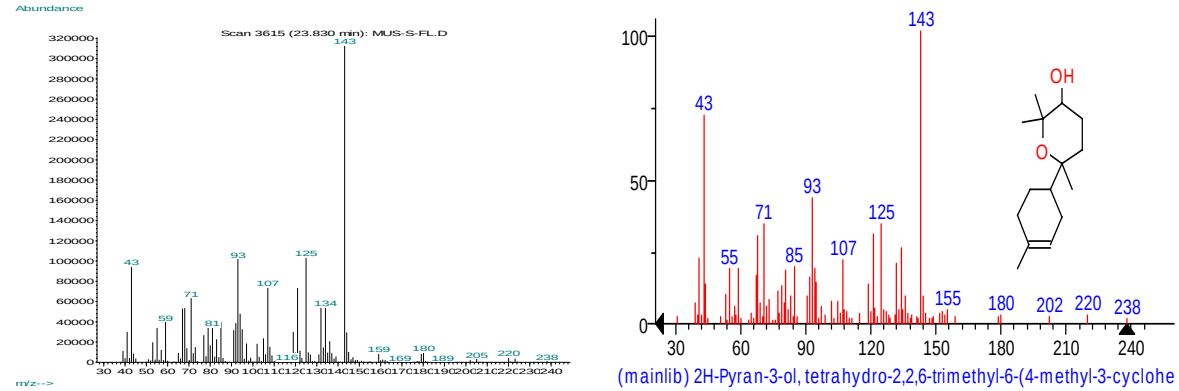

Figure 3. Experimental (left) and from the NIST database (right) MS spectrum for bisabolol-oxid A

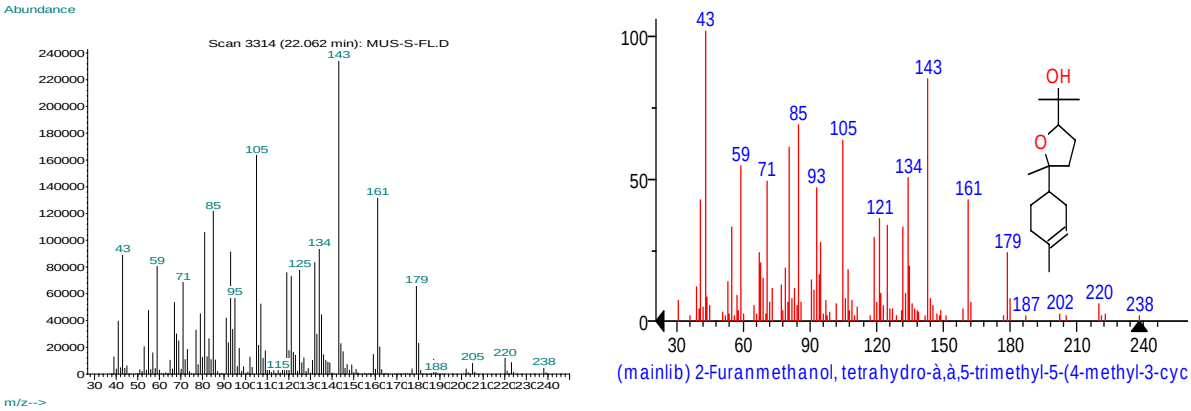

Figure 4. Experimental (left) and from the NIST database (right) MS spectrum for bisabolol-oxid B

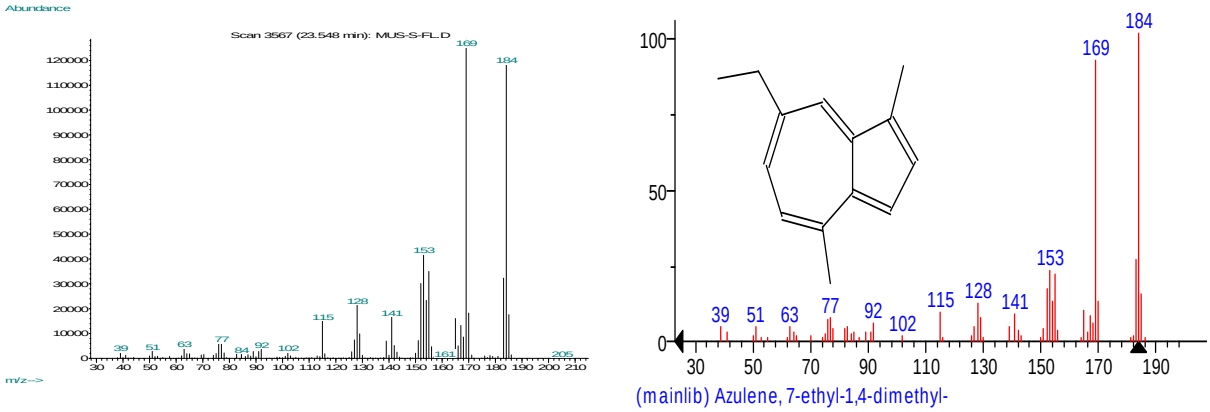

Figure 5. Experimental (left) and from the NIST database (right) MS spectrum for camazulene

Tabel 1. Relative concentrations (as percent area of total peaks area) of the main biocompounds from *Matricaria chamomilla* L. (from Salonta, all plant parts analyzed) separed by GC and identified by MS

No	RT (min)	KI	MS Identification	Area% (flower)	Area% (leaf)	Area% (root)	Area% (stem)
1	22.073	1454	alpha-Bisabolol oxid B	18.83	0.92	0.59	0.86
2	22.626	1472	alpha-Bisabolol	30.93	3.38	1.53	2.5
3	23.548	1503	Camazulene	3.62	18.69	16.08	27.4
4	23.836	1512	Bisabolol-oxid A	12.52	0.42	0.6	0.45

For the *Achillea millefolim* L. volatile oils from different plant parts, the main biocompounds were mono- and sesquiterpenes (pinenes, caryophyllene, cubebene), but in the case of flower extracts α-bisabolol was 0.7-2.6% (RT 22.6 min) and camazulene 11.7-12.9% (RT 23.6 min) (Table 2). These compounds were identified in concentration of 9.6-16% and 8.7-9.7%, respectively. The concentration of biocompounds in stem and root extracts were lower, only camazulene being in relatively higher concentration.

Tabel 2. Relative concentrations (as percent area of total peaks area) of the main biocompounds from *Achillea milefolium* L. (from Salonta, all plant parts analyzed) separed by GC and identified by MS

No	RT (min)	KI	MS Identification	Area% (flower)	Area% (leaf)	Area% (root)	Area% (stem)
1	22.073	1454	alpha-Bisabolol oxid B	-	7.3	3.48	0.69
2	22.626	1472	alpha-Bisabolol	0.68	16	10.27	0.76
3	23.548	1503	Camazulene	12.9	9.7	33.82	45.79
4	23.836	1512	Bisabolol-oxid A	0.08	2.8	0.97	-

For *Cynara scolymus* L. extracts the main compound was β-cubebene, especially in flowers, stem, and root extracts (38%, 39%, and 25%, respectively); in leaf extract (*E*)-2-hexenal was the major biocompound (20%) (Table 3).

The more concentrated compound in *Tussilago farfara* L. was α-bisabolol, especially in leaf extract (21%), but also in root extract (14%). Furthermore, phellandrene and cymene were identified in these last two samples (8.7-16.9% at RT 7.7 min and 12.7-22.3% at RT 8.1 min, respectively; Table 4).

Tabel 3. Relative concentrations (as percent area of total peaks area) of the main biocompounds from *Cynara scolymus* L. (from Câmpeni, all plant parts analyzed) separed by GC and identified by MS

No	RT (min)	KI	MS Identification	Area% (flower)	Area% (leaf)	Area% (root)	Area% (stem)
1	17.373	1305	Caryophyllene	5.01	0.55	3.49	4.68
2	18.654	1345	beta-Cubeben	38.24	6.46	25.21	39.07
3	18.954	1354	Elixen	5.43	2.59	3.32	4.95
4	20.74	1411	Caryophyllene oxide	3.71	4.51	4.61	4.17
5	22.073	1454	alpha-Bisabolol oxid B	1.22	1.33	13.31	1.16
6	22.626	1472	alpha-Bisabolol	2.66	0.51	1.32	5.79

Tabel 4. Relative concentrations (as percent area of total peaks area) of the main biocompounds from *Tussilago farfara* L. (from Câmpeni, only leaf and root were analyzed) separed by GC and identified by MS

No	RT (min)	KI	MS Identification	Area% (leaf)	Area% (root)
1	22.073	1454	alpha-Bisabolol oxid B	2.76	-
2	22.626	1472	alpha-Bisabolol	20.65	14.23
3	23.548	1503	Camazulene	7.18	3.17
4	23.836	1512	Bisabolol-oxid A	0.91	-

For the advanced statistical analysis of these samples from Compositae family, the GC-MS data were used in a Principal Component Analysis (PCA) approach.

A good classification for the Compositae extracts was obtained by using the relative GC concentrations of the main biocompounds identified. Thus, *Cynara scolymus* L. (***A*** samples) extracts were positioned in the left side of the loadings plot, while *Matricaria chamomilla* L. (***M*** samples), *Cynara scolymus* L. (***CS*** samples), and *Tussilago farfara* L. (***P*** samples) extracts were more grouped in the right side of the graph (Figure 6). The explained variance of the data was 52% for PC_1 and 19% for PC_2 and this classification is attributed especially to the data for β-pinene, bisabolol, and camazulene (Figure 7).

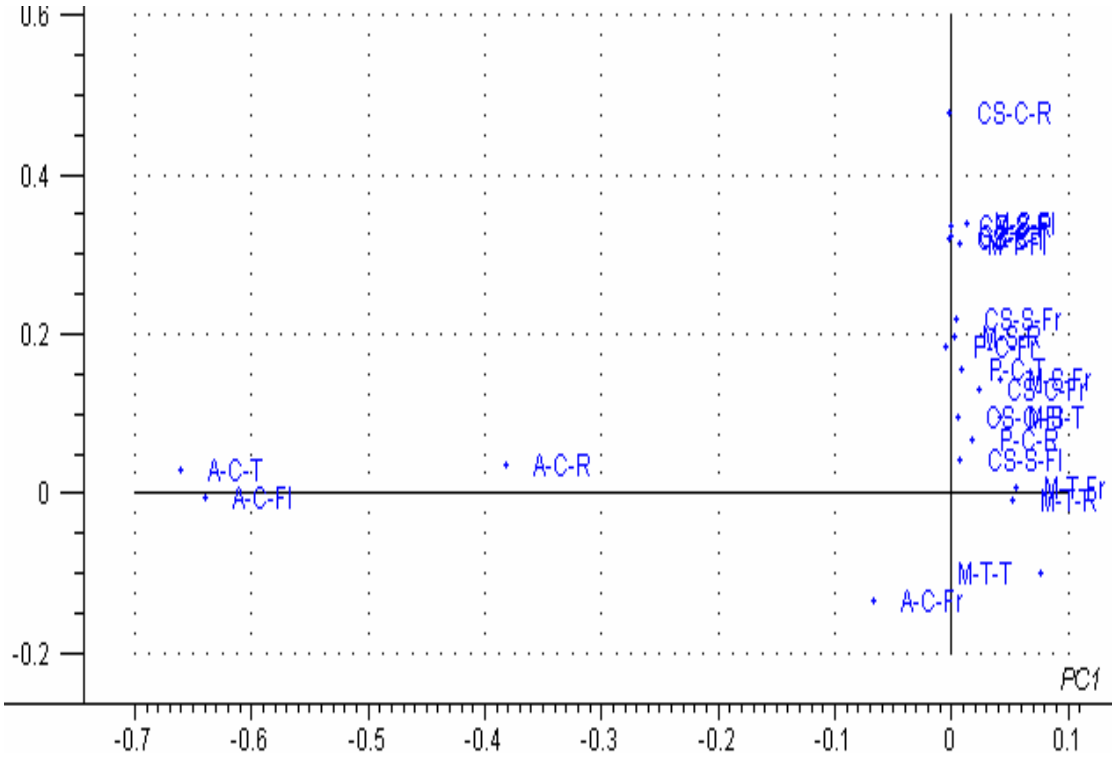

Figure 6. Loadings plot from the GC-MS analysis of the biocompounds from Compositae family plants extracts

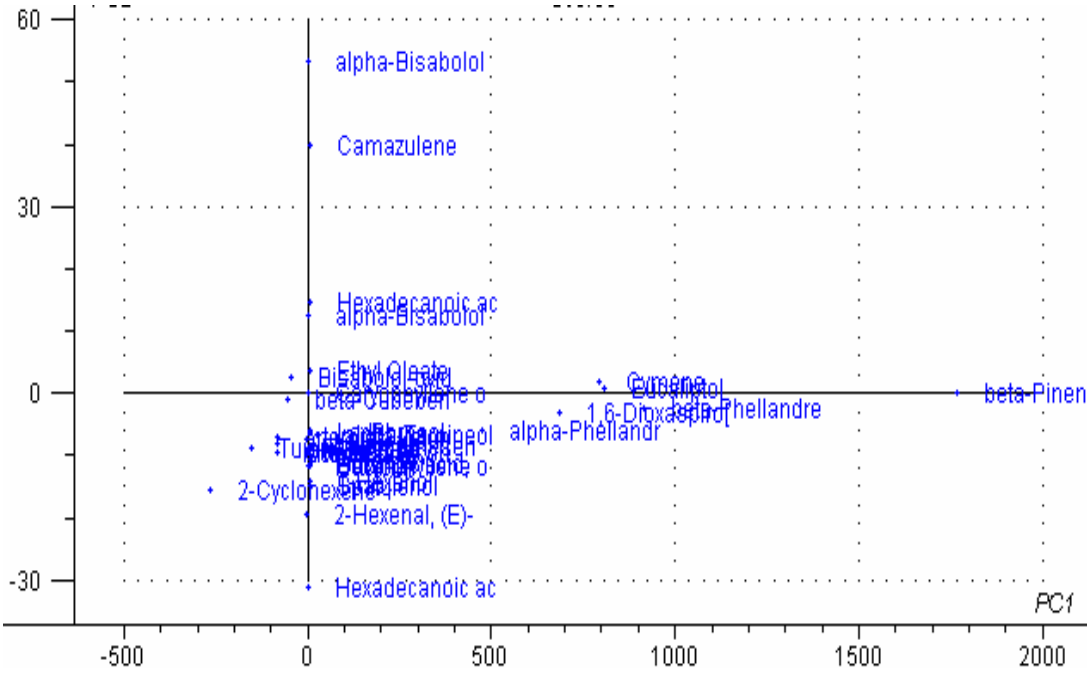

Figure 7. Score plot from the GC-MS analysis of the biocompounds from Compositae family plants extracts

4. Conclusion

The following conclusion can be draw according to the chromatographic and multivariate statistical analyses of the biocompounds from the Compositae family plant extracts: (1) twenty two samples of Compositae extracts were obtained by SDE with yield relatively low (up to 0.5%); (2) the higher concentrations were obtained for sesquiterpenoids like α-bisabolol, bisabolol-oxides A and B, and camazulene, especially in flower samples from *Matricaria chamomilla* L. (chamomile) and *Achillea millefolium* L. (yarrow); (3) the main compounds from *Cynara scolymus* L. (artichoke) was sesquiterpenes like β-cubebene, but also caryophyllene and elixen; (4) PCA analysis of the GC data revealed that the *Matricaria chamomilla* L., *Achillea millefolium* L., and *Tussilago farfara* L. samples were more similar comparatively with the *Cynara scolymus* L. samples, especially due to the sesquiterpenoids composition, therefore this advanced statistical multivariate analysis is very useful to classificate these sample types in order to evaluate the corresppondence between some biological activity (*i.e.* pharmaceutical or organoleptic properties) and important biocompounds from the essential oils from different plant parts.

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