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VARIATION IN THE COMPOSITION OF THE ESSENTIAL OIL OF COMMERCIAL ARTEMISIA ABSINTHIUM L. HERB SAMPLES FROM DIFFERENT COUNTRIES

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Wormwood (Artemisia absinthium L., Asteraceae) is an aromatic bitter herb that contains bitter-tasting metabolites and essential oil. The composition and biological effects of A. absinthium essential oil have been widely studied. However, the data on the content of the individual components vary significantly.

The aim. *The aim of the study was to research the compositions of essential oils from A. absinthium herb, which are on the market in various European countries and determine difference in their compositions, possible chemotypes, and compliance of the essential oil samples with the European Pharmacopeia requirements.*

Materials and methods. *The composition of 16 essential oil samples of A. absinthium herb from different countries was investigated using the gas chromatography method. Samples were obtained from retail pharmacies in 14 different countries.*

Research results. *A total of 41 compounds were identified in the studied A. absinthium essential oils. In all the samples, monoterpenes and monoterpenoids dominate (28.0–92.2 %), much less sesquiterpenes and sesquiterpenoids (0–18.9 %). The dominant components among the identified ones were sabinene (traces(tr.)–21,2 %), myrcene (0.1–25.6 %), p-cymene (0.2–6.5 %), 1,8-cineole (0.1–18.0 %), artemisia ketone (tr.–14.9 %), linalool (tr.–10.8 %), β-thujone (0.1–38.7 %), (E)-epoxyocymene (tr.–59.7 %), (E)-verbenol (tr.–7.9 %), borneol (tr.–11.7 %), (E)-sabinyl acetate (tr.–70.5 %), neryl butyrate (0–13.9 %), spathulenol (tr.–9.2 %), caryophyllene oxide (tr.–7.3 %). Both "pure"-chemotypes and "mixed"-chemotypes of A. absinthium have been defined.*

Conclusions. *Two"pure"-chemotype consist of 70.5 % (E)-sabinyl acetate and 59,2 % (E)-epoxyocymene, respectively. Also, eleven "mixed"-chemotypes of A. absinthium essential oils have been defined. Some correlations were established between the content of terpenes in the A. absinthium essential oils*

Keywords: *Artemisia absinthium L., essential oil, terpenes, chemotypes, (E)-sabinyl acetate, (E)-epoxyocymene, β-thujone*

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1. Introduction

The wormwood genus *Artemisia* belongs to the *Asteraceae* L. family and includes more than 500 species in the world flora [1]. *Artemisia absinthium* L. ranges from Europe to Siberia and W. Himalaya, N. Africa; it has been introduced and naturalized as a ruderal species in many countries [2, 3]. A large number of representatives of this genus grow in the countries of Western Europe [4, 5], as well as in Estonia [6]. They are also found in China, Japan, Russia, the countries of Central Asia [7], North Africa and the Middle East, India, the USA, and Canada [8, 9].

The wormwood herb (*Absinthii herba*) is an official plant raw material in European Pharmacopoeia (PhEur) [10]. The herb is collected at the beginning of flowering (July–August). In the case of gathering in a later period, the herb acquires a dark grey colour and flowers turn brown and fall apart. Wormwood is an aromatic bitter herb, which is known for bitter-tasting metabolites and essential oils [3, 11].

The essential oil of *A. absinthium* contains acyclic, monocyclic and bicyclic monoterpene(-oids) and their esters [12, 13]. These are: myrcene, nerol, lavandulol, α-terpinene, γ-terpinene, linalool, β-ocimene, cis- and trans-epoxy-ocimene, limonene, β-phellandrene, chrysanthenol, α-pinene, α-tuyol, α-thujone, β-thujone, camphene, camphor, 1,8-cineole [14], terpinolene, sabinyl acetate, thujyl acetate, neryl acetate [15], geraniacetate, geranylisovalerianate, isoborneol, thujene, thujyl alcohol, sabinene, sabinol, β-caryophyllene [16, 17], caryophyllene oxide, α-terpineol, geraniol, β-pinene [18, 19].

The sesquiterpenes of *A. absinthium* belong to different series of terpenoids, these are the acyclic (linear) and the guaiane, benzocycloheptene, germacrane, cadinane and eudesmane (selinane) groups [20, 21]. Acyclic sesquiterpenes are represented by β-farnesene and farnesol [22, 23]. Among the monocyclic sesquiterpene(-oids) of wormwood, the main ones are elemol, germacrene D, α-humulene, β-curcumene, bisabolene and α-bisabolol [24, 25].

Bicyclic sesquiterpenes of the azulene series are represented by 5,6-dihydrochamazulene, 3,6-dihydrochamazulene, chamazulene, methylchamazulene, ethylchamazulene [21, 22]. Bicyclic sesquiterpene(-oids) of the cadinene series [23, 24], naphthalene derivatives [25, 26]: α-cadinene, 7-epi-α-cadinene; eudesman series – eudesman and γ-selinene [27]. Bicyclic sesquiterpene(-oid)s of benzocycloheptene series: α-himachalene, himachalenol [28, 29]. Tricyclic sesquiterpenes of the azulene series are represented by aromadendren, copaene [30]. The aromatic monoterpene *p*-cymene (*p*-isopropyltoluene, 4-isopropyltoluene) is also typical of wormwood [31, 32].

Sesquiterpene lactones from *A. absinthium* have been well studied [33, 34]. Among the guayan lactones (guayanolides) are known artabsin, matricen, nor-sesquitepenoid absilactone, arlatin, artabsinolides A, B, C, D; dimers – absintin, absintolide, anabsintin. Among the germacrane lactones (germacranolides) are artabine, artabolide (artabolide), dihydrocostunolide, costunolide, 3α-hydroxypelenolide, ketopelenolide A, ketopelenolide B. Among the eudesmane lactones: hansonlactone, arabsin, α-santonin [33, 35]. Among the lactones, absinthine predominates at 0.28 %, artabsin at 0.04–0.16 % and matrixin up to 0.007 % [14, 31].

The composition and biological effects of the essential oil (EO) of *A. absinthium* have been widely studied. However, the data on the content of the individual components varies significantly. The composition of the EO exhibits a large intraspecific variability. It may vary depending on the growing conditions, the period of harvesting raw materials, and the conditions of its drying and storage [11, 15]. There are studies on changes in the composition of wormwood EO in the process of ontogeny, which confirm that the content of thujones changes during the growing season [2, 5]. Several chemotypes of volatile oils are known from different parts of the world according to the main constituent [31, 36]. Thujone, a major component in some essential oils, is neurotoxic. The toxicity of thujone has been extensively studied. Neurotoxicity is the principal toxic outcome in acute and chronic studies [36, 37].

Wormwood herb also contains amino acids [38] and phenolic compounds, including phenolcarboxylic and hydroxycinnamic acids, coumarins, and flavonoids [39, 40].

It has traditionally been used as an anthelmintic, choleretic, antiseptic, balsamic, depurative, digestive, diuretic, emmenagogue and in treating leukaemia and sclerosis [41]. Wormwood extracts have been used as a muscle relaxer, occasionally added to liniments, and as a mild sedative to treat anxieties [42, 43]. According to the European Medicines Agency, the comminuted and powdered herbal substance of wormwood herb is a traditional herbal medicinal product for temporary loss of appetite and for mild dyspeptic/gastrointestinal disorders [44].

In European countries, essential oil raw materials, as well as wormwood herbs, for the needs of pharmaceutical and food industries are supplied by specialized farms which cultivate medicinal herbs. These raw materials are cultivated according to strictly established rules (GAP), as well the period of collection is also regulated, and only standardized seeds can be used, therefore the information about their chemotypes is very important.

The study aims to research the compositions of samples of *A. absinthium* herb essential oils from various geographic regions and determine differences in content composition, possible chemotypes, and compliance of the essential oil samples with the PhEur requirements [10]. This study continues our previous article [9] and brings new samples and research aspects. Identification of various chemotypes of wormwood EOs allows us to predict, modulate and establish the mechanism of pharmacological activity at the molecular and cellular levels and predict their toxicity.

2. Planning (methodology) of research

The study protocol describing the different stages of the present research work is presented in the following flow chart (Fig. 1).

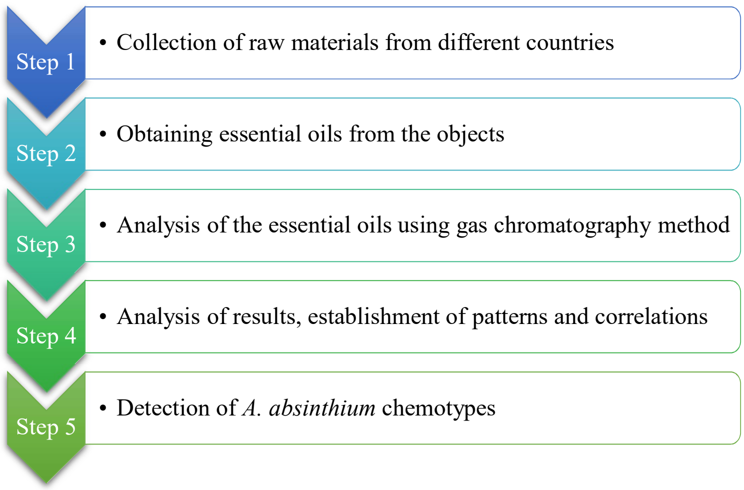

Fig. 1. Study protocol

3. Material and methods

Materials. The *A. absinthium* herbs commercial samples were obtained from retail pharmacies or health shops in different countries: Estonia 1–3, France, Belgia, Greece, Ukraine, Latvia, Lithuania, Italy, Spain, Germany, The Netherlands 1–2, England, Austria, and Georgia (in 2000–2011). They were partially studied previously [7, 9], and these results were used in our present research for settling correlations and chemotypes. Several packages of raw materials from each country were used, and average samples were made. Essential oils from the raw material samples were obtained by hydrodistillation according to the European Pharmacopoeia method and monograph “Absinthii herba” [10]. These essential oils were immediately analyzed by gas chromatography. All samples of *A. absinthium* herbs met the requirements of European Pharmacopeia [10].

Capillary gas chromatography: GC analysis was carried out using a Chrom-5 chromatograph (Laboratorni

Pristroe Prague, Czech Republic) with FID on two fused silica capillary columns with a bonded stationary phase: poly(5 %-diphenyl-95 %-dimethyl) siloxane) SPB-5 (30 m×0.25 mm, Supelco) and polyethyleneglycol SW-10 (30 m×0.25 mm, Supelco). The film thickness of both stationary phases was 0.25 µm. Carrier gas was He with a split ratio of 1:150, and the flow rate 35-40 (SPB-5) and 30–35 (SW-10) cm/s was applied. The temperature program was from 50–250 °C at 2 °C/min; the injector temperature was 200 °C. A Hewlett-Packard Model 3390A integrator was used for data processing [21].

The identification of the EO components was accomplished by comparing their retention indices (RI) using n-alkanes C6–C24 as standards on two columns with the RI values of reference standards, our RI data bank and with literature data [22, 23]. GC/MS confirmed the results obtained [45, 46]. The percentage composition of the EOs was calculated in peak areas using normalization method without correction factors. The relative standard deviation of percentages of oil components of three repeated GC analyses of a single EO sample didn't exceed 5 % [47, 48].

4. Results and Discussion

A total of seventeen wormwood EOs were used in our analyses. A total of 41 compounds were identified in *A. absinthium* EO samples studied. All identified components have been reported previously in wormwood herb EO [7, 9]. All samples of *A. absinthium* herbs met the requirements of European Pharmacopeia monograph "*Absinthii herba*" [10]. The content of essential oils in the raw materials was between 2.4 and 3.7 ml/kg. The identified compounds in EO samples from different countries, their range and mean %, and variation coefficients are presented in Table 1. The main components, whose content in EOs could be over 6 %, were sabinene (tr.–21.2 %), myrcene (0.1–25.6 %), *p*-cymene (0.2–6.5 %), 1,8-cineole (0.1–18.0 %), artemisia ketone (tr.–14.9 %), linalool (tr.–10.8 %), β-thujone (0.1–38.7 %), (E)-epoxyocymene (tr.–59.7 %), (E)-verbenol (tr.–7.9 %), borneol (tr.–11.7 %), (E)-sabinyl acetate (tr.–70.5 %), neryl butyrate (0–13.9 %), spathulenol (tr.–9.2 %), and caryophyllene oxide (tr.–7.3 %) (Table 1, Fig. 2).

High variation coefficients of the majority of compounds (>1) showed that the content of these compounds strongly differed from sample to sample. Low variation coefficients (0.56–0.76) could be seen for α-pinene, terpinolene, α-terpineol, neryl acetate, α-copaene, neryl propionate, (E)-β-caryophyllene, (E)-nerolidol and caryophyllene oxide.

In all the studied samples, monoterpenes and monoterpenoids dominate (28.0–92.2 %), much less sesquiterpenes and sesquiterpenoids (0–18.9 %). Aromatic monoterpenes are represented by *p*-cymene (0.2–6.5 %) (Fig. 3). A high content of oxygenated sesquiterpenes (6.8–16.6 %) characterized the samples from France, Austria, Ukraine, Germany, Spain, Greece, Latvia and Italy. The principal compounds in these groups were (E)-β-caryophyllene (tr.–2.1 %), caryophyllene oxide (tr.–7.3 %) and spathulenol (tr.–9.2). The EO from Germany, Italy and France contained more than 1 % chamazulene (2.1 %, 1.5 % and 1.4 %, respectively). Only Austrian wormwood EO was rich in viridiflorol (2.3 %).

In the samples from the Netherlands, England, Austria, and Georgia, the main (>10 %) compounds were also (E)-epoxyocymene (tr.–32.7 %), myrcene (0.8–29.9 %), sabinene (8.1–25.3 %), and (E)-sabinyl acetate (tr.–18.6 %) (Table 2).

Table 1

Composition of the essential oils of *Artemisia absinthium* herbs (*n*=17) from different countries

Compound	RI		Range, %	Mean, %, *n*=17	Variation coefficient
	SPB-5 SW-10	SPB-5 SW-10			
α-Thujene	924	1026	tr.–1.1	0.36	1.24
α-Pinene	929	1024	0.2–1.5	0.57	0.66
Camphene	953	1057	0–1.0	0.30	0.83
Sabinene	968	1110	tr.–21.2	7.16	1.09
β-Pinene	970	1103	tr.–0.8	0.25	0.85
Myrcene	990	1164	0.1–25.6	6.71	1.36
α-Fellandrene	1000	1165	0–4.5	0.85	1.51
***p*-Cymene**	1019	1266	0.2–6.5	1.85	1.06
1,8-Cineole	1026	1208	0.1–18.0	2.25	1.91
Limonene	1024	1202	tr.–0.4	0.20	0.42
(Z)-β-Ocimene	1035	1235	tr.–1.5	0.34	1.33
Artemisia ketone	1060	1350	tr.–14.9	2.04	2.36
γ-Terpinene	1054	1244	tr.–4.2	0.85	1.31
Terpinolene	1084	1276	0–0.5	0.20	0.61
(E)-Sabinenhydrate	1094	1548	tr.–0.3	0.22	0.33
Linalool	1100	1550	tr.–10.8	3.80	0.80
α-Thujone	1104	1415	tr.–2.5	1.05	0.96
β-Thujone	1113	1437	0.1–38.7	6.63	1.35
(E)-Epoxyocymene	1130	1468	tr.–59.7	7.90	2.10
Camphor	1139	1502	tr.–2.7	1.07	0.83
(E)-Verbenol	1158	1677	tr.–7.9	1.57	1.55
Borneol	1160	1702	tr.–11.7	2.75	1.42
Terpinen-4-ol	1172	1606	tr.–1.8	1.34	0.44
Myrtenal	1177	1645	tr.–2.1	0.50	1.32
α-Terpineol	1186	1702	tr.–1.1	0.47	0.73
Nerol	1223	1803	tr.–4.0	1.28	0.97
(E)-Sabinyl acetate	1288	1635	tr.–70.5	14.57	1.29
Neryl acetate	1368	1724	tr.–0.6	0.25	0.76
Geranyl acetate	1380	1758	tr.–0.4	0.25	0.52
α-Copaene	1373	1470	tr.–0.7	0.35	0.56
Neryl propionate	1423	1784	tr.–0.6	0.65	0.74
(E)-β-Caryophyllene	1408	1580	tr.–2.1	0.99	0.56
Neryl isobutyrate	1469	1803	0–3.2	1.20	0.87
Neryl butyrate	1505	1858	0–13.9	2.61	1.28
(E)-Nerolidol	1564	2040	tr.–0.8	0.38	0.60
Spathulenol	1568	2112	tr.–9.2	3.05	0.93
Caryophyllene oxide	1570	1958	tr.–7.3	3.23	0.75
Viridiflorol	1602	2078	tr.–2.3	0.57	0.95
Geranyl isovaleriate	1605	1905	tr.–4.9	1.10	1.23
Neryl valeriate	1639	1970	tr.–2.8	0.76	1.13
Chamazulene	1715	2363	tr.–2.1	0.60	1.05

Note: tr. – traces (<0.05 %); Bold – >1 %. The deviations of the results are within the deviations of the device

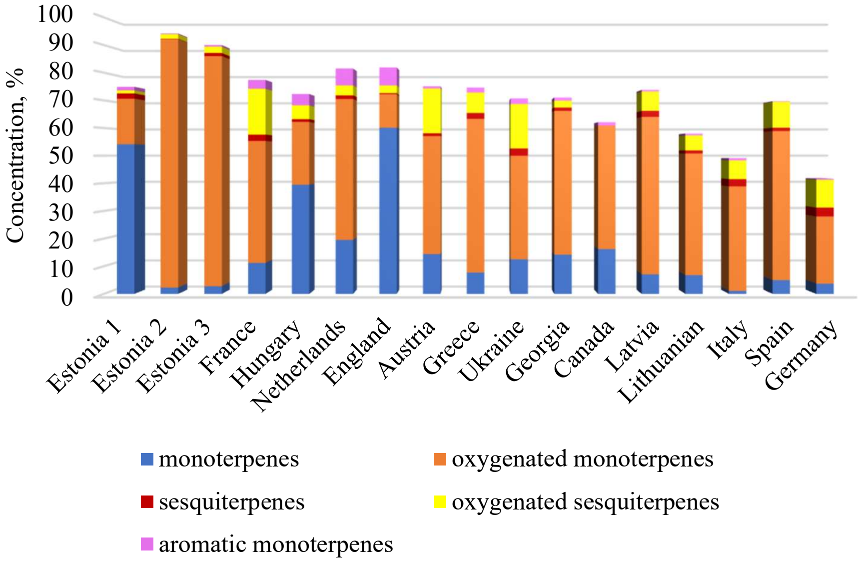

Fig. 2. Variation in the concentrations of the component groups of samples *Artemisia absinthium* oils from different countries

Table 2

Principal components of essential oil of *Artemisia absinthium* L. from different countries' origins

Compound	The Netherlands	England	Austria	Georgia
	Content of essential oils, %			
Sabinene	**9.3**	**25.3**	**9.3**	**8.1**
Myrcene	**5.4**	**29.9**	0.8	**3.9**
p-Cymene	**6.1**	**6.5**	0.8	**1.1**
1,8-Cineole	**3.9**	0.4	0.6	0.3
Linalool	**3.8**	**3.4**	**1.9**	0.4
β-Thujone	**3.5**	0.1	**1.7**	**8.5**
(E)-Epoxyocymene	0.4	**1.2**	**22.1**	**32.7**
Borneol	**1.4**	tr.	tr.	0.3
Terpinen-4-ol	**2.2**	**1.7**	0.6	**1.8**
Nerol	**3.6**	0.8	**3.1**	0.6
(E)-Sabinyl acetate	**18.6**	0.2	tr.	0.4
(E)-β-Caryophyllene	0.8	0.2	**1.0**	**1.0**
Neryl butyrate	**2.9**	0.1	**4.9**	**1.4**
Spathulenol	**1.7**	**1.3**	**7.6**	0.2
Caryophyllene oxide'	**1.5**	0.9	**5.5**	0.7
Geranyl isovaleriate	0.1	0.3	**1.9**	0.7

Note: tr. – traces (<0.05 %); Bold – >1 %; The deviations of the results are within the deviations of the device

In samples from Estonia 2, Georgia and Austria (E)-epoxyocymene predominated (59.7 %, 32.7 % and 22.1 %, respectively). According to the literature, EO *A. absinthium* from France, containing (Z)-epoxyocimene and chrysanthenylacetate as the main components, inhibited the growth of both the yeast *Candida albicans* and *Saccharomyces cerevisiae* var. *chevalieri* [34].

The five EOs studied, such as samples from Estonia 3, The Netherlands, Canada, Latvia and Lithuania, contain the maximum content of (E)-sabinyl acetate (70.5 %, 18.6 %, 26.4 %, 23.6 % and 13.7 % respectively). Comparatively large contents of (E)-sabinyl acetate were also found in the EOs from Estonia 2 (23.6 %), Italy (11.4 %) and France (9.3 %). It should be noted that the composition of the four dominant components, namely (E)-sabinyl acetate>borneol>β-thujone>-caryophyllene oxide, EOs from Latvia and Lithuania, coincide entirely [9].

β-Thujone predominated in EOs from Greece and Italy (38.7 % and 12.3 %). β-Thujone-rich EO was characteristic of samples from Ukraine (6.3 %), Latvia and Spain (6.2 % each) [9].

Wormwood EO is neurotoxic, embryo-fetotoxic and abortifacient; its toxicity is associated with the combined effects of thujone and sabinyl acetate. It is best to completely avoid sabinyl acetate-rich EOs and any medications containing them during pregnancy, especially in the first trimester [52].

The EO composition of three wormwood samples from Estonia was quite different. Sample 1 was dominated by monoterpenes, and samples 2 and 3 were dominated by oxygen-containing monoterpenes [7, 9]. Three samples that differ from the others in their dominant monoterpene content are those from Estonia 1, England and Hungary [7, 9]. All three have the highest myrcene content (25.6 %, 29.9 % and 17.1 %, respectively) and sabinene (21.2 %, 25.3 % and 18.1 %, respectively). Comparatively large contents of myrcene were also found in oils from Ukraine (5.9 %) and The Netherlands (5.4 %), sabinene – in the EOs from The Netherlands, Austria (9.3 % each) and Georgia (8.1 %). According to the literature, sabinene has antimicrobial, antifungal [49], anticonvulsant and antispasmodic effects [50, 51].

α-Thujone is more neurotoxic than β-thujone. When taken orally, thujone can affect the central nervous system and cause seizures, suggesting that it may cross the blood-brain barrier [53]. Thujone diastereomers have been shown to inhibit human gamma-aminobutyric acid type A (GABA) receptor current, a mechanism that causes muscle spasms and convulsions [53, 54]. α-Thujone has been found to inhibit CYP2A6 (IC50=2.34 mg/L) and CYP2B6 (IC50=2.66 mg/L), which may contribute to the long-term and enhanced toxicity of α-Thujone [55–57].

Thujone-rich EOs have been shown to have acaricidal, insecticidal and fungicidal effects and myrtenol-rich EOs repelled fleas, flies, mosquitoes and ticks [10]. Thujone-rich *A. absinthium* EO from Uruguay demonstrated antifungal activity against *Alternaria* sp. and *Botrytis cinerea* [58].

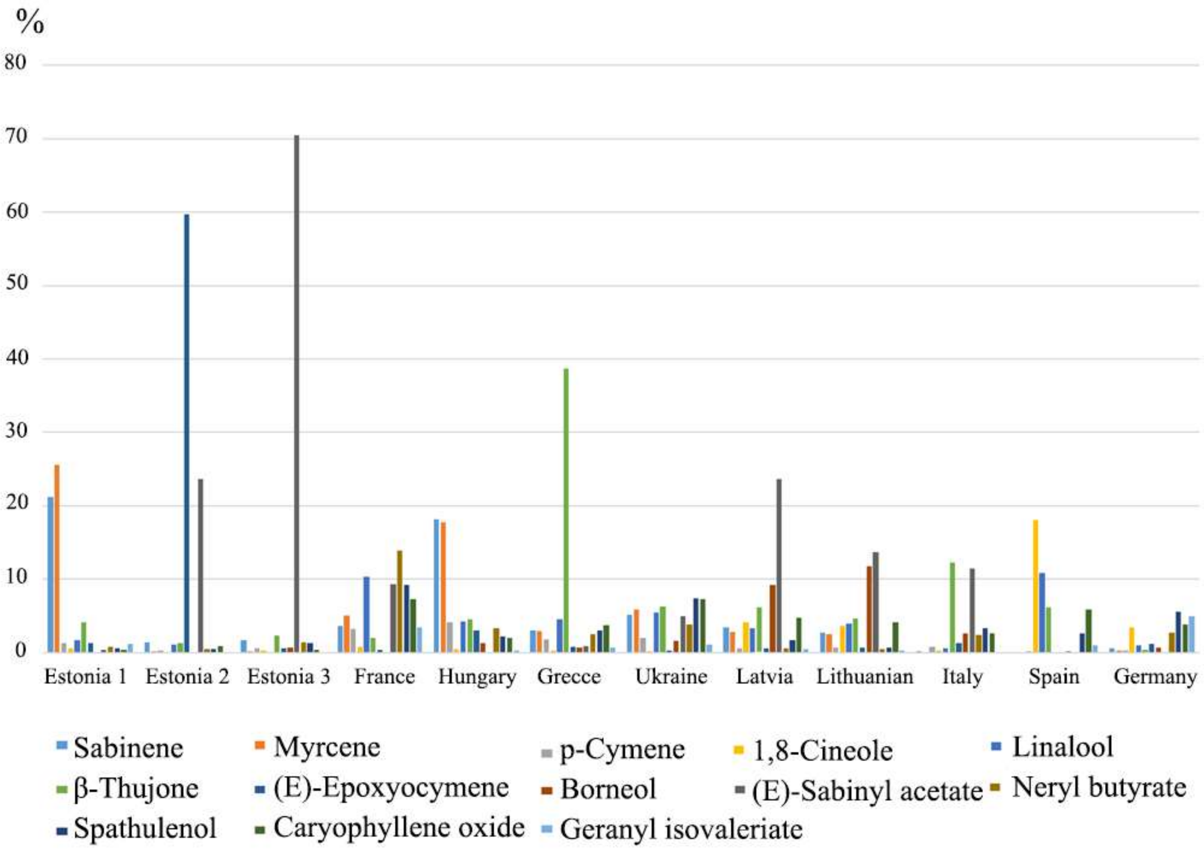

Fig. 3. Variation in the concentrations of the components in samples *Artemisia absinthium* oils from different countries [9]

Spathulenol predominated in EOs from Ukraine (7.4 %) and Germany (5.5 %). Comparatively large amounts of spathulenol were also found in the EOs in France (9.2 %) and Austria (7.6 %). Spatulenol is one of the immunomodulatory compounds capable of inhibiting lymphocyte proliferation and inducing apoptosis in these cells; treatment of activated lymphocytes with a concentrated fraction containing 62 % spatulenol shows a decrease in lymphocyte proliferation with an IC50 of 85.4±11.08 µg/ml [59]. Spatulenol has moderate to low cytotoxicity with an IC50 above 6 µM and is a good candidate for use in combination chemotherapy for multidrug-resistant cancers and, therefore, merits further in vivo studies [44, 60].

In samples from France neryl butyrate predominated (13.9 %). Neryl butyrate rich EO was also characteristic of samples from Austria (4.9 %) and Ukraine (3.8 %) [9].

In samples from Spain 1,8-cineole and *Artemisia* ketone predominated (18.0 % and 14.9 %, respectively). Wormwood EO from a Turkish population, whose main components are camphor, 1,8-cineole, and chamazulene, has been described as fungicidal against 34 species of fungi, including *Fusarium solani* and *Fusarium oxysporum* [21].

p-Cymene rich EO was characteristic of samples from England, The Netherlands and Hungary (6.5 %, 6.1 %, 4.1 %, respectively) [61]. *p*-Cymene exhibits antioxidant, anti-inflammatory, antiparasitic, antidiabetic, antiviral, antitumor, antibacterial and antifungal activity [62, 63].

Accordingly, in "Assessment report on *A. absinthium* L., herba" [44], the composition of EO depends on the different chemotypes. "Pure"-chemotype: α-Thujone is typical for plants grown in areas below 1,000 m a.s.l. (Z)-epoxy-ocimene is the main component in plants grown in Europe at altitudes higher 1,000 m a.s.l. In France, there are different chemotypes with *trans*-sabinyl-acetate and chrysanthenyl-acetate as main components, while Eastern European plants are mostly mixed types. In Spain, species were established the two most characteristic chemotypes of *A. absinthium*: chemotype A, with (Z)-epoxyocimene as the main component, and B, with (Z)-epoxyocimene and (Z)-chrysanthemyl acetate as major ones [30].

In our studies, both "pure"-chemotypes and "mixed"-chemotypes have been defined. "Pure"-chemotype are EOs from Estonia 3, which consists of 70.5 % (E)-sabinyl acetate and from Estonia 2, which consists of 59,2 % (E)-epoxyocymene. The obtained data are different from those previously known. This applies to the sabinyl acetate and epoxyocymene isomers. It was established that not only (Z)-epoxy-ocimene could be the main component of the essential oil of wormwood, but also (E)-epoxyocymene. At the same time, this is in no way related to the height of the plant growing. This also applies to isomers of sabinyl acetate: not only trans-sabinyl-acetate, but also cis-, as well (E)-sabinyl acetate can be the dominant component of the essential oil.

Accordingly, "Assessment report on *A. absinthium* L., herba" [44], "mixed"-chemotype:

– (Z)-epoxy-ocimene+chrysanthenyl-acetate+thujone-chemotype;

– (Z)-epoxy-ocimene+β-thujone-chemotype;

– (Z)-epoxy-ocimene+chrysanthenyl-acetate-chemotype;

– β-thujone-sabinyl-acetate-chemotype;

In the previously published work, three additional chemotypes of *A. absinthium* were revealed: sabinene+myrcene, neryl butanoate, and 1,8-cineole [9].

Some of the results we obtained confirm the existence of similar chemotypes:

– CT-(E)-epoxyocymene+β-thujone+sabinene: sample from Georgia (32.7 %+8.5 %+8.1 %, respectively);

– CT-β-thujone+(E)-sabinyl acetate+spathulenol+borneol and caryophyllene oxide: sample from Italy (12.3 %+11.4 %+3.3 %+2.6 %+2.6 %);

– CT-myrcene+sabinene: samples from Estonia 1 (25.6+21.2 % respectively) [9], England (29.9+25.3 % respectively) and Hungary (17.7+18.1 % respectively) [9];

– CT-neryl butyrate+linalool+(E)-sabinyl acetate+spathulenol: sample from France (13.9 %+10.3 %+ +9.3 %+9.2 %) [9];

– CT-1,8-cineole+Artemisia ketone+linalool+β-thujone: sample from Spain (18.0 %+14.9 %+10.8 %+ +6.2 %) [9, 33].

The results of this present study shows that there are numerous additional "mixed" chemotypes (CT) of *A. absinthium*:

– CT-(E)-epoxyocymene+sabinene+spathulenol: sample from Austria (22.1. %+9.3 %+7.6 %);

– CT-(E)-sabinyl acetate+sabinene+(E)-verbenol+p-cymene: sample from The Netherlands (18.6 %+9.3 %+7.9 %+6.1 %);

– CT-(E)-sabinyl acetate+borneol+β-thujone+-caryophyllene oxide: samples from Latvia (23.6 %+ +9.2 %+6.2 %+4.7 %) and Lithuania (13.7 %+11.7 %+ +4.6 %+4.1 %);

– CT-β-thujone+linalool+caryophyllene oxide+spathulenol and sabinene: sample from Greece: (38.7 %+4.5 %+3.7 %+3 %+3 %);

– CT-spathulenol+caryophyllene oxide+β-thujone+myrcene: sample from Ukraine (7.4 %+7.3 %+ +6.3 %+5.9 %);

– CT-spathulenol+geranyl isovaleriate+caryophyllene oxide+1,8-cineole: sample from Germany (5.5 %+4.9 %+3.8 %+3.4 %).

Literature data indicate a good correlation between some monoterpenes (e.g. nerol or limonene) and the antioxidant capacity of the natural extract [64]. However, the study of the correlation between the content of individual groups of compounds or between the content of individual substances in the essential oil of wormwood has not been conducted before.

Our results revealed relationships between the quantitative content of components in EOs that are characteristic of all objects (Table 3).

There is a strong positive correlation between the content of sabinene and myrcene (r=0.91), between the content spathulenol – caryophyllene oxide and neryl butyrate – spathulenol (r=0.81); moderate positive correlation between the content of: spathulenol and geranyl isovaleriate (r=0.68), sabinene and p-cymene (r=0.66), the sum of monoterpenes and p-cymene (r=0.64), linalool – caryophyllene oxide (0.62), myrcene – *p*-cymene (0.61), 1,8-cineole – linalool and neryl butyrate – geranyl isovaleriate (0.58), neryl butyrate – caryophyllene oxide (0.57), sum sesquiterpenes and sum oxygenated sesquiterpenes (0.55).

Table 3

Correlation between the content of groups and individual compounds in the essential oil of *Artemisia absinthium*

Couples	Correlation coefficient
Sabinene – Myrcene	0.91
Spathulenol – Caryophyllene oxide	0.81
Neryl butyrate – Spathulenol	0.81
Spathulenol – Geranyl isovaleriate	0.68
Sabinene – *p*-Cymene	0.66
Linalool – Caryophyllene oxide	0.62
Myrcene – *p*-Cymene	0.61
1,8-Cineole – Linalool	0.58
Neryl butyrate – Geranyl isovaleriate	0.58
Neryl butyrate – Caryophyllene oxide	0.57
Monoterpenes – aromatic monoterpenes	0.64
Sesquiterpenes – Oxygenated sesquiterpenes	0.55
Monoterpenes – Oxygenated monoterpenes	–0.69
Monoterpene – Sesquiterpene	–0.60

There is a strong inverse correlation between the content of monoterpenes and oxygenated monoterpenes (r=–0.69) and a moderate inverse correlation between the content of monoterpenes and sesquiterpenes (r=–0.60). The identified correlations can serve as a generalized characteristic of EOs of wormwood of different origins.

Practical Relevance. The established chemotypes make it possible to more accurately classify and sort *Artemisia absinthium* L. raw material and essential oils, predict the pharmacological activity of its medicinal products, and provide the possibility of a targeted search for the necessary raw materials according to the specified parameters. The correlation of substances' content allows us to predict the content of target molecules in *Artemisia absinthium* L. essential oils.

Study limitations. The used samples of *Artemisia absinthium* L. herb were only from European countries. It would be appropriate to expand the geography of the origin of raw materials.

The prospects for further research. The prospects for further research consist of expanding the geography of the origin of commercial raw materials and establishing new chemotypes and correlations with growth regions. The results of the research create conditions for a targeted search for biologically active substances and seed materials.

6. Conclusions

Based on research, 16 brands of EOs and bitters are sold in 15 countries: Estonia, France, Hungary, The Netherlands, England, Austria, Greece, Ukraine, Georgia, Canada, Latvia, Lithuania, Italy, Spain, Germany, 2 "pure"-chemotypes and 11 "mixed"-chemotypes have been defined. "Pure"-chemotype are EOs from Estonia 3, which consists of 70.5 % (E)-sabinyl acetate and from

Estonia 2, which consists of 59.2 % (E)-epoxyocymene. For the first time, correlative deposits have been installed between instead of adjacent shelves in the warehouse of EO of Pauline bitter. The strongest correlations are the pairs sabinene – myrcene (*r*=0.91), spathulenol – caryophyllene oxide and neryl butyrate – spathulenol (*r*=0.81). The revealed patterns can be used to predict, modulate and establish the mechanism of possible pharmacological activity and toxicity of polyhydric EO.

Conflicts of interest

The authors declare that they have no conflict of interest concerning this research, whether financial, personal, authorship or otherwise, that could affect the research and its results presented in this paper.

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Data availability

The datasets used and/or analyzed during the current study are available from the author and/or corresponding author upon reasonable request.

Use of artificial intelligence

The authors confirm that they did not use artificial intelligence technologies when creating the current work.

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