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Review

Biological and Chemical Diversity of *Angelica archangelica* L. —Case Study of Essential Oil and Its Biological Activity

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Abstract: Garden angelica (*Angelica archangelica* L.), native to the northern temperate region, is widespread in Europe and Asia. Since the middle ages, it has been used for healing and as a vegetable in traditional dishes. In the modern era, it has been proven that *A. archangelica* has a complex chemical composition. The main derivatives that contribute to the plant's biological activities are essential oil and coumarins. In this review, the focus is on the cross-analysis of the taxonomy of *A. archangelica*, and its distribution in different regions, with the presentation of the richness of its biochemical composition, which overall contributes to the widespread use of the roots of this plant in folk medicine. It belongs to the plants that were introduced to the wider area of Central, Eastern, and Southern Europe; as a medicinal plant, it represents a significant part of the medical flora of many areas. Cluster analysis of pooled data indicates a clear differentiation of chemotypes.

Keywords: angels root; Apiaceae; chemotypes; subspecies; volatiles

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1. Introduction

Angelica archangelica L. (syn. *A. officinalis Hoff.*), garden angelica, or The Root of the Holy Ghost, is a well-known medicinal plant with doubtful native range, but best known as Norwegian angelica. Distribution is limited to the northern temperate region of Europe, from Northern Fennoscandia to Eastern Siberia, and the natural habitat of this plant extends up to the Himalayas, while it is cultivated in most other regions [1–3]. It mostly grows in moist places in the mountains and in mountain valleys. It can be found in the lowlands of the far north [4]. It was highly valued in the Middle Ages and traded to Continental Europe by the Vikings as food (for flavoring liqueurs and aquavits, omelets, trout, to be made into jam, and as a preservative for reindeer milk) and a medicinal plant (as a calming remedy for treating hysteria, seizures, hypertension, rheumatism, and biliary diseases, as well as plague) [2,5,6]. It is known that this plant was associated with the magic of protection against evil spirits and witchcraft, as well as for healing [7–9]. Furthermore, the whole plant can be used as a vegetable (roots, young shoots, leaves, and seeds) if harvested appropriately [10].

In Europe, apart from Nordic countries (Finland, Sweden, Norway, Denmark, Greenland, the Faroe Islands, and Iceland), *A. archangelica* is cultivated in Poland, Germany, the

Netherlands, Belgium, France, Austria, Hungary, and Romania, while it is often grown in Asia in Central Russia, as well as in India and Thailand [11–16]. In Serbia, *A. archangelica* is a rare plant in natural and semi-natural habitats [17]; however, due to good prices and the constant demand for essential oil, there is considerable interest in cultivating this essential-oil-bearing crop [18,19].

This study is aimed at systematically describing *A. archangelica*'s biology, phytochemistry, and chemotaxonomy according to the essential oil composition as well as the biological activities associated with the essential oil. It is based on the more than 70 literature references collected from available scientific databases, books, and other resources. Therefore, this review article could present a valuable update on current knowledge about *A. archangelica* and to improve the cultivation processes, concerning species diversity. Further, this study could give an explanation of the chemical diversity of the root/seed essential oil between subspecies and distribution areas of *A. archangelica*.

2. Biological Characteristics

Angelica archangelica L. 1753 is a bi-annual or perennial plant from the Apiaceae family. In the first year of growing, it produces a rosette of large (30–70 cm in length), compound leaves with a hollow, tubular leaf stalk. During the first year, it accumulates nutrients in long, spindle-shaped, thick roots with a yellowish–grey epidermis. If the fresh root is bruised, it oozes honey-colored juice. In the second year, it forms erect flower stalks, up to 2 m tall, with ridges and grooves, hollow and tinged with purple, not glaucous. Basal leaves are huge, two-pinnate, and glabrous. Cauline leaves are two-pinate with petioles strongly sheathed at the base, while upper leaves are reduced to inflated sheaths, which enclose the development of inflorescences, of the umbel type. Umbels are spherical (10–15 cm or more in diameter), with greenish–white flowers. It is a self-pollinated plant. Fruit is a schizocarp consisting of two mericarps, oblong, slightly dorso-ventrally flattened, glabrous, with prominent and acute dorsal ridges and developed marginal wings. The monocarpic plant wilts and dies after seed maturation. If the flowering stem is gathered before flowering and seed maturation, the plant's lifetime is prolonged (perennial). When damaged, the whole plant emits a strong aromatic scent, which could be described as terpenic, fresh, celeriac, and sweet [2–4,8,20–22].

The native range of the species covers the northern temperate region of Europe and Asia, from Northern Fennoscandia to Eastern Siberia, and the natural habitat of this plant extends up to the Himalayas. In the native range, the species are distributed along riverbanks and coastal zones, moving towards higher altitudes, where it also prefers moist or wet habitats [1,23–26].

Genus Angelica comprises 15 species with distribution in Europe and the Mediterranean, while in Serbia, five are present [17,27]. Among them, *Angelica archangelica* stands out as well known in folk medicine as angel root, primarily due to its traditional medicinal use. Within the species *A. archangelica*, more infraspecific taxa have been identified over time [28]. According to modern taxonomic treatment, three subspecies are accepted within the species *A. archangelica* subsp. *archangelica, A. archangelica* subsp. *litoralis* (Fr.) Thell, earlier known as *A. litoralis Fr*., and *A. archangelica* subsp. *decurrens (Ledeb.) B. Fedtsch*., formerly accepted as a species [29]. The populations from the Himalayas are recognized as taxon *A. archangelica* subsp. *himalaica* (C.B.Clarke) G.Singh & G.M.Oza [30]. Although numerous authors have lately classified populations from the Himalayas as A. angelica subsp. *archangelica* var. *himalaica* [29], differences in fruit size and the chemical composition of the root essential oil, followed by the geographical isolation of the population, indicate that it should be treated as a subspecies *A. archangelica* subsp. *himalaica* (C.B.Clarke) G.Singh & G.M.Oza, or eventually species, *A. himalaica* Clarke, due to geographical and ecological isolation. Further investigations need to be conducted to resolve this taxonomical and nomenclature problem. In addition, it is noted that a correlation exists between habitat preferences and fruit morphology, i.e., the smallest fruits are characteristic for subsp. *litoralis* (distributed at the seashore), followed by subsp. *archangelica* (distributed in continental and mountain regions), while the largest are in the populations from the Himalayas [22,30].

Contrary to some authors, who describe some characteristics as useful for Angelica species identification, followed by studies in which even subspecies can be clearly distinguished, [22,31,32], there are also scientists who claim that the genus Angelica has highly variable morphological traits, which leads to difficulty in recognition of both species and infraspecific taxa [21,33,34]. By comparing the native range of the above infraspecies taxa, geographical separation in four areas is noticeable. On the other hand, considering that Central Europe (excluding Poland, which belongs to the native range of species), moving further south and southeast, is treated as an arched area for *Angelica archangelica*, overlapping distribution areas of European subspecies in this region support the given taxonomic approach [27,35–37].

Nowadays, it is valued primarily as a cultivated species, often used as a medicinal herb. In Southern and Southeastern Europe, both subsp. *archangelica* and subsp. *litoralis* are recorded as cultivated and as naturalized along river banks or in moist forests [17,21,31,35,36]. Since representatives out of cultivation are rare, it is not considered an invasive species, but rather a casual alien without or with a negligible impact on nature. This trait is important considering the need to grow this plant for pharmaceutical and medicinal use.

3. Chemical Composition and Biological Activities

A. archangelica has a complex chemical composition [38]. Apart from essential oil and coumarins, which contribute to the plant's biological activities [39], it contains glycosides, carbohydrates, phytosterols, saponins, phenols, fixed oil, and fats [40], which influence its nutraceutical potential [10].

Furanocoumarins (such as archangelicin, bergapten, xanthotoxin, imperatorin, osthole, and others) [41,42] are constituents responsible for the antibacterial, [43] antiviral, [44] anti-inflammatory, [45] antitumor [46,47], hepatoprotective, [48] antidepressant [42], and other activities, as well as for phototoxicity [49]. For these reasons, the European Medicines Agency (EMA) commission pointed out risks associated with furanocoumarins in preparations of *A. archangelica* [50]. However, this chemical class of compounds is not addressed in this paper; rather, only volatile compounds in the essential oil are presented.

4. Statistical Analysis

All available data dealing with the chemical composition of both root and seed (fruit) essential oils were used for the construction of tables, which systematically show ten main compounds (in average), in descending order.

Principal Component Analysis (PCA) was introduced to investigate the chemical compositions of different *A. archangelica* L. root and seed (fruit) essential oil volatile compounds. The perspective trend for a more profound comprehension of the essential oil feature profile could be assessed by embracing the grouped samples' PCA plot. Correlation analysis was applied to examine the similarity in the active compound content of the different samples. A statistical study of the data was accomplished using the Statistica 10 software. Correlation analysis and an unrooted cluster tree were performed using the R software 4.0.3 (64-bit version) to investigate the likeness among various samples visually.

5. Root Essential Oil

The plant is generally cultivated for its root (*Angelicae radix*), an official drug according to the European Pharmacopoeia [51]. The essential oil (*Angelicae radix aetheroleum*) is a yellow liquid with a fresh, herbaceous, and gently pungent aroma, with earthy and woody notes. The minimum essential oil content in dried drugs needs to be 2.0 mL/kg. However, the essential oil is usually obtained from fresh roots by steam distillation, and ranges between 0.1 and 1.0% [17]. Drying raw material before distillation is to be avoided because of volatile compound loss, which may alter the top fragrance notes of the oil [11]. Apart from steam distillation and hydrodistillation [9,52–58], other advanced techniques can be used for essential oil isolation, such as supercritical fluid extraction and solvent extraction [5,11,59,60].

The chemical compositions of different *A. archangelica* root volatile compounds of different accessions according to the literature are given in Table 1, while the unrooted tree (Figure 1) was created using these data, in order to apply the neighbor-joining method to identify various groups (chemotypes). Obtained results strongly support the separation of the *A. archangelica* subsp. *himalaica* taxon. Furthermore, Eurasian samples indicate the coincidence of isolated chemotypes in relation to non-widespread subspecies. While expected, in a certain part of Europe, there are more chemotypes, where the distributions of the subspecies partially overlap, or the species was introduced for cultivation.

Table 1. Chemical compositions of different *A. archangelica* root volatile compounds of accession according to the literature.

No	Region	Ref.	1	2	3	4	5	6	7	8	9	10
			α-Pinene	Dillapiole	δ-3-Carene	β-Phellandrene	Sabinene	Limonene	α-Phellandrene	Nothoapiole	p-Cymene	Myrcene
1	Finland	[54]	4.8	0.0	2.7	4.0	5.9	1.9	0.4	0.0	0.6	1.3
2	Finland	[54]	9.9	0.0	6.7	2.1	14.8	4.6	1.0	0.0	1.2	3.1
3	Finland	[54]	9.1	0.0	0.2	12.3	3.9	1.5	0.4	0.0	0.7	0.5
4	Finland	[54]	2.2	0.0	3.5	15.4	3.3	3.4	0.2	0.0	1.0	2.4
5	Lapland	[5]	21.4	0.0	21.6	0.0	22.2	10.8	0.0	0.0	4.2	2.7
6	Lapland	[5]	47.6	0.0	0.0	0.0	29.1	6.7	0.0	0.0	1.7	1.4
7	France	[52]	9.8	0.0	13.0	2.0	0.0	7.3	0.0	0.0	2.3	2.9
8	France	[53]	32.2	0.0	16.2	1.3	0.5	6.6	2.0	0.0	6.4	5.3
9	Romania	[11]	16.7	0.0	8.7	8.9	0.6	13.1	11.3	0.0	5.6	3.9
10	Canada	[54]	15.7	0.0	5.7	26.6	0.7	5.9	19.1	0.0	5.0	2.8
11	Lithuania	[55]	17.5	0.0	16.3	1.4	6.5	8.5	2.5	0.0	3.3	2.9
12	Lithuania	[55]	20.2	0.0	13.9	14.7	3.2	0.0	8.6	0.0	2.0	1.9
13	Lithuania	[55]	13.7	0.0	11.4	16.2	1.7	0.0	7.4	0.0	8.4	3.0
14	China	[56]	24.5	0.0	13.8	10.1	6.3	8.4	1.7	0.0	8.8	4.8
15	Italy	[61]	21.3	0.0	16.5	0.0	5.1	16.4	8.7	0.0	2.2	5.5
16	India	[9]	0.0	35.9	0.0	0.0	0.0	0.0	0.0	62.8	0.0	0.0
17	India	[9]	0.0	66.1	0.0	0.0	0.0	0.0	0.0	21.9	0.0	0.0
18	India	[9]	0.3	91.6	0.0	0.0	0.0	1.1	0.0	0.1	0.5	0.0
19	Serbia	[58]	29.7	0.0	14.2	13.2	6.1	0.0	5.7	0.0	3.8	4.1
20	Finland	[60]	11.1	0.0	7.4	26.8	8.7	4.6	20.8	0.0	8.4	3.2
AVERAGE			15.4	9.7	8.6	7.7	5.9	5.0	4.5	4.2	3.3	2.6

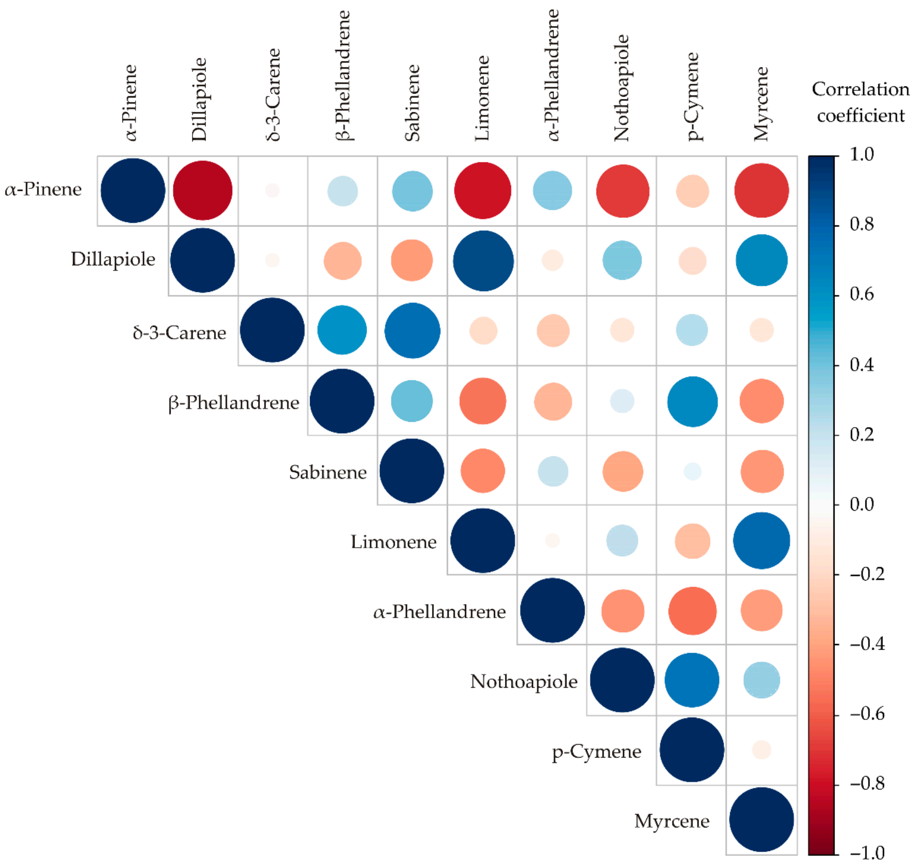

Figure 1. Correlations between different *A. archangelica* root volatile compounds.

The compositions of volatile compounds varied greatly due to the weather, soil, [62,63] locality, [64], and altitude [9]. Such great variations in the essential composition of the oil may be attributed to the existence of chemotypes and the adaptation of the species to a particular habitat [9]. Large intra-population variation occurs due to hybridization [13,65]. Apart from this, the composition of volatile compounds depends on the development stage [66], storage period [67], extraction method, and conditions [20], while different harvest dates (summer and spring) caused slight changes only in the root essential oil composition [54].

A. archangelica root essential oil is used extensively in the alcoholic beverage industry for flavoring liquors and vines, such as vermouths, Benedictine, Becherovka, Boonekamp, and Chartreuse [38,68]. In addition, in the perfume industry, *A. archangelica* is a high-grade ingredient, as it imparts a musky note and is used as a fixative [9].

Correlation between Different A. archangelica Root Volatile Compounds of Accession According to Literature

The correlation analysis was performed to investigate the similarities in the active compound content of the different *A. archangelica* root samples (1–20), and the results are visually displayed in Figure 1. The darker blue color of the circles, which shows the two samples' relation, presents a stronger correlation between these samples, i.e., the more pronounced similarity in the active compound content. On the other hand, the lighter tone suggests a certain dissimilarity between samples. Therefore, if the color tone is lighter, the correlation is lower.

The content of α-pinene is negatively correlated with dillapiole content ($r = -0.504$), and positively correlated with the content of sabinene and myrcene ($r = -0.573$ and $r = -0.529$, respectively), statistically significant at the $p \leq 0.05$ level. The content of dillapiole is negatively correlated with δ-3-carene and myrcene content ($r = -0.502$ and $r = -0.618$, respectively), statistically significant at the $p \leq 0.05$ level. The content of δ-3-carene is positively correlated with myrcene content ($r = 0.759$), statistically significant at the $p \leq 0.01$ level, and positively correlated with limonene and p-cymene content ($r = 0.520$ and $r = 0.520$, respectively), at the $p \leq 0.05$ level. The content of β-phellandrene is positively correlated with α-phellandrene content ($r = 0.774$, $p \leq 0.01$), and positively correlated with p-cymene content ($r = 0.506$, $p \leq 0.05$ level). The content of limonene is positively correlated with myrcene content ($r = 0.640$, $p \leq 0.05$). The content of α-phellandrene is positively correlated with p-cymene content ($r = 0.552$, $p \leq 0.05$ level). The content of myrcene is positively correlated with p-cymene content ($r = 0.665$, $p \leq 0.05$ level) and negatively correlated with nothoapiole content ($r = -0.469$, $p \leq 0.05$ level).

The PCA analysis was performed to test the correlations between *A. archangelica* root volatile compounds, and the results are presented in Figure 2. The points shown in the PCA graphics, which are geometrically close to each other, indicate the similarity of patterns representing these points. The vector's orientation describing the variable in factor space indicates an increasing trend in these variables, and the length of the vector is proportional to the square of the correlation values between the fitting value for the variable and the variable itself. The angles between corresponding variables indicate the degree of their correlation (small angles corresponding to high correlations). The first PC explained 41.88% and the second 21.23% of the total variance between the experimental data. The parting within samples could be seen from the PCA figure, where the samples from *A. archangelica* root volatile compounds were presented.

The unrooted cluster tree (Figure 3) constructed according to *A. archangelica* root volatile compounds (listed in Table 1) shows the presence of four chemotypes. However, α-pinene is noted in all samples except in No. 16, 17, and 18, originating from India, with dillapiole and nothapiole as the main compounds (dillapiole+nothapiole chemotype {1}). The most prevalent is a combination of α-pinene and δ-3-carene in the root essential oil (α-pinene+δ-3-carene chemotype {2}), which could be divided into three subgroups: solely α-pinene and δ-3-careneis present in samples No. 8 (from France), No. 14 (from China), and No. 19 (from Serbia). The second subgroup is α-pinene and δ-3-carene in combination with limonene (α-pinene+δ-3-carene+limonene), which is noted in samples No. 7 (from France), No. 9 (from Romania), No. 11 (from Lithuania), and No. 15 (from Italy), while in the third group α-pinene and δ-3-carene occur in combination with α-phellandrene and β-phellandrene (α-pinene+δ-3-carene+α-phellandrene+β-phellandrene chemotype), which is noted in samples No. 10 (from Canada), No. 12 and 13 (from Lithuania), and No. 20 (from Finland). A chemotype with the domination of α-pinene and β-phellandrene (α-pinene+β-phellandrene chemotype {3}) is noted in samples No. 1, 2, 3, and 4, originating from Finland, while a chemotype with α-pinene and sabinene (α-pinene+sabinene chemotype {4}) is noted in samples No. 5 and 6, originating from Lapland.

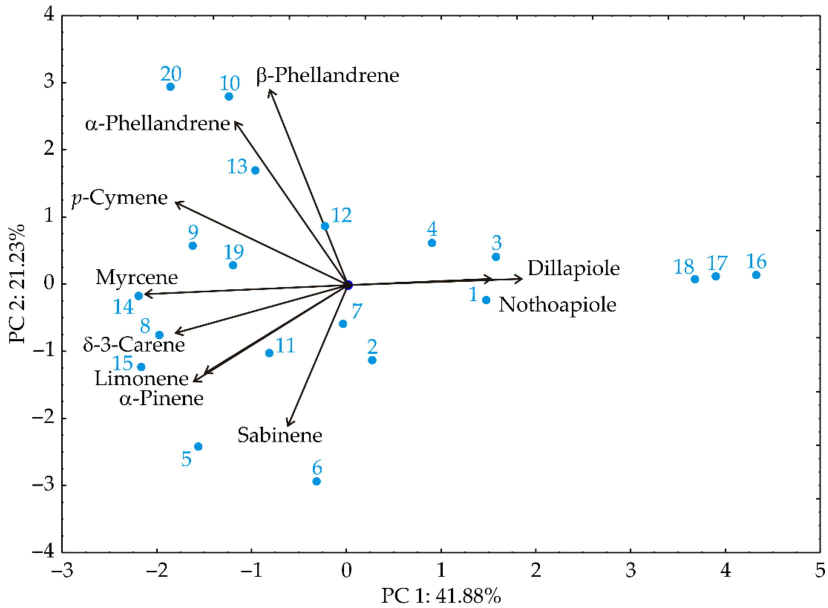

Figure 2. The PCA biplot diagram describing the relations between *A. archangelica* root volatile compounds.

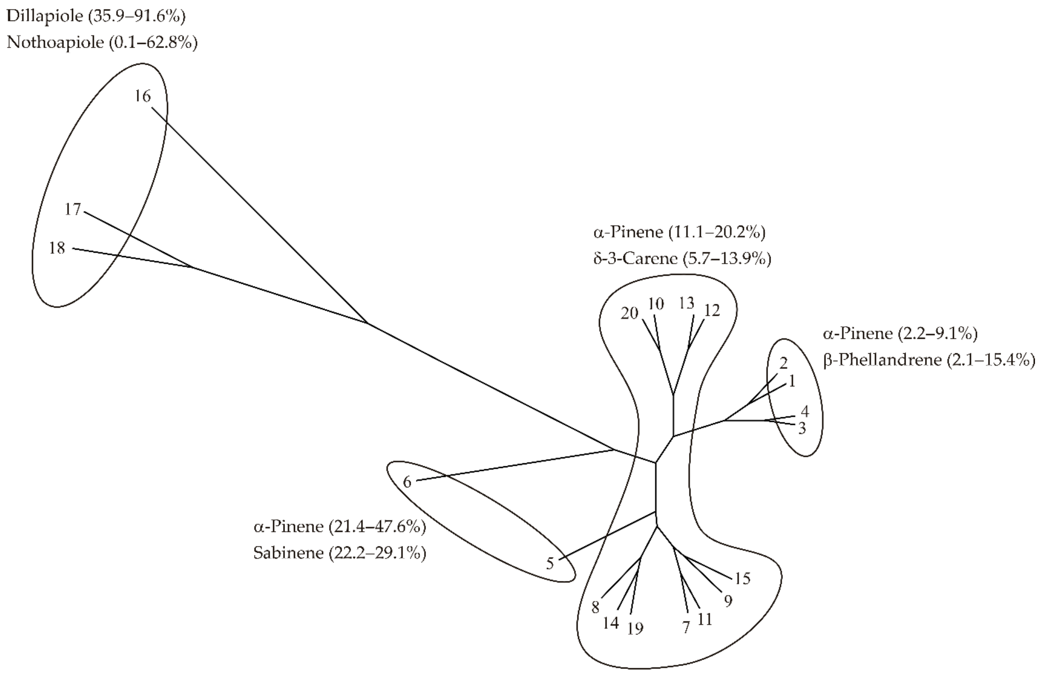

Figure 3. Unrooted cluster tree of *A. archangelica* root essential oil (samples are numbered according to Table 1).

The composition of volatile compounds varied greatly due to the weather, soil, locality, and altitude [9,62–64]. Such great variations in the essential composition of the oil may be attributed to the existence of chemotypes and the adaptation of the species to a particular habitat [9]. Large intra-population variation occurs due to hybridization [13,65]. Apart from this, the composition of volatile compounds depends on the development stage [66], storage period [67], and extraction method and conditions [20], while different harvest dates (summer and spring) cause slight changes only in the root essential oil composition [54].

6. Seed Essential Oil

The seed essential oil is a light yellow liquid with a fresh, sweet, and peppery odor [54]. Chemical compositions of different *A. archangelica* seed (fruit) essential oils of different accessions according to the literature are shown in Table 2. As can be seen, the dominant compound in seed essential oil in almost all samples is β-phellandrene, with 57.0% on average; however, its content ranges between 33.6 and 84.7%. In one sample from Iceland, the dominant compound was α-pinene, with 41.4%, followed by bicyclogermacrene (11.9%) [69].

Table 2. Chemical composition of different *A. archangelica* seed (fruit) essential oil accessions according to the literature.

			1	2	3	4	5	6	7	8	9	10
No	**Region**	**Ref.**	**β-Phellandrene**	**α-Pinene**	**Sabinene**	**α-Phellandrene**	**Myrcene**	**Bicyclogermacrene**	**Limonene**	**β-Pinene**	**α-Humulene**	**α-Zingiberene**
1	Lapland	[5]	82.1	8.3	0.5	3.8	3.4	0.0	2.0	0.0	0.0	0.0
2	Lapland	[5]	66.4	9.4	11.3	3.1	7.3	0.0	1.7	0.0	0.0	0.0
3	Lapland	[5]	74.0	10.3	5.4	4.3	4.0	0.0	2.1	0.0	0.0	0.0
4	France	[70]	65.8	6.6	0.0	0.0	2.4	1.5	2.6	0.6	0.0	0.0
5	France	[70]	64.9	2.3	0.2	1.9	3.2	0.7	1.8	0.3	0.8	0.0
6	France	[70]	76.0	4.2	0.5	3.4	0.0	0.0	0.6	0.0	0.0	0.0
7	Canada	[54]	74.7	6.6	0.4	3.7	2.9	0.0	2.7	0.6	0.6	0.0
8	Lithuania	[64]	43.8	9.1	2.5	2.7	2.5	0.0	0.0	2.4	1.5	1.3
9	Lithuania	[64]	33.6	12.8	4.6	7.4	2.0	0.0	0.0	3.7	3.4	0.0
10	Lithuania	[64]	63.4	4.2	3.3	2.6	2.0	0.0	0.0	0.7	1.0	1.9
11	Iceland	[69]	0.0	41.4	2.1	0.0	0.0	10.1	0.5	1.7	0.0	3.6
12	Iceland	[69]	37.8	28.9	0.3	1.7	0.0	3.0	1.2	1.2	0.0	0.4
13	Iceland	[69]	55.2	14.4	2.4	3.4	2.1	3.0	1.7	0.7	0.0	0.6
14	Czech	[71]	60.0	8.4	15.0	7.7	6.0	0.0	0.0	0.0	1.4	0.0
15	Hungary	[72]	84.7	2.5	0.4	3.4	2.1	0.0	0.0	0.4	0.6	0.4
	AVERAGE		57.0	11.9	3.5	3.3	2.7	1.3	1.2	0.8	0.6	0.6

Correlation between Different A. archangelica Seed (Fruit) Volatile Compounds of Accession According to Literature

The correlation analysis was performed to investigate the similarities in the active compound content of the different *A. archangelica* seed (fruit) essential oils (1–15), and the results are visually displayed in Figure 4.

The content of β-phellandrene is negatively correlated with α-pinene (r = −0.853), statistically significant at the $p \leq 0.01$ level, and negatively correlated with bicyclogermacrene, β-pinene, and α-zingiberene content (r = −0.783; r = −0.693, and r = −0.704, respectively), statistically significant at the $p \leq 0.05$ level. The content of α-pinene is positively correlated with bicyclogermacrene and α-zingiberene (r = 0.892 and r = 0.649, respectively), statistically significant at the $p \leq 0.01$ level. The content of sabinene is positively correlated with myrcene (r = −0.759), statistically significant at the $p \leq 0.01$ level, and positively correlated with α-phellandrene (r = −0.592), statistically significant at the $p \leq 0.05$ level. The content of α-phellandrene is negatively correlated with bicyclogermacrene (r = −0.759, $p \leq 0.05$) and positively correlated with α-humulene content (r = −0.633, $p \leq 0.05$). The content of bicyclogermacrene is positively correlated with α-zingiberene (r = 0.770, $p \leq 0.01$).

The content of limonene is negatively correlated with α-humulene (r = −0.554, $p \leq 0.05$). The content of β-pinene is positively correlated with α-humulene (r = 0.726, $p \leq 0.01$).

The first PC explained 42.61% and the second 27.68% of the total variance between the experimental data. The parting within samples could be seen in the PCA figure (Figure 5), where the samples from *A. archangelica* seed volatile compounds were presented.

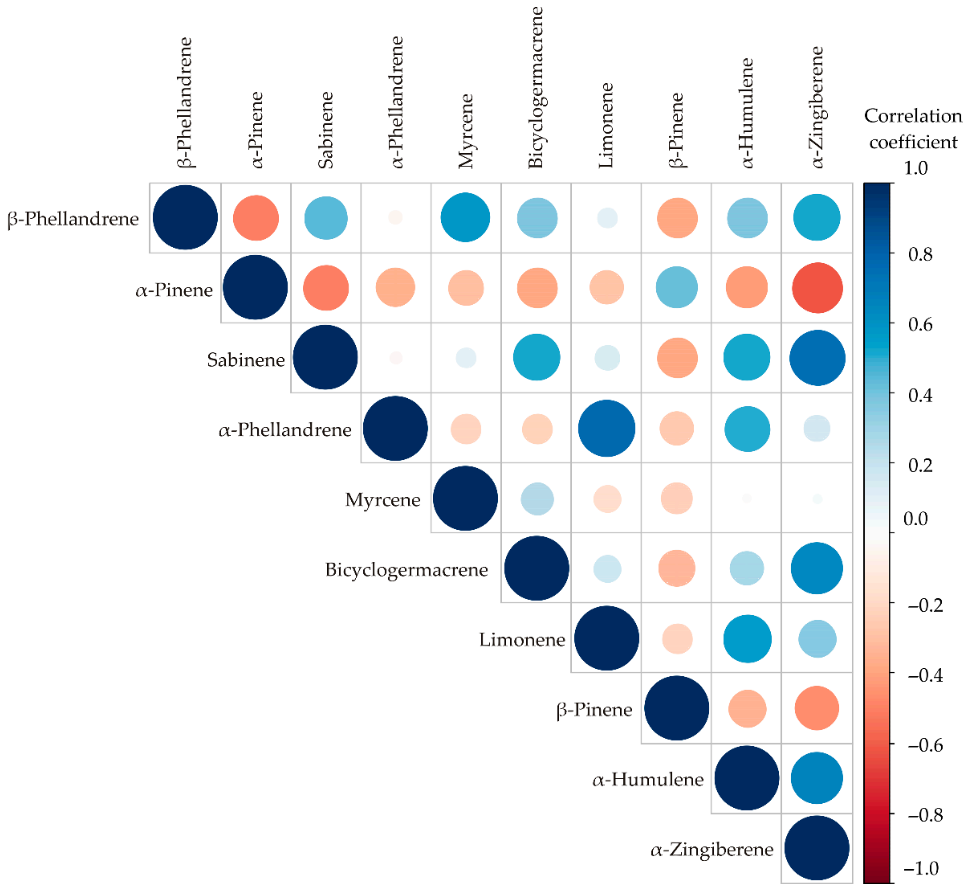

Figure 4. Correlations between different *A. archangelica* seed volatile compounds.

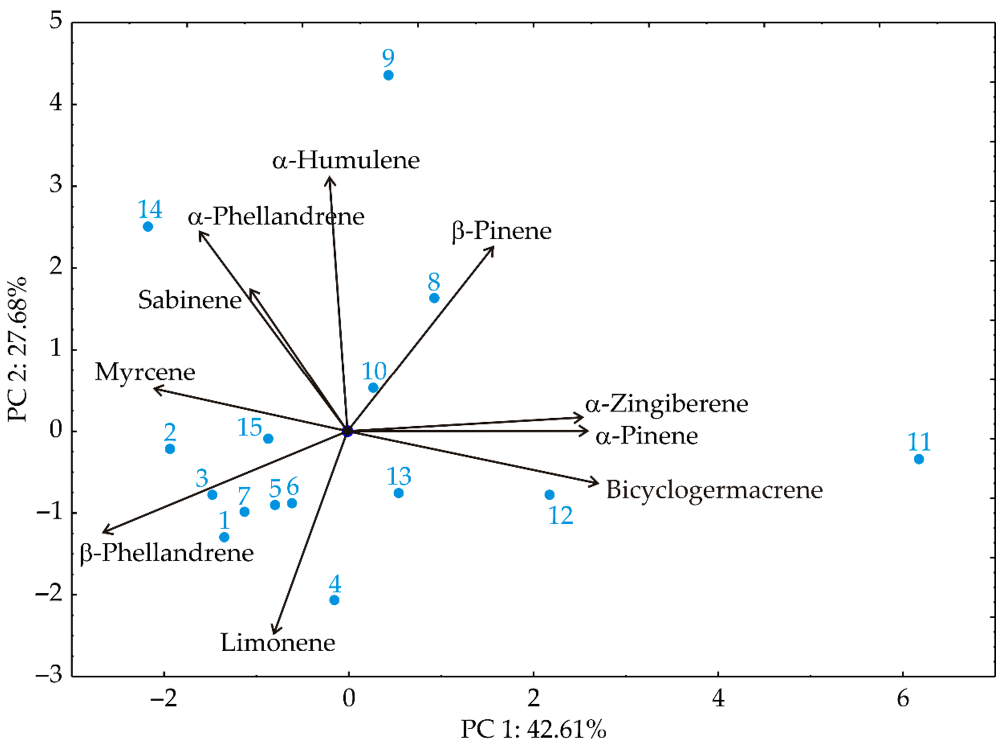

Figure 5. The PCA biplot diagram describing the relations between *A. archangelica* seed (fruit) volatile compounds.

Cluster analysis based on these data was used for drawing an unrooted tree (Figure 6). Moreover, vice versa in relation to the morphological characteristics of the fruit, which are extremely conservative among species and subspecies according to the individual (discussed earlier), essential oils cannot easily be analyzed for their chemotypes as in the previous group. However, these conclusions should not be completely rejected, as, potentially, these results may be important in identifying the origins of the plants.

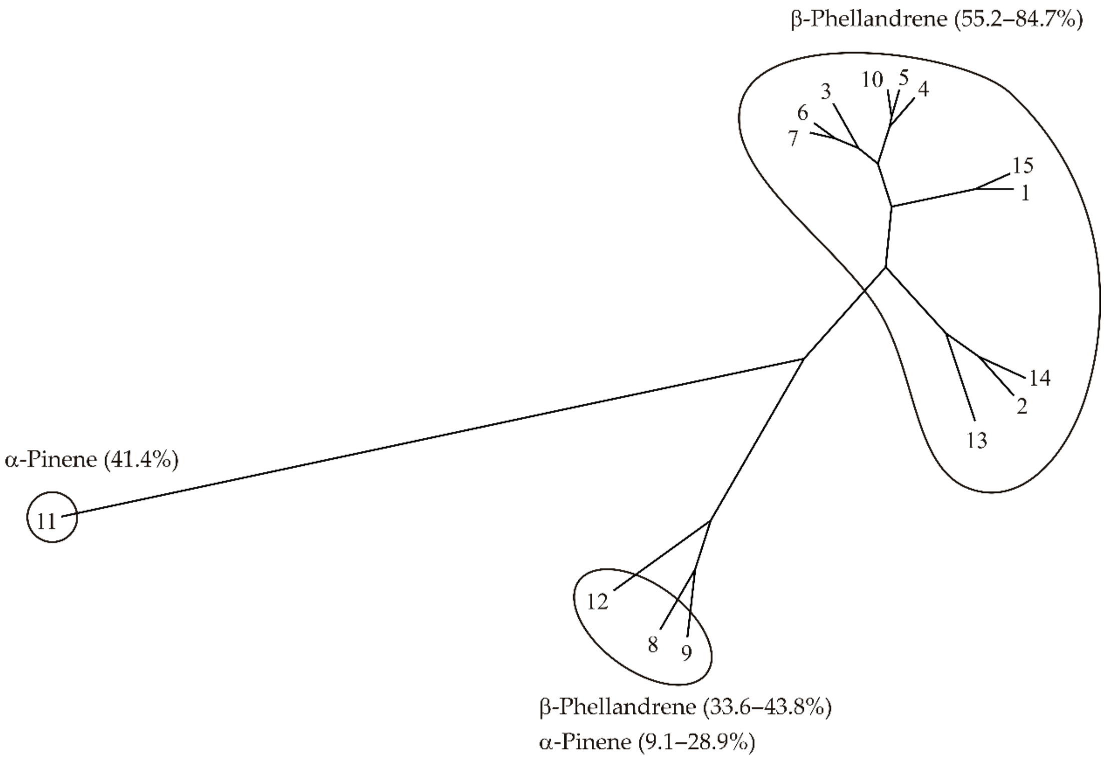

Figure 6. Unrooted cluster tree of *A. archangelica* seed (fruit) essential oil (samples are numbered according to Table 2).

The unrooted tree of *A. archangelica* seed (fruit) essential oil (samples were numbered according to Table 2) indicated the presence of three chemotypes; the first with β-Phellandrene, second with α-Pinenen and the third with β-Phellandrene and α-Pinenen as main volatile compound. The main volatile compound in *A. archangelica* seeds is β-phellandrene (total 11 accessions), and this chemotype could be divided into four subgroups. The extremely high content of β-phellandrene (with variation between 82.1 and 84.7%) is noted in accessions No. 1 from Lapland and No. 15 from Hungary. The very high content of β-phellandrene (variation between 74.0 and 76.0%) is noted in accessions No. 3 (Lapland), No. 6 (France), and No. 7 (Canada). The high content of β-phellandrene (variation between 63.4 and 65.8%) is noted in accessions No. 4 and 5 (France), as well as in No. 10 (Lithuania). An accession rich in β-phellandrene (with variation between 55.2 and 66.4%) is noted in No. 2 (Lapland), No. 13 (Iceland), and No. 14 (Czech). A combination of β-phellandrene (33.6–43.8%) and α-pinene (9.1–28.9%) is noted in accessions No. 8 and 9 (from Lithuania) and No. 12 (from Iceland). Accessions with dominant α-pinene (41.4%) from Iceland.

7. Biological Activities Associated with Essential Oil

A number of *Angelica* species have been used in traditional medicine and ethnoveterinary care to treat many ailments [73–76]. Traditionally, *A. archangelica* has been used as a cure for nervous headaches, fever, skin rashes, wounds, rheumatism, toothaches, digestive problems, bronchitis, excess mucus, the flu, chronic fatigue, and menstrual and obstetric complaints [73]. In addition, volatile compounds from angelica essential oils give a specific fragrance and biological properties to every plant part [74].

Scientific results show that the *A. archangelica* root essential oil expressed good antimicrobial activity against *Aspergillus niger*, *Candida albicans*, *Cladosporium cladosporioides*, *Clostridium difficile*, *C. perfringens*, *Enterococcus faecalis*, *Escherichia coli*, *Eubacterium limosum*, *Penicillium venetum*, *Peptostreptoccocus anaerobius,* and *Staphylococcus aureus* [58,60,74], as well as against *Alternaria solani*, *Botrytis cinerea*, and *Fusarium* sp. [57]. According to these results, *A. archangelica* root essential oil can be used as a natural preservative and as a natural antibiotic for treating infectious diseases caused by these pathogens, as well as serving as a control agent for plant pathogenic fungi in natural formulations [57,58,74].

A. archangelica fruit essential oil expresses cytotoxic activity towards human pancreatic cancer lines (PANC-1) and Crl mouse breast cancer cells [47], while the root essential oil at high doses (from 219.9 µg/mL) induced significant apoptosis and necrosis in human histocystic lymphoma cells (U937) [61]. In addition, *A. archangelica* root essential oil at low doses, which are nontoxic, showed anti-inflammatory effects. These results provide an important basis for developing adjuvant formulations for pharmacological therapies and new food products or dietary supplements for antagonistic inflammation [61]. However, the Committee for Veterinary Medicinal Products has limited the usage of *A. archangelica* root essential oil in products used as nose sprays to facilitate breathing in newborn animals [73].

8. Conclusions

Angelica archangelica L. is often grown throughout Asia and Europe, but only in one region is it a natural species. A systematic approach to the species is still often the goal of many papers, and new research on chemical diversity is equally present.

Our research has shown that within a species, four subspecies can be clearly defined: *A. archangelica* subsp. *archangelica*, A. archangelica subsp. *litoralis* (Fr.) Thell, *A. archangelica* subsp. *decurrens* (Ledeb.) *B. Fedtsch*., and *A. archangelica* subsp. *himalaica* (C.B.Clarke) G.Singh & G.M.Oza. This conclusion is supported by the distribution area, morphological traits, and differentiated chemotypes that resulted from the analysis of the volatiles of the essential oils. The results of the unrooted cluster tree constructed according to *A. archangelica* root volatile compounds showed the presence of four chemotypes. However, α-pinene is noted in all samples except in No. 16, 17, and 18, originating from India, with dillapiole and nothapiole as the main compounds. On the other hand, the unrooted tree of *A. archangelica* seed (fruit) essential oil indicated the presence of three chemotypes. The main volatile compound in *A. archangelica* seeds is β-phellandrene, and this chemotype could be divided into four subgroups. The unrooted cluster tree of *A. archangelica* root volatile compounds clearly shows that samples from India, probably subsp. *himalaica*, were significantly different from others (with dillapiole and nothapiole), while other samples, both for roots and seeds, are very similar, with α-pinene in root oil and β-phellandrene and α-pinene in seed oil. This indicates the origination of *Angelica archangelica* from the northern temperate regions of Europe, and the existence of two subspecies: subsp. *archangelica* and subsp. *litoralis*. According to this theory, subsp. *himalaica* could be an ecologically distinct species.

All these results have been cross-analyzed and are particularly important for planning and defining the process of cultivation and use of this species in both traditional and official medicine.

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