



Wild plants are found in temperate climate zones: in the forest zones of the continents of Eurasia, North and South America, Australia. Hops have a wide range of growth in the Russian Federation, covering the entire European part of Russia, the Caucasus, Western Siberia, and are widespread in the flora of the Republic of Bashkortostan. The wild plant is found in forest and forest-steppe zones, in broad-leaved forests, on forest edges, in ravines, among bushes, along river banks and swamps [12, 13, 14, 15]. If we talk about cultivated plants, then in many countries, in particular England, France, the Czech Republic, Germany, China, and the USA, hops have long been introduced into production and are grown as an industrial crop for the needs of the food and pharmaceutical industries. World hop production is concentrated in the USA, Germany, the Czech Republic, Poland and China, these countries account for 70% of world production [16]. In the Russian Federation, commercial hop production is concentrated in 11 administrative regions. The main producers are the Chuvash Republic (82%), the Mari El Republic (about 6.5%) and the Altai Territory (3.3% of Russian hops). The remaining regions - Bryansk, Nizhny Novgorod, Ulyanovsk, Omsk regions and Khabarovsk Territory produce slightly more than 8% [16].

Hop cones are rich in biologically active substances such as: essential oils, bitter glycosides, phytohormones, organic acids, flavonoids (quercetin, rutin, myricetin, kaempferol, etc.), prenylated flavonoids, vitamins B, PP, C, H, tocopherol, amino acids, coumarins, tannins, pectin substances, alkaloids [15, 17, 18, 19, 20, 21, 22, 23].

The most important quality indicator that determines the consumer properties of hops for the food and especially the brewing industry is the content of bitter acids, especially α -acids. According to the quantitative content of bitter acids, three varieties of common hops are noted: aromatic, bitter-aromatic and bitter [6, 24]. Among the cultivated plants in the Russian Federation, the following cultivars are grown. The aromatic cultivar (the cultivars "Ranniy", "Mikhailovsky", "Istrinsky", "Clone 18", etc.) has 3-6% of α -acids, a significant content of essential oils up to 4%, and is characterized by a pronounced hop aroma.

The bitter-aromatic cultivar (the cultivars "Krylatsky", "Polesky", "Sumer", etc.) has a significant content of bitter acids (6-10% α -acids), a sufficient content of essential oils (0.5-2.65%), and a characteristic hop aroma. The essential oil of this cultivar contains resinous and balsamic substances. Plants of the bitter variety type (varieties "Podvyazny", "Silny", "Granat") with an α -acid content of more than 10% have a less pronounced hop aroma, terpenoids are represented mainly by resinous substances [6].

An equally important quality indicator is the ratio of the proportion of α -acids to the proportion of total hop resins. For plants of the bitter variety type, it should be at least 35%, for the aromatic - at least 20% [6].

For the needs of the brewing industry, plants of the bitter variety type are mainly used, for the needs of the food industry - bitter-aromatic [25, 26]. In the pharmaceutical industry, common hops are used regardless of the variety type, including wild plants.

Hops are included in a number of well-known drugs and many fortified specialized food products, biologically active food supplements. Hop preparations have sedative, neurotropic, anti-inflammatory, antiulcer, capillary-strengthening, antioxidant, analgesic, and hypnotic effects [21, 26, 28, 29, 30, 31].

Analysis of literary data shows that the chemical composition and biological properties of common hop fruits are well studied. Other parts of the plant have been little studied in terms of chemical composition. Common hop stems contain phytosterols (β -sitosterol, stigmasterol), as well as a large amount of lignin and a relatively small amount of pentosan and cellulose [14, 32]. Hop leaves contain a small amount of cannabidiol. Young shoots and leaves of hops are used (especially in Belgium) to prepare salads, added to borscht, soup, and sauces. In Romania, young shoots of hops are used like asparagus. Food products made with the addition of hops stimulate appetite, stimulate digestion and calm the nervous system [33, 34]. It should be noted that the urgent task of practical pharmacy and the agricultural sector of the economy is the complex processing of plant raw materials. In this regard, the phytochemical study of new types of raw materials, namely, the leaves of common hops, which have a large vegetative mass, which today are waste products of hop production, is an urgent task, since it will expand the possibility of



complete processing of raw materials and the scope of its application, both in medical practice and in the food industry and other sectors of the national economy.

The aim of our study was to investigate the qualitative and quantitative composition, as well as to conduct a comparative analysis of polyphenolic compounds in various samples of leaves and cones of cultivated and wild *Humulus lupulus* L.

Materials and Methods

The objects of the study were dried leaf and cone samples of wild *Humulus lupulus* L. collected in the Russian Federation (in several districts of the Republic of Bashkortostan: Ufimsky, Blagoveshchensky, Davlekanovsky, Belebeysky, Tuymazinsky, and others). Cultivated plant material was collected in the Chuvash Republic from the hop varieties 'Ranniy' (aromatic type), 'Krylatkiy' (bitter-aromatic type), and 'Podvyazny' (bitter type) during different vegetation phases between 2015 and 2023 (Cheboksary, urban-type settlement Urmariy). In our previous studies, the main groups of biologically active compounds (BACs) were identified, including phenolic compounds (flavonoids, isoflavonoids, coumarins, tannins, stilbenes, and hydroxycinnamic acids). The identification of these BAC groups was carried out in aqueous, aqueous-alcoholic, butanol, chloroform, and ethyl acetate extracts of the studied plant materials using specific qualitative reactions and chromatography methods [21]. It was experimentally established that a 70% ethanol solution is the most effective solvent for the preparation of aqueous-alcoholic extracts [22]. In the present study, high-performance liquid chromatography (HPLC) and spectrophotometry were used.

To study the composition of phenolic compounds, the HPLC method was used using the following technique and the specified equipment. The qualitative composition of phenolic compounds was studied using a high-performance liquid chromatograph by Gilson, model 305 (France); manual injector, model Rheodyne 7125 (USA) with subsequent computer processing of the research results using the program Multichrom for Windows. A metal column measuring 4.6 x 250 mm Kromasil C 18 with a particle size of 5 microns was used as a stationary phase. The mobile

phase was methanol-water-concentrated phosphoric acid in a ratio of 400:600:5. The analysis was carried out at room temperature. The eluent feed rate was 0.8 ml/min. The duration of the analysis was 120 min. Detection was carried out using a UV detector Gilson UV/VIS model 151, at a wavelength of 254 nm. For the study, the raw material was ground to a particle size passing through a sieve with a hole diameter of 2 mm according to GOST 214-83.

About 2.5 g of raw material (accurately weighed) was placed in a 200 ml flask, 40 ml of 70% ethyl alcohol were added, connected to a reflux condenser and heated in a boiling water bath for 1 hour from the moment the alcohol-water mixture in the flask boiled. After cooling, the mixture was filtered through a paper filter into a 50 ml measuring flask and brought to the mark with 70% ethyl alcohol (solution A, the test solution).

To prepare the mobile phase, methyl alcohol (special purity), concentrated phosphoric acid (special purity), purified distilled water were used. In parallel, a series of 0.02% solutions of standard samples (Fluka, Sigma) in 70% ethyl alcohol were prepared: rutin, quercetin, luteolin, cynaroside, kaempferol, coumarin, hyperoside, hesperidin, apigenin, gallic acid, caffeic acid, chlorogenic acid, neochlorogenic acid, cinnamic acid, ferulic acid, arbutin, catechin, umbelliferone, o-coumaric acid, epigallocatechin gallate, epicatechin, dicoumarin.

50 µl of the test solutions and comparison solutions were introduced into the chromatograph and chromatographed under the above conditions.

Identification of the separated substances was carried out by comparing the retention times of the peaks obtained on the sample chromatogram with the retention times of the standard solutions. The internal normalization method was used to determine the relative content of some phenolic compounds in the sample under study [35, 36].

In our previous studies, we experimentally determined the optimal extraction parameters, marker compound, and developed a method for quantitatively determining the amount of flavonoids in common hop raw materials in terms of rutin. Quantitative determination was performed by differential spectrophotometry in the UV region of the spectrum. To obtain characteristic UV



spectra, we used the reaction of complexation of flavonoids with aluminum chloride in a 70% ethyl alcohol medium with acidification with acetic acid [21, 22].

To study resveratrol, HPLC was used using the following method and equipment.

Methodology. Common hop raw material of about 0.5 g (accurately weighed), crushed to 2 mm in accordance with GOST 214-83, placed in a 50 ml flask, was filled with 20 ml of methanol. The flask with the raw material under study, connected to a reflux condenser, was heated from the moment the extractant boiled for 1 hour. After cooling, the mixture was filtered into a 25 ml measuring flask through a paper filter, washed with two portions of methanol (2 ml), brought up to the mark with methanol. The resulting extract was placed in a water bath and evaporated to a volume of 2 ml (test solution). In parallel, a 0.02% solution of resveratrol CO in methanol was prepared. Chromatography conditions: stationary phase – metal column «Kromasil C 18» measuring 4.6x250 mm (particle size 5 microns); mobile phase: mixture of TFA solution pH 2.5 – acetonitrile, in a ratio of 140:60; eluent feed rate – 1 ml/min; analysis time – 30 min; t °C – room temperature; UV detector («Gilston UV/VIS», model 151); wavelength 307 nm; the volume of the studied solutions and CO solutions introduced into the chromatograph – 50 μ l.

The standard sample solution was prepared using the resveratrol standard from «Sigma-aldrich» and methyl alcohol (special purity grade). TFA, acetonitrile (special purity grade), purified water suitable for HPLC were used to prepare the mobile phase. The determination of separated biologically active substances was carried out by comparing the retention times of sample peaks reflected in the chromatograms with the retention times of CO solutions.

HPLC was also used to investigate isoflavonoids using the following technique and equipment.

Methodology. Common hop raw material of about 1.0 g (accurately weighed), crushed to 2 mm in accordance with GOST 214-83, placed in a 250 ml measuring flask, was poured with 50 ml of 70% ethyl alcohol solution. The flask with the raw material under

study, connected to a reflux condenser, was heated from the moment the extractant boiled for 1 hour. After cooling, the mixture was filtered into a 50 ml measuring flask through a paper filter, washed with two portions of ethanol (3 ml), brought to the mark with 70% ethyl alcohol solution (test solution). In parallel, a 0.02% solution of genistin, genistein, daidzein CO in a 70% ethyl alcohol solution was prepared. Chromatography conditions: stationary phase – metal column «Luna C18» measuring 4.6x250 mm (particle size 5 microns); mobile phase: mixture of acetonitrile – 0.1% phosphoric acid (ratio 350:650); eluent feed rate – 0.8 ml/min; analysis time – 120 min; t °C – room temperature; UV detector («Gilston UV/VIS», model 151); wavelength 255 nm; volume of studied solutions and CO solutions introduced into the chromatograph – 20 μ l.

CO of standard samples were prepared using standards of genistin, genistein, daidzein from «Sigma-aldrich», «Fluka» and ethyl alcohol (special purity). The mobile phase was prepared using phosphoric acid, acetonitrile (special purity), purified distilled water. The determination of separated biologically active substances was carried out by comparing the retention times of sample peaks reflected in the chromatograms with the retention times of RSO solutions.

Results and discussion

Study of phenolic compounds

The results of the study of phenolic compounds by HPLC allowed to identify 19 compounds of phenolic nature, 13 of which were identified for the first time. Substances of phenolic nature are mainly represented by flavonoids (rutin, cynaroside, hyperoside, luteolin-7-glycoside, dihydroquercetin, quercetin, kaempferol, luteolin), coumarin, derivatives of phenolic carboxylic and oxycinnamic acids (gallic, chlorogenic, chicory, caffeic, neochlorogenic, ferulic, cinnamic), tannins (tannin, epigallocatechin gallate, epicatechin), are presented in Tables 1 and 2. It was established that all the studied samples of raw materials from flavonoid compounds contain rutin, hyperoside, kaempferol; from derivatives of phenolic carboxylic and oxycinnamic acids - gallic, chlorogenic, chicory, coffee, neochlorogenic, ferulic acids; from tannins - epigallocatechin gallate. From tables 1, 2 it is clear that the qualitative composition of various samples of



common hop leaves is very diverse, represented by compounds of the main groups of phenolic substances and are similar in composition. But the richest were samples of wild plants collected in the Russian Federation, namely in the Republic of Bashkortostan (Ufa and Davlekanovsky districts), as well as a sample of the cultivated variety "Ranniy", belonging to the aromatic variety. Thus, in samples of common hop leaves collected in the Ufa and Davlekanovsky districts of the Republic of Bashkortostan, 17 and 16 phenolic

compounds, respectively, were found, and the variety "Ranniy" - 17 compounds. In the leaves of common hops of the bitter-aromatic cultivar "Krylatsky", 14 phenolic compounds were identified, and in the bitter cultivar "Podvyazny" - 15 compounds. Quantitative determination of the amount of flavonoids in terms of rutin in the raw material of common hops was carried out according to the method developed by us for the raw material of common hop leaves [21]. The results of the quantitative determination are presented in Table 3.

Table 1 – Content of polyphenolic compounds in different samples of common hop leaves

Name of the compound	Raw material samples			
	Wild sample from Davlekanovo district		Wild hop raw material, Ufa district	
	Cones	Leaves	Cones	Leaves
	Retention time, min (internal normalization)	Retention time, min (internal normalization)	Retention time, min (internal normalization)	Retention time, min (internal normalization)
Umbelliferone	–	–	3,24	–
Tannin	3,28	3,23	3,28	3,22
Gallic acid	3,41	3,43	3,43	3,42
Epigallocatechin gallate	3,92	3,96	3,81	3,87
Chlorogenic acid	4,38	4,31	4,38	4,35
Caffeic acid	5,78	5,82	5,85	5,84
Cichoric acid	5,94	5,95	5,96	5,98
Ferulic acid	7,98	7,96	7,95	7,97
Neochlorogenic acid	9,58	9,62	9,58	9,52
Cynaroside	10,83	10,94	10,86	10,88
Cinnamic acid	–	–	11,04	11,07
Epicatechin	12,78	12,75	12,64	–
Rutin	14,08	14,11	14,14	14,12
Hyperoside	16,39	16,38	16,38	16,41
Coumarin	21,12	21,09	21,08	21,09
Quercetin	41,65	41,62	40,44	40,40
Kaempferol	58,52	58,49	58,76	58,78



Dihydroquercetin	59,99	59,97	–	–
Luteolin	69,29	69,32	69,35	69,34

Table 2 – Content of polyphenolic compounds in different samples of common hop leaves

Name of the compound	Raw material samples					
	Cultivar "Ranniy"		Cultivar "Krylatsky"		Cultivar "Podvyazny"	
	Cones	Leaves	Cones	Leaves	Cones	Leaves
	Retention time, min (internal normalization)	Retention time, min (internal normalization)	Retention time, min (internal normalization)	Retention time, min (internal normalization)	Retention time, min (internal normalization)	Retention time, min (internal normalization)
Umbelliferone	–	–	–	–	–	–
Tannin	–	–	–	–	–	–
Gallic acid	3,39	3,44	3,38	3,36	3,54	3,59
Epigallocatechin gallate	3,96	3,95	3,89	3,92	3,94	3,93
Chlorogenic acid	4,34	4,38	4,35	4,33	4,36	4,41
Caffeic acid	5,76	5,77	5,78	5,81	5,74	5,76
Cichoric acid	6,02	5,98	6,05	6,07	6,04	6,04
Ferulic acid	7,97	7,95	7,87	7,89	7,92	7,89
Neochlorogenic acid	9,56	9,39	9,75	9,69	8,85	8,76
Cynaroside	10,83	10,88	10,87	10,92	–	–
Cinnamic acid	11,12	11,09	–	–	–	–
Epicatechin	12,63	12,52	–	–	–	–
Rutin	14,08	14,09	14,05	14,09	14,12	14,14
Hyperoside	16,36	16,44	16,45	16,49	16,43	16,45
Coumarin	21,14	21,17	–	–	21,15	21,17
Quercetin	40,05	40,07	40,18	40,21	40,08	40,09
Kaempferol	58,73	58,69	58,76	58,79	58,76	58,77
Dihydroquercetin	59,99	59,98	59,95	59,98	59,93	59,96
Luteolin	–	–	69,29	69,34	69,41	69,43

Table 3 – Content of total flavonoids in different samples of hop leaves



Name of the compound	Flavonoid content, %
Cultivar "Ranniy"	3,05±0,06
Cultivar "Krylatsky"	2,36±0,09
Cultivar "Podvyazny"	2,66±0,08
Wild raw material collected in the Ufa district	3,23±0,11
Wild raw material collected in the Davlekanovo district	2,97±0,10

The data in the table show that the content of the sum of flavonoids in hop leaves is quite high, fluctuates depending on the variety and in the samples we studied ranges from 2.36 to 3.23%. The maximum content of flavonoids was noted in the wild variety collected in the Ufa region of the Republic of Bashkortostan, the minimum - in the leaves of the cultivated variety "Krylatsky".

Resveratrol Study

According to literature data, common hop cones contain resveratrol, a promising antioxidant widely used in medical practice [35]. The meal of common hop cones, remaining during the production of common hop cones extract, is proposed by the authors [36] as a source for obtaining a class of polyphenolic compounds of the stilbene group – resveratrol. In this regard, it was of great interest to determine the presence of this substance in common hop leaves. For this purpose, we used the HPLC method. The results of the studies are shown in Figures 1, 2, and Table 4.

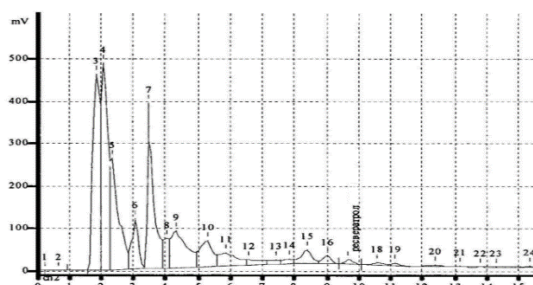


Figure 1. HPLC chromatogram of methanol extract from hop cones (resveratrol)

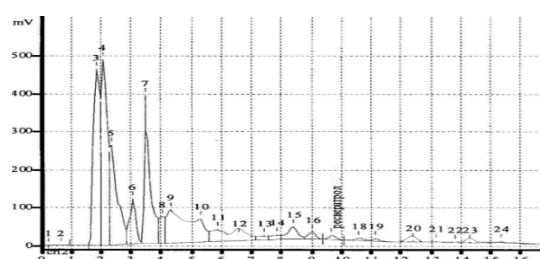


Figure 2. HPLC chromatogram of methanol extract from hop leaves (resveratrol)

Quantitative determination of resveratrol in common hop raw materials

Quantitative determination of resveratrol in common hop raw materials was carried out by HPLC according to the method described above, by the absolute calibration method, using a standard sample (SS) of resveratrol as a standard. Calculation of the quantitative content of resveratrol in dry raw materials was carried out using the computer program "Multichrome" for "Windows" according to the formula (X,%) (1):

Quantitative Determination Formula for Resveratrol

$$X = (S_{\text{sample}} \times C_{\text{standard}} \times V \times 100 \times 100) / (S_{\text{standard}} \times a \times (100 - W))$$

Where:

- S_{sample} – peak area of resveratrol in the test solution
- S_{standard} – peak area of the resveratrol standard
- C_{standard} – concentration of the resveratrol standard, g/mL
- a – weight of the sample (g)
- W – moisture loss on drying (%)
- V – dilution volume (mL)



Table 4 – Results of quantitative determination of resveratrol in common hop raw materials

Name of the compound	Type of raw material	Resveratrol content (%)
Common hop (Davlekanovo district)	Cones	0,0250±0,0002
	Leaves	0,0211±0,0001
Common hop (Ufa district)	Cones	0,0380±0,0002
	Leaves	0,0252±0,0002
Cultivar "Ranniy"	Cones	0,0284±0,0001
	Leaves	0,0242±0,0002
Cultivar "Krylatsky"	Cones	0,0341±0,0002
	Leaves	0,0265±0,0001
Cultivar "Podvyazny"	Cones	0,0211±0,0001
	Leaves	0,0182±0,0001

The results of the conducted studies showed the presence of resveratrol in all the studied samples of raw materials. It was found that the content of resveratrol in the fruit of the studied plants ranges from 0.0211 to 0.0380%, which is slightly higher than in the leaves - from 0.0182 to 0.0265% (Table 4). The content of this component in the samples of wild plants is not inferior to that of cultivated hop varieties.

Isoflavonoids study

According to literature data, the fruit of common hop contains phytoestrogens. From the point of view of the complex use of the whole plant, it was of interest to determine the presence of this group of biologically active substances in the leaves of common hop. For this purpose, we used the HPLC method. The results of the studies are presented in tables 5, 6, figures 3, 4.

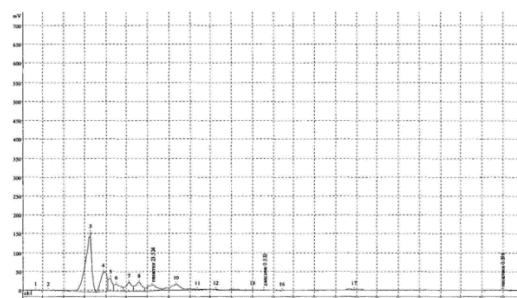


Figure 3. HPLC chromatogram of the aqueous-alcoholic extract from hop cones (isoflavonoids)

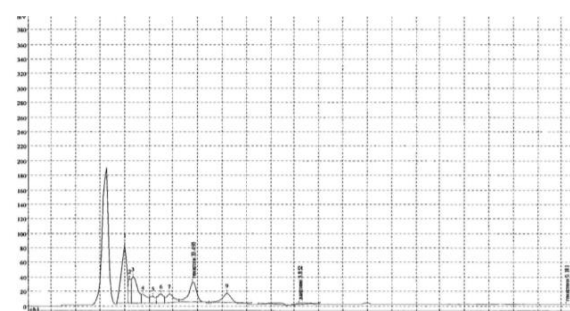


Figure 4. HPLC chromatogram of aqueous-alcoholic extract from hop leaves (isoflavonoids)

Table 5 – Results of the study of the composition of isoflavonoids in the raw material of common hops using the HPLC method

Name of the compound	Raw material of common hop leaves	Raw material of common hop cones
	Retention time, min (internal normalization)	Retention time, min (internal normalization)
Genistin	6,77	6,76
Daidzein	11,14	11,12
Genistein	22,12	22,12



Quantitative determination of isoflavonoids in common hop raw materials

Quantitative determination of isoflavonoids in common hop raw materials was carried out by HPLC according to the method described above, by the absolute calibration method, using genistin, genistein, daidzein as a standard. The quantitative content of isoflavonoids in dry raw materials was calculated using the Multichrome computer program for Windows using the formula (X, %) (2):

Quantitative Determination Formula for Isoflavonoids

$$X = (S_{\text{sample}} \times C_{\text{standard}} \times V \times 100 \times 100) / (S_{\text{standard}} \times a \times (100 - W))$$

Where:

- S_{sample} – peak area of isoflavonoids in the test solution
- S_{standard} – peak area of the isoflavonoid standard
- C_{standard} – concentration of the corresponding isoflavonoid standard, g/mL
- a – weight of the test sample (g)
- W – moisture loss during drying (%)
- V – dilution volume (mL)

Table 6 – Results of quantitative determination of isoflavonoids in common hop raw materials

Name of the compound	Type of raw material	Isoflavonoids found (mg%)		
		Genistin	Genistein	Daidzein
Common hop (Davlekanovo district)	Cones	4000±20,12	50±0,21	70±0,39
	Leaves	1900±8,21	18±0,13	60±0,18
Common hop (Ufa district)	Cones	2800±16,75	31±0,35	50±0,27
	Leaves	900±7,29	9±0,07	20±0,14
Cultivar "Ranniy"	Cones	4100±26,16	60±0,21	90±0,28
	Leaves	1500±11,36	12±0,11	70±0,34
Cultivar "Krylatsky"	Cones	3400±22,87	45±0,28	80±0,26
	Leaves	1100±9,34	13±0,12	60±0,18
Cultivar "Podvyazny"	Cones	3900±18,45	70±0,19	40±0,12
	Leaves	1400±13,21	21±0,12	10±0,03

The results of the conducted studies showed the presence of genistin, genistein, daidzein in all the studied raw material samples. It was found that the content of genistin in all the studied raw material samples is higher than genistein and daidzein (Table 6). Thus, the content of genistin in the fruit buds of the studied plants varies from 28 to 4100 mg%, which is higher than in the leaves - from 900 to 1900 mg%. The

content of genistein in the fruit buds varies from 31 mg% to 70 mg%, in the leaves - from 12 mg to 21 mg%; the content of daidzein in the leaves was from 10 mg% to 0 mg%, in the fruit buds - from 50 mg% to 90 mg%. The samples of wild plants are not inferior to cultivated varieties in terms of isoflavonoid content. These studies also showed the prospects for using common hop leaves.



Conclusion

Thus, a comparative analysis of the composition of phenolic compounds showed that the leaves of the common wild hop species and cultivated varieties are not inferior to the fruit pods in the content of the main groups of polyphenols. 24 compounds of polyphenolic nature were identified. The leaves and fruit pods of common hop contain flavonoids (rutin, cynaroside, hyperoside, dihydroquercetin, quercetin, kaempferol, luteolin), derivatives of phenolic carboxylic acids (gallic, chlorogenic, chicory, coffee, neochlorogenic, ferulic, cinnamic), tannins (tannin, epigallocatechin gallate, epicatechin), coumarins (coumarin, umbelliferone), stilbenes (resveratrol), isoflavonoids (genistin, genistein, daidzein). The conducted studies have shown the similarity of the qualitative composition of the main groups of biologically active substances in the leaves and fruit sets of cultivated varieties and wild common hops. In terms of quantitative content of flavonoids, wild types of raw materials are not inferior to cultivated varieties, and in some cases even surpass them. Studies of the chemical composition of polyphenolic compounds have shown the prospects of further study of common hop leaves as an additional source of their production.

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