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Chemical Composition and Biological Active Substances from Hazelnut Green Leafy Covers

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Abstract: This investigation aims to study the perspectives for obtaining natural remedies and food additives from raw plant materials that can be used in food, pharmaceutical, and other industries. The selection of hazelnut green leafy cover as an item is based on the fact that it is a natural organic resource that is now being discarded as waste. In the article, the results are presented about the determination of mineral elements and bioactive compounds in the bio-extracts of 70% ethyl alcohol (BE-III) and distillation water (BE-IV) obtained from the green leafy cover of the plant (Corylus avellane L.) where grow in the northwestern region of Azerbaijan. According to our study, BE-III has 25 chemical elements, excluding Rb, for a total of 12.797%, while BE-IV contains 26 chemical elements for a total of 21.347%. Amounts of macroelements are 10.4%, and microelements are 2.69% in the content of BE-III, while amounts of macroelements are 17.82%, and amounts of microelements are 3.53% in the content of BE-IV. Amounts of organic compounds are 87.2% in the content of BE-III, while their amounts are 78.65% in the content of BE-IV. The amount of Zn, which has antioxidant activity, is 0.009%, and the amount of Se is 0.002% in the content of BE-IV. These values vary in the content of BE-III, the amount of Zn is 0.01%, but the amount of Se is 0.001%. 15 bioactive substances were identified in the content of BE-III bio-extract; however, 5 bioactive substances were identified in the content of BE-IV bio-extract. According to our research results, the bio-extract obtained from hazelnut green leafy cover is abundant with antioxidants and bioactive substances with antibacterial activity. For this reason, these bio-extracts can be used as both a food supplement and a means of treatment.

Keywords: Hazelnut green leafy covers, bio-extract, bioactive compound, macro- and microelements, antioxidant, antibacterial, chromato-mass spectrometry.

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INTRODUCTION

Researchers studying the common hazelnut plant (*Corylus avellana* L.) growing in different world countries have found that, along with other organs, the green leafy covers also are rich in bioactive compounds (1). However, despite the information that the kernel, shell, leaves, twigs, and other parts of the hazelnut plant are rich in mineral elements (2), no literature data has been found on the presence of mineral elements in hazelnut green leafy covers grown in Azerbaijan. While studying green leafy covers of the hazelnut plant, Turkish researchers S.B.Oguzkhan et al., 2016 found that the bio-extract contained bioactive compounds with high antioxidant and antibacterial properties. They obtained hazelnut green leafy covers extract with methanol at room temperature for 72 h and studied it by diffusion method using 8 different bacterial strains and determined that they had high antirad-

ical activity and antibacterial effect (3). Other researchers A.Hoffman and F.Witness in 2009 found that the extracts obtained from its leaves, brown and green leafy covers with 80% ethyl alcohol in a ratio of 1:10 during 12 h at 40ºC contain 10-deacetylbaccatin III, cephalomannine, and paclitaxel, but green contained only baccatin III (4). The studies of S.S.Siriwardhana and F.Shahidi in 2002 showed that the bio-extract obtained from the hazelnut green leafy covers had a hydrogen peroxide radical scavenger activity of 66% at 100 ppm and 91% at 200 ppm concentrations, which removes organic free radicals effectively (5). F.Shahidi et al.,2007 evaluated the total antioxidant activity (TAA) and free radical scavenger activity of ethanol-derived bio-extract from hazelnut green leafy covers using activity tests such as hydrogen peroxide, superoxide, and DPPH (diphenyl-l-picrylhydrazyl), and have confirmed its high antioxidant activity (6). Extracts obtained from the hazelnut green leafy covers with 80% ethyl alcohol and 80% acetone contain 5 phenolic acids - gallic acid, caffeic acid, p-coumaric acid, ferulic acid, and sinapinic acid, having a high antioxidant activity and free radical scavenger capacity (7). Therefore, it is recommended to consider hazelnut green leafy covers as a potential source of antioxidants. Hexadecanoic acid methyl ester ($C_{17}H_{34}O_2$) determined in green leafy covers had been tested for activity against fungi and proven its a high antifungal effect. It is recommended to use this substance to prepare antifungal drugs (8). The results of our research on the mineral elements and bioactive compounds found in the extracts of the hard shell of this plant have been presented in the articles by F. Azizov et al.,2021 (9, 19). This article presents the results of the determination and identification of minerals and bioactive compounds in bio-extracts obtained by extraction of green leafy covers of common hazelnut plants grown in the north-western region of Azerbaijan with aqueous extract and ethanol, as well as information on the results of quantitative and qualitative changes of the bioactive compounds depends on the extragents used and their comparative analysis.

MATERIAL AND METHODS

Plant material. The research object is the green leafy covers of the common hazelnut plant in Azerbaijan's Sheki region. Firstly, the green leafy covers were washed with ordinary water, then with distilled water, dried, and grounded, and the extracts were obtained using distilled water and 70% ethyl alcohol. The yield extractive substances and extraction regimes were studied separately for each.

Preparation of extracts. Samples of hazelnut green leafy covers dried at room temperature were grounded. 50 g grounded sample was added into a 500 mL flask. And then, 300 mL of distilled water was added to the grounded sample. The mixture was extracted in the water bath at 75-80 °C temperature for 30 minutes, and obtained extract solution was filtered. Then 100 mL of distilled water was added to the residual grounded sample and extracted for 15 minutes. The obtained extract was filtered and added to the first extract. Again 100 ml distilled water was added to the residual in the flask and extracted for 15 minutes. The obtained extract was filtered and added to the first extract.
Extraction in alcohol was carried out in the same way. Both extracts were powdered in an SPT-200 Vacuum-Drier device (10).

Determination of mineral elements. 0.2 g of powder of both samples was dissolved in 5.2 ml of acid solution (HNO_3: $HClO_4$ in the ratio of 5:0.5). It was heated until it turned white. Solutions were diluted with 40 mL of distilled water and filtered. Mineral elements were determined using the AA220FS atomic absorption spectrometer at the Center for Nuclear Research of the Azerbaijan Republic (11).

Determination of organic compounds. Biologically active substances in the extracts were determined using the gas-chromato-mass-spectroscopy method. For this purpose, Agilent Technologies 6890 N Network CG System, a chromatograph with 5975 inert Mass Selective Detector mass spectrometer, and as a detector Split/Splitless, injection-Split, Inlet pressure 60,608 kpa, Split-100, Low Mass-40, High Mass-400, Threshold 150 were used.

In experiments, a 30-meter quartz capillary column "HP-5MS 5% Methyl Siloxane" (internal diameter 0.25 mm, stationary phase thickness 0.25 μ) was used. Analyzes were performed in temperature programming mode at 50 °C to 280 °C at 15 °C/min.

Temperature regime of the column: starting temperature of the column 50 °C - constant for 2 minutes;
- temperature rise from 15 °C to 200 °C - 2 minutes constant;
- temperature rise from 15 °C to 280 °C - constant for 10 minutes;
- vacuum HiVac - 3.38e-005.

Diluted with a mixture of methanol - chloroform (1:2 ratio).

The flow rate of the gas (He) is 1 mL/min. The standard mass spectroscopic NIST library was used to identify the substances. The analysis lasted 33 minutes (12).

Comparative analysis of the number of minerals in the hazelnut green leafy covers extracts, as well as the identification of bioactive compounds, their synonyms, and therapeutic properties, were performed based on the available literature, Internet data, and the results of researchers from different countries.

RESULTS AND DISCUSSION

In the research work, mineral elements and bioactive compounds were determined separately in hazelnut green leafy covers BE-III and BE-IV extracts. The amounts of mineral elements determined in the content of BE-III and BE-IV extracts have been shown in Table 1.

Table 1: Amounts of mineral elements in the aqueous and ethanol bio-extracts.

Mineral elements	Amount, %	
	BE-III	**BE-IV**
K	4.380	9.133
Na	2.804	3.124
Mg	1.150	1.759
Ca	1.447	3.466
Ti	0.079	0.042
V	0.004	0.002
Cr	0.013	0.008
Mn	0.017	0.021
Fe	0.071	0.078
Ni	0.034	0.017
Cu	0.038	0.020
Zn	0.010	0.009
Ga	0.002	0.001
Zr	0.013	0.009
Sn	0.001	0.001
Sr	0.009	0.012
Y	0.004	0.002
Se	0.001	0.002
Al	1.718	2.476
Si	0.631	0.717
P	0.254	0.270
S	0.043	0.045
Ba	0.057	0.027
Pb	0.003	0.002
Nb	0.014	0.008
Rb	0	0.005
Total	**12.80**	**21.35**

As can be seen from the table, the composition of both BE-III and BE-IV is qualitatively similar except for Rb in BE-III extract, consisting mainly of 26 mineral elements K, Na, Mg, Ca, Ti, V, Cr, Mn, Fe, Ni, Cu, Zn, Ga, Zr, Sn, Sr, Y, Se, Al, Si, P, S, Ba, Pb, Nb, Rb. However, the amounts of mineral elements in BE-IV are noticeably higher (21.35%) than in BE-III (12.80%).

In the composition of BE-III, the amount of macroelements K, Na, Mg, Ca, Fe, and P is 10.11%, other microelements 2.69%, but in the composition of BE-IV, the amount of macroelements K, Na, Mg, Ca, Fe, P is 17.82%, other microelements 3.53%. As can be seen, the total amount of mineral elements and macro and microelements in the bio-extract BE-IV is about twice as high relatively in the bio-extract BE-III. In other words, the aqueous extract contains 21.35% inorganic and 78.65% organic substances, and the ethanol extract contains 12.80% inorganic and 87.20% organic substances. Antioxidant properties and vital elements such as Zn is 0.01% in BE-III, 0.009% in BE-IV, and Se is 0.001% in BE-III, 0.002% in BE-IV (13-16).

The results of the study of bioactive compounds of the bio-extracts have been given in Table 2. The bioactive compound listed in the table were selected sequentially according to the differences in their peaks on the chromatogram. The substances having peaks with lower height indicators have not been included in the table due to their lack of pharmacological properties and economic importance.

Table 2: Biologically active substances in BE-III and BE-IV extracts obtained from hazelnut green leafy covers.

No	Identified components	
	Ethanol extract (BE-III)	**Aqueous extract (BE-IV)**
1	Benzene-1,2-diol ($C_6H_6O_2$)	Benzene-1,2-diol ($C_6H_6O_2$)
2	2,3-dihydro-1-benzofuran (C_8H_8O)	5-(hydroxymethyl) furan-2-carbaldehyde ($C_6H_6O_3$)
3	5-(hydroxymethyl) furan-2-carbaldehyde ($C_6H_6O_3$)	3,5-dihydroxy-6-(hydroxymethyl)oxan-2-one $C_6H_{10}O_5$)
4	3,5-dihydroxy-6-methyl-2,3-dihydropyran-4-one ($C_6H_8O_4$)	Methyl hexadecanoate ($C_{17}H_{34}O_2$)
5	4-ethenyl-2-methoxyphenol ($C_9H_{10}O_2$)	Methyl octadecenoate ($C_{19}H_{38}O_2$)
6	Methyl 3-hydroxybenzoate ($C_8H_8O_3$)	
7	2,6-dimethoxyphenol ($C_8H_{10}O_3$)	
8	3,5-dihydroxy-6-(hydroxymethyl)oxan-2-one ($C_6H_{10}O_5$)	
9	1-methylsulfanyl-4-propan-2-ylbenzene ($C_{10}H_{14}S$)	
10	4-((1E)-3-Hydroxy-1-propenyl)-2-methoxyphenol ($C_{10}H_{12}O_3$)	
11	Methyl hexadecanoate ($C_{17}H_{34}O_2$)	
12	Dibutyl benzene-1,2-dicarboxylate ($C_{16}H_{22}O_4$)	
13	Methyl octadecenoate ($C_{19}H_{38}O_2$)	
14	Ethyl icosanoate ($C_{22}H_{44}O_2$)	
15	Gamma-sitosterol ($C_{29}H_{50}O$)	

As can be seen in Table 2, the extracts obtained by these methods differ from the composition of the main bioactive compound. Thus, 15 main bioactive compounds have been identified in BE-III and 5 in BE-IV. Each identified substance was studied separately according to its synonyms; information on their therapeutic properties and applications were obtained based on available literature data. The chromatograms obtained for determining the main bioactive compounds in BE-III and BE-IV are given below (Fig. 1-10).

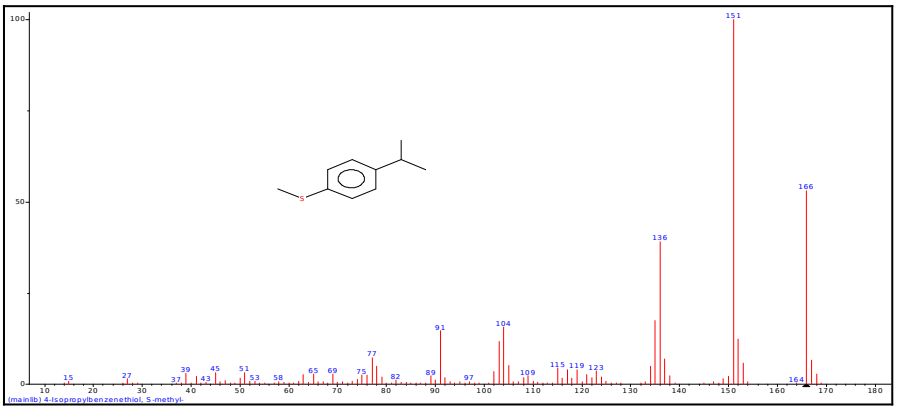

Figure 1: 1-Methylsulfanyl-4-propan-2-ylbenzene; $C_{10}H_{14}S$; MW=166.

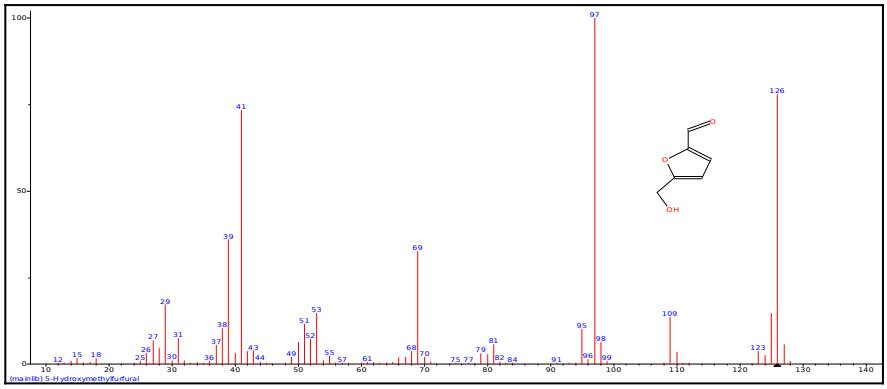

Figure 2: 5-(Hydroxymethyl)furan-2-carbaldehyde; $C_6H_6O_3$; MW=126.

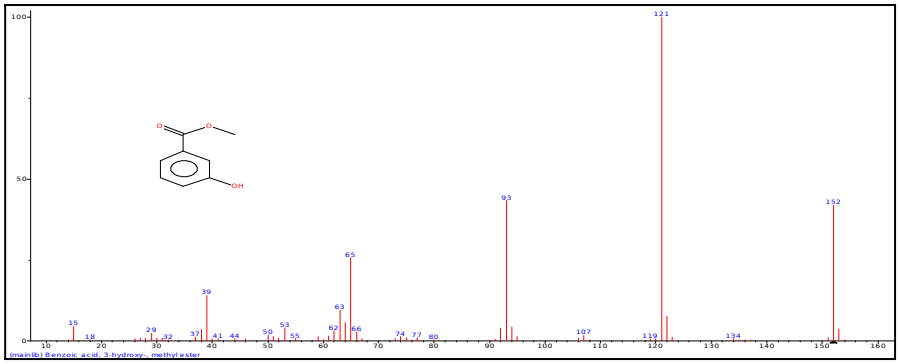

Figure 3: Methyl 3-hydroxybenzoate; $C_8H_8O_3$; MW=152.

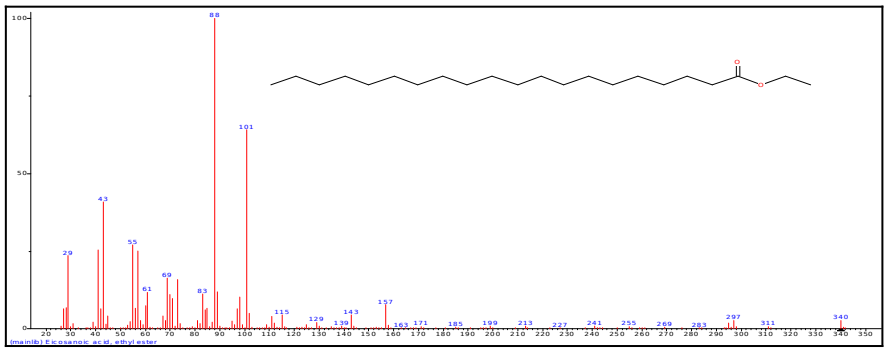

Figure 4: Ethyl icosanoate; $C_{22}H_{44}O_2$; MW=340.

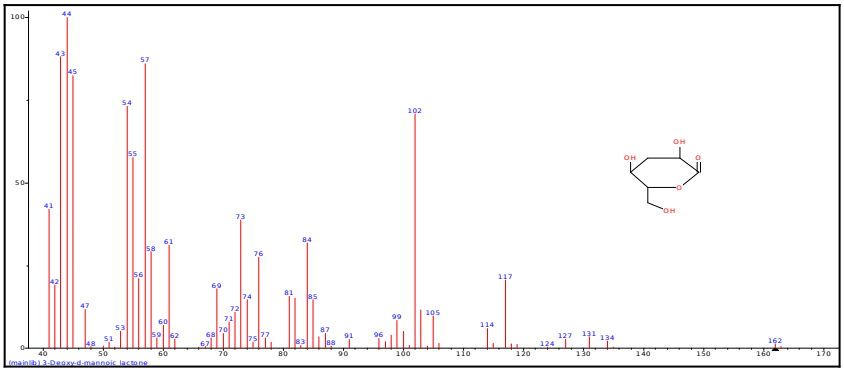

Figure 5: 3,5-Dihydroxy-6-(hydroxymethyl)oxan-2-one; $C_6H_{10}O_5$; MW=162.

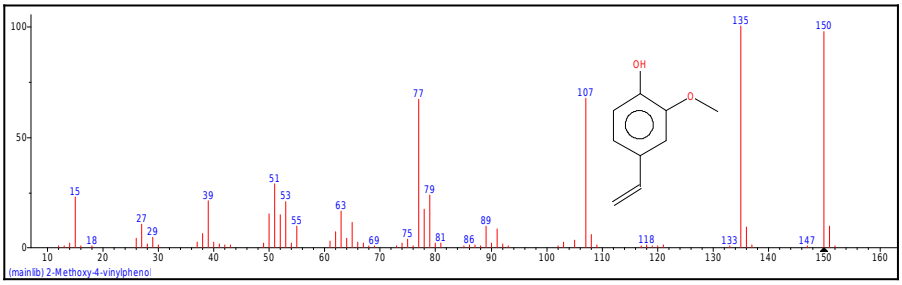

Figure 6: 2-Methoxy-4-vinylphenol; $C_9H_{10}O_2$; MW=150.

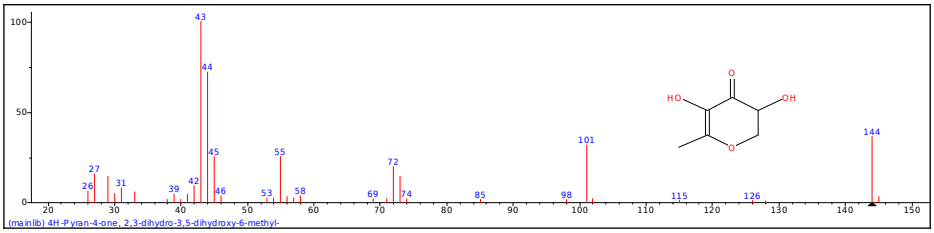

Figure 7: 4H-Pyran-4-one, 2,3-dihydro-3,5-; $C_6H_8O_4$; MW=144.

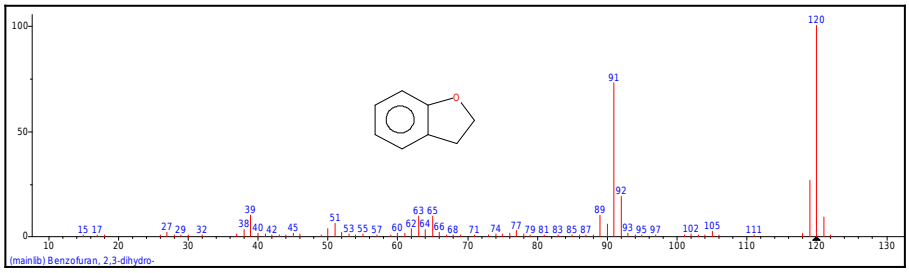

Figure 8: 2,3-Dihydrobenzofuran; C_8H_8O; MW=120.

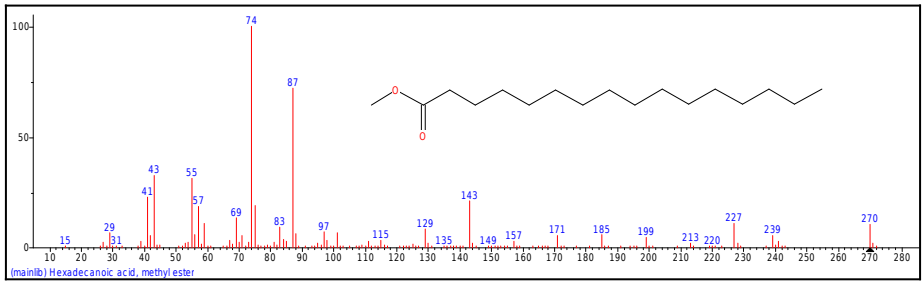

Figure 9: Methyl hexadecanoate; $C_{17}H_{34}O_2$; MW=270.

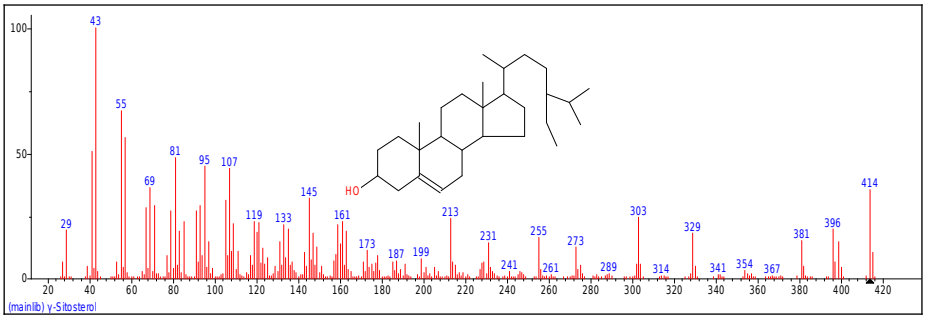

Figure 10: γ-Sitosterol; $C_{29}H_{50}O$; MW=414.

Analysis of the results of the study indicates that bioactive compounds of BE-III hazelnut green leafy covers are rich in organic compounds, such as antioxidant, antibacterial and antifungal properties. Particularly important among them are methyl hexadecanoate ($C_{17}H_{34}O_2$), dibutyl benzene-1,2-dicarboxylate ($C_{16}H_{22}O_4$), methyl octadecanoate ($C_{19}H_{38}O_2$), ethyl icosanoate ($C_{22}H_{44}O_2$), especially gamma-sitosterol ($C_{29}H_{50}O$), which has antimicrobial activity ten times more than beta-sitosterol (17,18). Our previous researches have revealed that the bio-extract obtained from the hard shell of hazelnuts has a wider spectrum range and higher amounts of bioactive compounds (19). However, in the composition of bio-extracts obtained from green leafy covers, these bioactive compounds are in short supply, both in quantity and quality. Besides, in the hazelnut green leafy covers extracts (BE-III and BE-IV) obtained by both methods 5 new organic compounds have been identified: benzene-1,2-diol ($C_6H_6O_2$), 5-(hydroxymethyl)furan-2-carbaldehyde ($C_6H_6O_3$), methyl hexadecanoate ($C_{17}H_{34}O_2$), methyl octadecanoate ($C_{19}H_{38}O_2$), 3,5-dihydroxy-6-(hydroxymethyl)oxan-2-one ($C_6H_{10}O_5$) (Figure 1-5). The presence of 5-(hydroxymethyl) furan-2-carbaldehyde ($C_6H_6O_3$), which has pharmacological properties, especially antioxidant and anti-inflammatory properties, increases the possibility of its use in the treatment of skin diseases (20,21). Other substances in the extracts are also very important and play an important role in the development of the body, the regulation of metabolism, and the strengthening of the immune system (22). The comparative results show that the bio-extracts contain 5 new organic substances such as 1-methylsulfanyl-4-propan-2-ylbenzene ($C_{10}H_{14}S$), 5-(hydroxymethyl)furan-2-carbaldehyde ($C_6H_6O_3$), methyl 3-hydroxybenzoate ($C_8H_8O_3$), ethyl icosanoate ($C_{22}H_{44}O_2$), 3,5-dihydroxy-6-methyl-2,3-dihydropyran-4-one ($C_6H_8O_4$) unlike the bio-extracts obtained from the hazelnut shell in previous studies by F. Azizov et al.,2021 (9, 19).

CONCLUSION

1. In BE-III and BE-IV extracts obtained from hazelnut green leafy covers, there are 26 mineral elements such as K, Na, Mg, Ca, Ti, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, Ga, Zr, Sn, Sr, Y, Se, Al, Si, P, S, Ba, Pb, Nb, Ge, Rb. Their total amount in BE-III is 12.80%, and in BE-IV is 21.35%. In BE-III, macroelements (K, Na, Mg, Ca, Fe, P) is 10.11%, and microelements are 2.69%; in BE-IV macroelements are 17.82%, microelements are 3.53%.

2. The content of organic compounds in BE-III is 87.5%, and in BE-IV is 78.5%. In contrast to the hazelnut hard shell extract, the green leafy covers extracts contain 5 new organic compounds: 1-methylsulfanyl-4-propan-2-ylbenzene ($C_{10}H_{14}S$), 5-(hydroxymethyl)furan-2-carbaldehyde ($C_6H_6O_3$), methyl 3-hydroxybenzoate ($C_8H_8O_3$), ethyl icosanoate ($C_{22}H_{44}O_2$), 3,5-dihydroxy-6-methyl-2,3-dihydropyran-4-one ($C_6H_8O_4$). It provides a basis for obtaining a bio-extract rich in bioactive compounds.

3. It provides a basis for obtaining a bio-extract rich in bioactive compounds with antioxidant, antibacterial, and antifungal properties, as well as vital macro and microelements for the human organism, which has the potential to be used in the treatment and prevention of many diseases.

4. Based on the results, a two-stage extraction regimen is recommended: (I) keep dried and ground hazelnut green leafy covers in 70% ethyl alcohol solution in a 1:3 ratio of solid-liquid phases at 20-22 °C for 3 hours; (II) after evaporation of ethyl alcohol the extraction should be continued with distilled water at 70-80 °C for 3 hours.

5. Bio-extracts obtained from hazelnuts with distilled water BE-IV and BE-III with 70% ethyl alcohol contain 12.797% 25 elements, except for Rb in BE-III, and 26 elements in BE-IV 21.347%. In BE-IV, macronutrients K, Na, Mg, Ca, Fe, and P are 17.82%, microelements are 3.53%, and in BE-III, macroelements are 10.11%, and microelements are 2.69%. Elements with antioxidant activity are Zn-0.01%, Se-0.01%, Mn-0.017% in Be-III, and Zn-0.009%, Se-0.001%, Mn-0.021% in BE-IV.

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