



RESEARCH ARTICLE

CHEMICAL COMPOSITION AND BIOLOGICAL ACTIVE SUBSTANCES OF
BIOEXTRACTS FROM HAZELNUT SHELL

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ABSTRACT

The article provides a comparative analysis of data on the content of macro- and micronutrients, as well as the determination and identification of biologically active substances in the bioextracts obtained with distilled water (BE-I) and 70% ethanol (BE-II) from the shell of the common hazelnut (*Corylus avellana* L.) plant widespread in the northwestern region of Azerbaijan. It was established that the bioextracts BE-I and BE-II have the same mineral composition and contain 25 mineral elements. The bioextracts obtained by extraction with distilled water and 70% ethanol contain 28.51% and 14.61% mineral elements respectively. The amount of macronutrients (K, Na, Mg, Ca, Fe, P) in BE-I is 22.97%, micronutrients (Ti, Cr, Mn, Ni, Cu, Zn, Ga, Zr, Sn, Sr, Y, Al, S, Se, Si, Ba, Pb, Rb, V) – 5.54%; in BE-II 11.60% and 3.01%, respectively. It was established that the BE-II contains 85.4% biologically active substances (BAS) and 28 major therapeutic substances, while the BE-I contains 71.5% BAS and 14 major therapeutic substances. Phenolic compounds with high antioxidant, anticancer and antibacterial properties were found among the BAS, of which the following components dominate: 2-methoxy phenol (C₇H₈O₂), 2,3-dihydrobenzofuran (C₈H₈O), 2-methoxy-4-vinylphenol (C₉H₁₀O₂), 4-Hydroxy-3-methoxybenzaldehyde (C₈H₈O₃), 2-methoxy-4-propyl-phenol (C₁₀H₁₄O₂), 4-((1E)-3-hydroxy-1-propenyl)-2-methoxyphenol (C₁₀H₁₂O₃), dibutyl phthalate (C₁₆H₂₂O₄), 1-naphtalenamin (C₁₀H₉N), 5-cholestene-ol, 24-methyl- (C₂₈H₄₈O), γ-sitosterol və β-sitosterol (C₂₉H₅₀O), stigmast-4-en-3-one (C₂₉H₄₈O), 4H-pyran-4-one-, 2,3-dihydro-3,5-dihydroxy-6-methyl- (C₆H₈O₄), trans-4-fluoro-4'-(methyltio) chalcone (C₁₆H₁₃FOS). The bioextracts obtained by the proposed methods contain vital macro- and microelements and BAS with high therapeutic effect, which allows them to be used as a therapeutic agents in the treatment and prevention of many diseases. Based on the results of the study for obtaining bioextracts rich in mineral elements, BAS, coloring pigments and flavorings the optimal regime was determined using two-stage extraction by 70% ethanol and distilled water.

Keywords: Hazelnut, Bioextract, Macro- and micronutrients, Biologically active substances (BAS), Antioxidant

1. INTRODUCTION

Common hazelnut (*Corylus avellana* L.) is one of the wildgrowing shelly plants found in different areas of Azerbaijan in the natural conditions, as well as cultivated by the population on the farm. As a result of our research in previous years, information has been obtained about the ancient growth of various species of this plant as an endemic plant in the north-western region and its rich biodiversity [1].

Hazelnut plant has a special role and importance in the economy of Azerbaijan and is an export-oriented product. Azerbaijan ranks fourth in the world for hazelnut production. President Ilham Aliyev's decree on increasing the production of this plant and the development of hazelnut growing envisages expanding its sown areas in the country and increasing crop production [2].

Hazelnut plant widely used by the population as an important food and medicinal plant since ancient times. Products made from its leaves, twigs, shoots, shells and kernels are widely used for medicinal purposes.

As a result of research it is established that different parts of hazelnut plants contain following substances: twigs: tannins - 0.85-2.54%, flavonoids, mainly quercetin, myricetin; leaves: essential oils - 0.043%, alkaloids - 0.012%, tannins - 7.7-10.6%, vitamin C, carotenes, higher fatty acids; shoots: carotenes, steroids, higher aliphatic hydrocarbons, higher fatty acids; fruits: sugars - 13.7%, mainly milibiose, raffinose, mannobiose, stachyose, vitamins: B1 0.33 mg, B2 0.12 mg, B6 0.24 mg, E 31.4 mg, PP, carotene, proteins: 10.0-19.6%, mainly globulins; fat 50.0-71.5%, unsaturated fatty acids 90.0-91.0%, saturated fatty acids 9.0-10.0%, mucus - 3.0%, minerals: Fe 5.0 mg/kg, Ca 160.0 mg/kg, Zn 2.2 mg/kg, K 665 mg/kg, etc. [3].

Aqueous and alcoholic extracts of hazelnut plants made from different vegetative organs are widely used in folk and scientific medicine as an effective remedies in the treatment and prevention of various diseases. The drug L-2 obtained by dry evaporation from its twigs, is used in scientific medicine in the treatment of many skin diseases as eczema, psoriasis, neurodermatitis, streptoderma, epidermophyte. Aqueous and alcoholic extracts of hazelnut leaves are effective drugs in many intestinal diseases, anemia, avitaminosis, rickets, pancreatic hypertrophy, as well as antibacterial agents. Aqueous and alcoholic extracts from the dried plant shells have a positive effect on intestinal diseases, colitis, chronic and acute prostatitis [4].

In recent years, various researchers have confirmed that hazelnut shells is also rich in BAS and is effective agents in the treatment and prevention of many diseases. Infusions (brewings) made from hazelnut shells and barks can be used to treat colitis [5].

Aqueous infusion made from the bark of the plant is used in folk medicine as an antipyretic, as well as in dysentery, varicose veins, periphlebitis, varicose wounds, capillary hemorrhoids, and essential oils as a vasodilator. Aqueous and alcoholic extracts from the bark of the plant are used in scientific medicine as effective means in the treatment of adenomas of the pancreas and prostate, and chronic prostatitis [6].

The therapeutic effect of the water extract obtained from the bark is associated with the presence of a tannin with a special structure and bicyclic chlorogenic acid [7,8]. In recent years large-scale researches have been conducted on the chemical and biochemical composition of hazelnut shell, the detection of its BAS.

Studies conducted by scientists from different countries in different years have shown that hazelnut shells are rich in biologically active substances with high therapeutic effect, composition and quantity of which varies depending on the type of extragents used, their ratio and concentration in water, as well as the applied extraction regime.

Italian researchers T.Esposito et al. has studied the antioxidant properties of phenolic compounds of hazelnut shell extract and their cytotoxic effects on human cancer cells. For this purpose obtained extract from hazelnut shells by extraction with methanol contain high-activity polyphenol compounds, concerning to the classes of neolignanes and diaryl heptanoils: lawsonicin, cedrusin, cyclic diaryl heptanoid, caprinontriol-B and C-verateoyl glycol, hydroxypropio vanillin, amount of which is range within 0.71-2.93%. The extract was tested in humans and its cytotoxic effect against cancer cells was established [9].

Another Italian researchers M.Contini et al. studied the phenolic content of extracts from hazelnut shells using three solvent systems - ethanol, methanol and 80% acetone solution, and found that the extract

obtained with 80% acetone had the richest phenolic content. The extract has been shown to have a high percentage of tannins and antioxidant activity [10].

Italian researchers C.Stevigny et al. studied the extraction mode of hazelnut shell using a mixture of two different solvents, methanol and ethanol in different proportions with distilled water, and using the response surface method, it was determined that the extract with the highest phenolic compounds is obtained during 108.7 minutes when 55.7% ethanol is used. The content of phenolic compounds in the extract was determined to be 6.67 GAS according to the equivalent of gallic acid [11].

Turkish researchers S.B.Oguzkhan et al. studied the effect of adsorbents on the extraction of taxols with anticancerogenic properties from hazelnut shells. The composition of stock solution extracted by dichloroethane solution and filtered using 7 different adsorbents are studied by high performance liquid chromatography and the adsorbent with the highest activity was found to be graphene oxide. According to the results of this study the extract from the shell was confirmed to be a source of taxol with anticancer effect. Hazelnut shell contains paclitaxel, which has a high antioxidant effect, plays an important role in neutralizing free radicals in the body and enhances immunity, and is effective in the treatment of cancer [12].

Another Turkish researchers A.Demirbash and F.Akdeniz studied the extraction of a supercritical liquid extract from hazelnut shells. For this purpose extracts were obtained using a mixture of acetone and water, dichloroethane, benzoyl alcohol, diethyl ether, petrol ether, and methanol, and the extraction regime was investigated. It was established that when using mixture of acetone and water, the yield of the extract is higher (4.2%). The extraction mode was determined for acetone-water mixture with a critical temperature of 508°K and a critical pressure of 4.76 MPa [13].

USA researchers B.Yuan et al. conducted research on the extraction and quantification of antioxidant phenolic compounds from hazelnut shells and found that the highest yields of phenolic compounds could be obtained by extraction with 58% acetone at 50°C for 12 hours. 27 phenolic compounds were determined in the extract obtained by this method [14].

Chinese researchers Q.Xu et al. studied the physical-chemical properties of pigments from hazelnut shells. For this purpose, extraction of hazelnut shells performed by 60% ethanol at 80°C during 80 minutes. The results showed that the thermal stability of the pigments to water is positive, the pigments are stable in the range of pH4-pH12. In addition, it was found that the elements Na, K, Ca, Al and Mg have little effect on pigment stability, Fe, Cu and Zn have a significant effect. It has been shown that citric acid reduces color density and that the removal of brown pigments is not technically difficult [15].

Another Chinese researcher Z.Wu studied the extraction of taxols from hazelnut shells. For this purpose, hazelnut shells were first kept in an acetone solution at 45-70°C during 20 hours, after filtration the obtained solution was treated with methanol and an emulsifier, filtered after storage for 12 hours, and after washing of the precipitate and treating with methyl alcohol obtained a mixture of taxols in the form of powder with a purity of 97.7%. This method was patented [16].

Chinese researchers Z.Wang et al. studied the extraction of pigments from hazelnut shells and obtained 85-92% pigment yield by 60% ethanol using the ultrasonic testing. The purity of the obtained pigment was 50-70%. The possibility of its use as a food additive has been confirmed and the method has been patented [17].

As a result of our researches conducted and patented in previous years in the bioextract obtained by water from hazelnut shells have been identified 25 macro- and microelements such as K, Na, Ca, Mg, Ti, Cr, Fe, Mn, Ni, Cu, Zn, Ga, Zr, Sn, Sr, Y, Al, Se, P, Si, S, Ba, Pb, Rb, V and it has been found that the bioextract is rich in vital chemical elements for the human organism [18].

Hazelnut kernels are also an effective remedy for anemia, general sexual weakness, as a wound healing remedy and emollient in rheumatism, to increase the body's defenses. Obtained from kernels Oleum corylus oil has a high therapeutic effect on gastrointestinal diseases, as a cholesteric agent in gallstone disease, intestinal worms, especially against ascarids, and is also important in the treatment of tumors [19].

As can be seen from the above, the separate parts of the hazelnut plant and the remedies made from them have a very wide range of effects, and the field of application is multifaceted.

The article presents the results of determination and identification of the amount of minerals and biologically active substances in bioextracts obtained by applying various extragents from the shells of hazelnut plant grown in the north-western region of Azerbaijan, as well as the results of qualitative and quantitative changes in the amount of minerals and biologically active substances depending on the extragents used and their comparative analysis.

2. PREPARATION OF MANUSCRIPT

The object of the research was the shells of common hazelnut plant grown in the territory of Sheki region, Azerbaijan Republic. For this purpose, the shells were first washed with water, dried and then crushed, extracted by distilled water and 70% ethanol using particles of 2-3 mm size, the yield percent of extractives and the regimes of extraction were studied separately for each solution.

For the determination of mineral and biologically active substances, bioextracts obtained with distilled water and 70% ethanol, which are evaluated as optimal variants for the percentage of extractive substances, extraction regime and economic efficiency of the technological process, were studied in powder form.

Determination of minerals in the bioextracts was performed at the Center for Nuclear Research of the Azerbaijan Republic using an atomic absorption spectrometer USA. 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 was 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.

The analyzes were performed in temperature programming mode at a temperature of 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 velocity 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.

The results of determination of the amount of minerals in hazelnut shell extracts obtained with different methods, as well as the identification of BAS, their synonyms and therapeutic properties, were compared with available literature and Internet data, based on the results of research on hazelnut shells by researchers from different countries.

3. RESULTS AND DISCUSSION

Initially, experiments were carried out to determine the optimal extraction regimes of industrial production of bioextract from hazelnut shell patented in previous years. For this purpose, extracts from hazelnut shell were obtained using distilled water (BE-I) and 70% ethanol (BE-II), and the extraction regimes was studied for each of them separately. It was determined that the maximum yield of BE-I and BE-II is 0.40% and 0.48%, the optimal time of maximum yield of BE-I and BE-II make 6 hours and 3 hours, respectively.

According to the results of the research, it is expedient to extract the shell extract in two stages using distilled water and 70% ethanol solution as an efficient, technologically safe, and economically rentable regime for obtaining bioextracts.

To determine the optimality of the proposed method, mineral elements and biologically active substances were identified separately in the BE-I and BE-II (table 1).

Table 1. The content of mineral elements in the bioextract obtained by extracting hazelnut shell with distilled water and 70% ethanol, in %

Mineral elements	Amount, %	
	Water extract	70% ethanol extract
K	12.622	4.694
Na	5.214	3.408
Al	3.310	1.798
Mg	2.588	2.100
Ca	2.342	1.381
Si	1.442	0.698
P	0.413	0.278
Fe	0.206	0.104
S	0.114	0.050
Ti	0.055	0.040
Cu	0.041	0.035
Ba	0.039	0.025
Ni	0.026	0.019
Mn	0.021	0.018
Sr	0.015	0.008
Zn	0.013	0.012
Zr	0.010	0.009
Cr	0.010	0.008
Rb	0.006	0.003
Pb	0.003	0.003
V	0.003	0.003
Y	0.003	0.003
Ga	0.001	0.001
Sn	0.001	0
Se	0.001	0.001
Total	28.499	14.599

As can be seen from the table 1, the mineral content of the extracts obtained as with distilled water (BE-I), as well as with 70% ethanol (BE-II), is qualitatively the same and consists mainly of 25 mineral elements: K, Na, Mg, Ca, Ti, V, Cr, Mn, Fe, Ni, C, Zn, Ga, Zr, Sn, Sr, Y, Se, Al, Si, P, S, Ba, Pb, Nb, Rb. However, while the mineral elements in the bioextract BE-I were 28.51%, but in the BE-II was 14.61%.

In BE-I obtained with distilled water 22.57% of total amount are macroelements K, Na, Mg, Ca, Fe, and remaining 5.54% other microelements; analogically in BE-II obtained with 70% ethanol macroelements K, Na, Mg, Ca, Fe are 11.60% and other microelements are 3.01%. As can be seen, the total amount of mineral elements, as well as the amount of macro- and microelements in the bioextract obtained with distilled water is approximately twice as much as in the bioextract obtained from 70% ethanol. This suggests that the bioextract obtained with distilled water was richer in minerals, consists of 28.50% inorganic, 71.50% organic matter, and the extract obtained with 70% ethanol consists of 14.61% inorganic, 85.39% organic matter.

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It is known that the mineral elements take an active part in the oxidation-reduction processes in the organism and play an important role in its life and activity. It has been confirmed that the element K and Na ensure the normal functioning of the heart muscle cells; Ca, P and Mg strengthens the musculoskeletal system, increases the body's resistance to physical stress; Fe present in synthesis of hemoglobin, included in the structure of blood and enzymes such as catalase, peroxidase, cytochromoxidase; Cu regulates liver function; as an antioxidants Mn and Se enhances the body's defenses, strengthens the immune system; Zn regulates the synthesis of sex hormones in the body and the activity of the reproductive system; Co element participates in blood formation by forming a component of vitamin B12; Ni and Cr elements take an active part in the sugar metabolism, regulate insulin biosynthesis [4].

Taking into account the above mentioned facts and the given the high content of vital minerals in the hazelnut shell bio-extracts it can be said that it is promising to use them as a remedy.

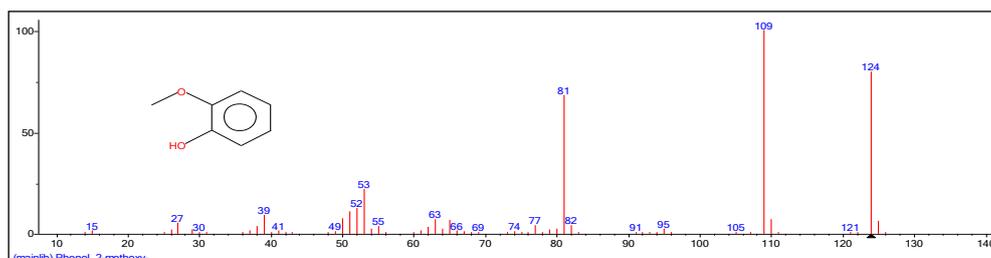
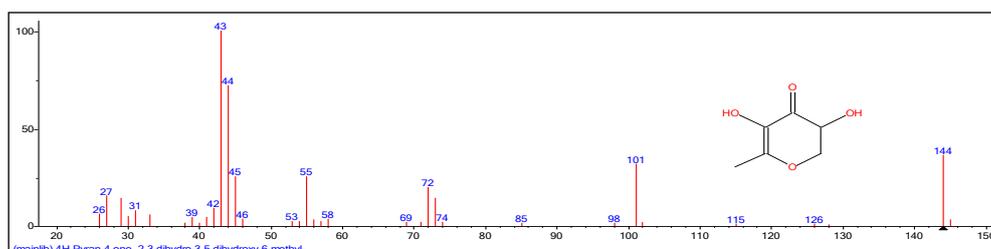
In the next experiment determination and identification of the bioactive substances extracted from hazelnut shell with distilled water and 70% ethanol were performed (Table 2).

Chromatograms obtained at the determination of main biologically active substances in bioextracts BE-I and BE-II are given below (Figures 1-10).

Table 2. Biologically active compounds identified in bioextracts obtained with distilled water and 70% ethanol.

Identified components	
Water extract (BE-I)	70% ethanol extract (BE-II)
Phenol, 2-methoxy-	Phenol, 2-methoxy-
4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl-	2,3-dihydrobenzofuran
Benzene-1,2-diol	2-Methoxy-4-vinylphenol
Benzofuran, 2,3-dihydro-	4-Hydroxy-3-methoxybenzaldehyde
2-Methoxy-4-vinylphenol	Phenol, 2-methoxy-4-propyl-
Phenol, 2,6-dimethoxy-	2,4'-Dihydroxy-3'-methoxyacetophenone
4-Hydroxy-3-methoxybenzaldehyde	(4-Hydroxy-3-methoxyphenyl)acetic acid
Phenol, 2-methoxy-4-(1-propenyl)-	4-((1E)-3-Hydroxy-1-propenyl)-2-methoxyphenol
2,4'-Dihydroxy-3'-methoxyacetophenone	Methyl tetradecanoate
Benzeneacetic acid, 4-hydroxy-3-methoxy-, methyl ester	Benzeneacetic acid, 4-hydroxy-3-methoxy-, methyl ester
4-((1E)-3-Hydroxy-1-propenyl)-2-methoxyphenol	Hexadecanoic acid, methyl ester
Hexadecanoic acid, methyl ester	Dibutyl benzene-1,2-dicarboxylate
Methyl octadecanoate	9,12-Octadecadienoic acid (Z,Z)-, methyl ester
trans-4-Fluoro-4'-(methylthio)chalcone	9-Octadecenoic acid, methyl ester, (E)-
	11-Octadecenoic acid, methyl ester, (Z)-
	Methyl octadecanoate
	9-Octadecenoic acid, (E)-
	Ethyl (Z)-octadec-9-enoate
	Naphthalen-1-amine
	5-cholestene-ol, 24-methyl-
	γ -Sitosterol
	Stigmast-4-en-3-one

As can be seen from the table 2, the extracts obtained by both methods differ in the composition of biologically active substances. Thus, while 28 main biologically active substances were found and identified in the bioextract obtained with 70% ethanol, 14 substances were identified in the bioextract obtained with distilled water. Each substance was identified and studied separately according to its synonyms, referring to the available literature information on their therapeutic properties and applications was obtained.

**Figure 1.** Phenol, 2-methoxy-dihydroxy-6-methyl-; $C_7H_8O_2$; MW=124**Figure 2.** 4H-Pyran-4-one, 2,3-dihydro-3,5-; $C_6H_8O_4$; MW=144

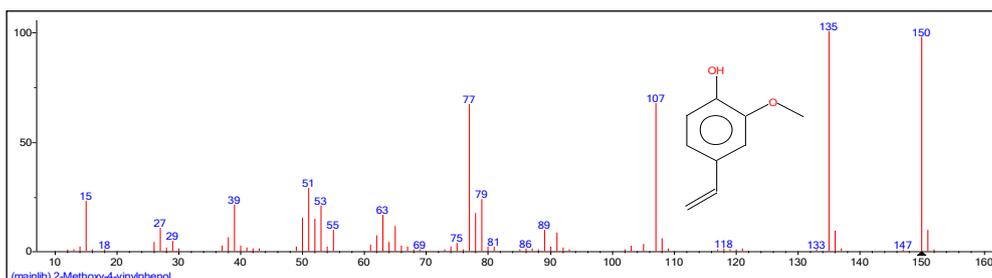


Figure 3. 2-Methoxy-4-vinylphenol; $C_9H_{10}O_2$; MW

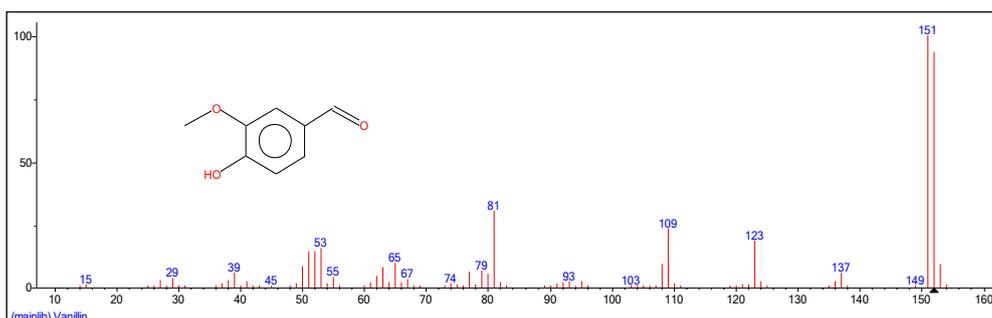


Figure 4. 4-Hydroxy-3-methoxybenzaldehyde; $C_8H_8O_3$; MW=152

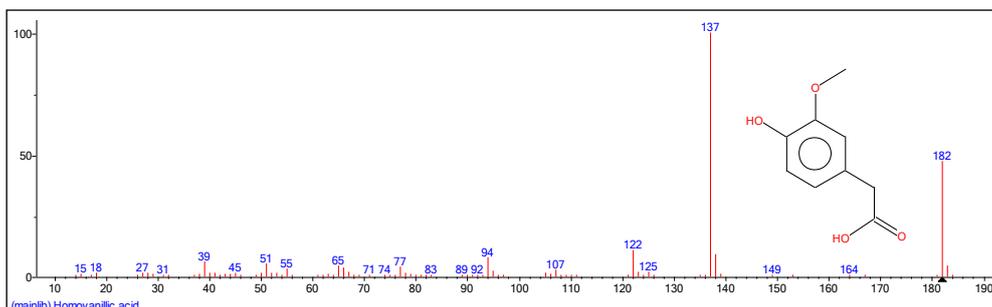


Figure 5. (4-Hydroxy-3-methoxyphenyl)acetic acid; $C_9H_{10}O_4$; MW=182

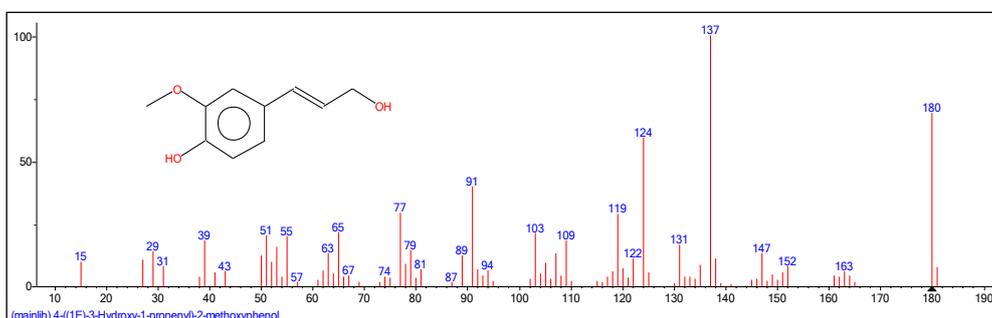


Figure 6. 4-((1E)-3-Hydroxy-1-propenyl)-2-methoxyphenol; $C_{10}H_{12}O_3$; MW=180

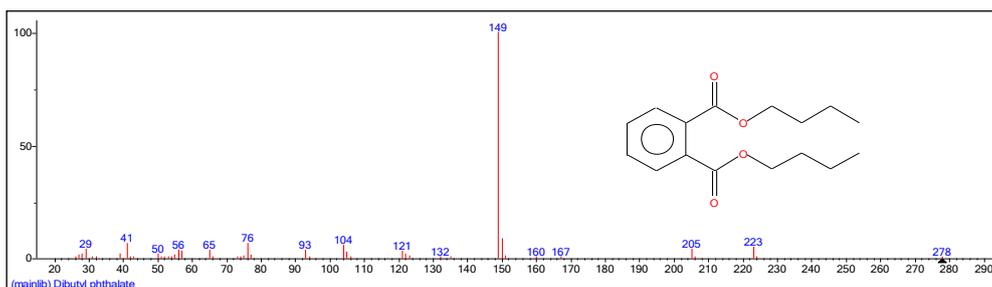


Figure 7. Dibutyl benzene-1,2-dicarboxylate; $C_{16}H_{22}O_4$; MW=278

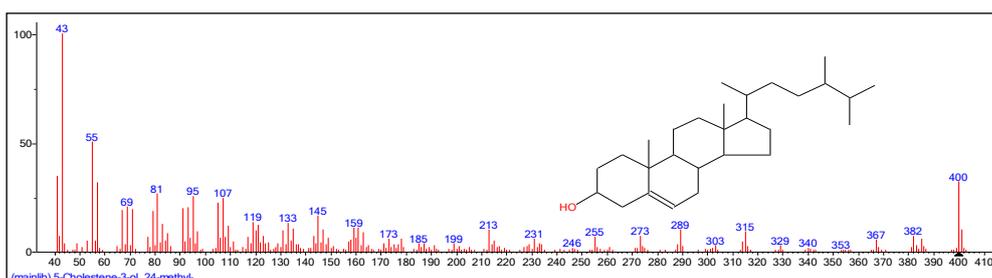


Figure 8. 5-Cholestene-3-ol, 24-methyl-; $C_{28}H_{48}O$; MW=400

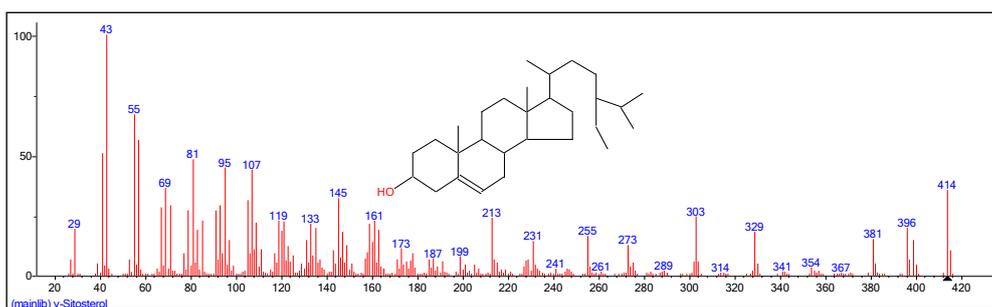


Figure 9. γ -Sitosterol; $C_{29}H_{50}O$; MW=414

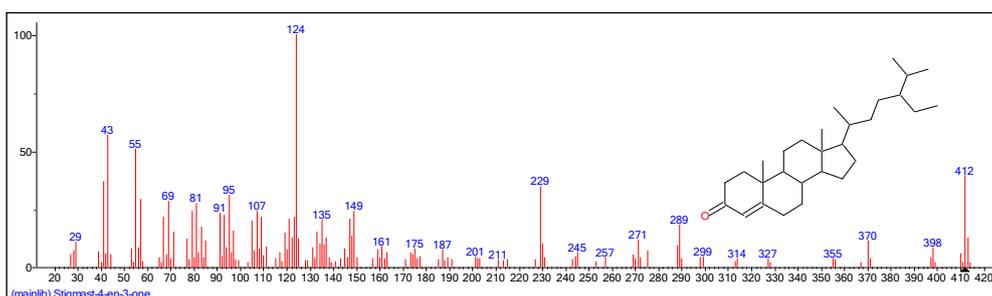


Figure 10. Stigmast-4-en-3-one; $C_{29}H_{48}O$; MW=412

The both extracts contain 2-methoxy phenol ($C_6H_4OHCH_3$) and 4-((1e)-3hydroxy-1-propenyl)-2-methoxyphenol ($C_{10}H_{12}O_3$), 2-methoxy-4-vinylphenol ($C_9H_{10}O_2$) and 4-Hydroxy-3-methoxybenzaldehyde ($C_8H_8O_3$) with high antioxidant, antibacterial and antiinflammatory activity, has expectorant effect, is used in the treatment of Parkinson's disease, as well as has antiseptic and anesthetic effects [20, 21].

Another very important biologically active substance is campesterol – 5-cholesteene-ol, 24-methyl- ($C_{28}H_{48}O$), which has an anticancer effect, prevents the growth of venous blood vessels involved in the growth and metastasis of malignant tumors, eliminates inflammation, reduces blood cholesterol level [22]. Gamma-sitosterol and betta-sitosterol ($C_{29}H_{50}O$) are antihyperglycemic agents that maintain normal blood glucose levels. Increases insulin biosynthesis, is used as an anticancer agent in lung and breast cancer [23, 24].

Stigmast-4-en-3-one ($C_{29}H_{48}O$) has an antiemetic properties, is used as agent against vomiting (regurgitating) [25].

Phenol, 2-methoxy-4-propyl- ($C_{10}H_{14}O_2$) is a taste giving, (4-Hydroxy-3-methoxyphenyl)acetic acid ($C_9H_{10}O_4$) is a source of dopamine metabolites, methyl tetradecanate ($C_{15}H_{30}O_2$) is a food additive and dyeing, as well as participate in the transport of anticancer substances, dibutylphthalate ($C_6H_4(COOC_4H_9)_2$) is an antibacterial and enhancing of metabolism substance [26,27].

Other biologically active substances identified in the extracts are also very significant and play an important role in the development of the organism, ensuring normal metabolism and boosting the immune system.

The presence of 4-Hydroxy-3-methoxybenzaldehyde ($C_8H_8O_3$) as an aromatic and taste giving, methyltetradecanate ($C_{15}H_{30}O_2$) as a food additive and dyeing compounds in the bioextracts obtained by both methods, allows to recommend their use in the food industry, as well as in the confectionery industry, also in the light industry in the dyeing of silk, wool and cotton threads in different colors.

Thus, the results of research show that depending on the type of extragent used, their concentration ratios and regimes, the content of mineral elements in the obtained bioextracts varies, and the composition of biologically active substances differs strongly both qualitatively and quantitatively.

Therefore, based on the results, the extraction of mineral elements and biologically active substances from hazelnut shells as a technologically simple and safe, cost-effective and profitable method for obtaining a bioextract rich in mineral elements and substances with antioxidant, antibacterial and anticancer properties, it is advisable to apply a two-stage extraction regimen, first keeping the shells reduced to 2-3 mm in a 70% ethanol solution at 20-22°C for 3 hours, and then after expelling the ethyl alcohol extracting it again with distilled water at 70-80°C for 3 hours.

4. CONCLUSIONS

1. Bioextract obtained from hazelnut shell with distilled water (BE-I) and 70% ethanol (BE-II) contains 25 mineral elements, their total content in the BE-I is 28.51%, in the BE-II is 14.61%. In the BE-I amount of macronutrients (K, Na, Mg, Ca, Fe) are 22.97%, microelements are 5.54%, in the BE-II macroelements are 11.60% and microelements are 3.01%.
2. The organic matter content in the BE-I is 71.50%, in the BE-II is 85.4%. In the BE-I 14 biologically active substances (BAS), in the BE-II 29 BAS were identified. The main BAS in the bio-extracts obtained by both methods are: Phenol, 2-methoxy- ($C_7H_8O_2$), 2,3-dihydrobenzofuran (C_8H_8O), 2-

methoxy-4-vinylphenol (C₉H₁₀O₂), 4-Hydroxy-3-methoxybenzaldehyde (C₈H₈O₃), Phenol, 2-methoxy-4-propyl- (C₁₀H₁₄O₂), 2-methoxyphenol, 4-((1E)-3-hydroxy-1-propenyl)- (C₁₀H₁₂O₃), dibutylphthalate (C₁₆H₂₂O₄), Naphthalen-1-amine (C₁₀H₉N), 24 methyl-5-cholesterol-ol (C₂₈H₄₈O), γ -sitosterol (C₂₉H₅₀O), stigmaster-4-en-3-one (C₂₉H₄₈O), 2,3-dihydro-3,5-dihydroxy-6-methyl-4H-pyran -4-one (C₆H₈O₄), trans-4-Fluoro-4'-(methyltio) chalcone (C₁₆H₁₃FOS).

3. Based on the results of the research the optimal regime for the maximal extraction of macro- and micronutrients, as well as active biologically active substances from hazelnut shells it is advisable to apply a two-stage extraction regimen, first keeping the shells reduced to 2-3 mm in a 70% ethanol at 20-22°C for 3 hours, and then after expelling the ethyl alcohol extracting it again with distilled water at 70-80°C for 3 hours.
4. Given the presence of biologically active substances with antioxidant, antibacterial, anticancer and other therapeutic properties, as well as vital macro-and micronutrients for the organism, the bioextract obtained by the proposed method can be used in the treatment and prevention of many diseases. The bioextract is also rich in coloring pigments, taste giving and aromatic properties substances such as phenol, 2-methoxy-4-propyl-(C₁₀H₁₄O₂), 4-Hydroxy-3-methoxybenzaldehyde (C₈H₈O₃), methyl-tetradecanate (C₁₅H₃₀O₂), methyltetradecanate (C₁₅H₃₀O₂), can be used as food dye, food additives and flavorings in food industry, and in dyeing silk, wool and cotton threads in different colors in light industry.

CONFLICT OF INTEREST

The author stated that there are no conflicts of interest regarding the publication of this article.

REFERENCES

- [1] Azizov FŞ, Halilov ZM, Memmedov CI. Azərbaycan'ın Kuzeybatı bölgəsində fındık bitkisinin bioçeşitliliği və sürdürülebilir kullanımı. İktisadi ve Sosyal Boyutlarıyla Fındık Uluslararası Sempozyumu, Türkiye: Ordu, 2018. s. 217-222.
- [2] Decree of president of the Azerbaijan Republic about to strengthen of state support for the development of Sericulture and Hazelnut growing, №1081, 02 March 2015.
- [3] Damirov I, Prilipko L, Shukurov A, Kerimov Yu. Medicinal plants of Azerbaijan. Baku: Maarif, 1982; 319 p. (in Azerbaijan).
- [4] Lovkova MYa, Rabinovich AM, Ponomareva SM, Buzuk GN, Sokolova SM. Why plants treat? Moscow: Nauka, 1990; 290 p. (in Russian).
- [5] Plant resources of the USSR. Flowering plants, their chemical composition, use. Families *Magnoliaceae* and *Limonaceae*. Leningrad: Nauka, 1985; 1: 165-169 (in Russian).
- [6] Kuvayev VB, Jukov VM, Nikolayeva AB. Plants and agents for the prevention and treatment of prostate adenoma. Plant Resources (Rastitelniye Resursy), 1988; 24(4): 615-621 (in Russian).
- [7] Wehmer S. Die Pflanzenstoffe. Jena: 1929; Bd. 1: 640 S.
- [8] Hegnauer P. Chemotaxonomie der Pflanzen. Basel, Stuttgart, 1964; Bd 8: 741 S.
- [9] Esposito T, Sansone F, Franceschelli S, DelGaudio P, Picerno P, Aquino RP, Mencherini T.

- Hazelnut (*Corylus avellana* L.) shells extract: Phenolic composition, antioxidant effect and cytotoxic activity on human cancer cell lines. *Int J Mol Sci*, 2017; 18: 392 (12 p.).
- [10] Contini M, Baccelloni S, Massantini R, Anelli G. Extraction of natural antioxidants from hazelnut (*Corylus avellana* L.) shell and skin wastes by long maceration at room temperature. *Food Chemistry*, 2008; 110(3): 659-669.
- [11] Stévigny C, Rolle L, Valentini N, Zeppa G. Optimization of extraction of phenolic content from hazelnut shell using response surface methodology. *Journal of the Science of Food and Agriculture*, 2007; 87(15): 2817-2822.
- [12] Oguzkan SB, Karadeniz Sh, Karagul B, Uzun A, Aksoy ES, Guler OO, Cakir U, Ugras HI. Effects of some adsorbents on the pre-purification of taxol (anticancer drug) from hazelnut nutshells. *International Journal of Pharmacology*, 2018; 14: 835-840.
- [13] Demirbash A, Akdeniz F. Supercritical fluid extraction of hazelnut shell. *Energy Sources*, 2001; 23(1): 55-62.
- [14] Yuan B, Lu M, Eskridge KM, Isom LD, Hanna MA. Extraction, identification, and quantification of antioxidant phenolics from hazelnut (*Corylus avellana* L.) shells. *Food Chemistry*, 2018; 244: 7-15.
- [15] Xu Q, Ming X, Li B. The extraction of brown pigment from hazelnut shells and its stability. *Journal of Shenyang Agricultural University*, 2009; 40(1): 58-61.
- [16] Wu Z. Patent. Method for extracting taxol from filbert shells. 2016.
- [17] Wang Z, Wang T, Jiao Y. Patent. Method for extracting pigment of hazelnut shell. 2009.
- [18] Azizov FSh, Shukurlu YH, Khalilov ZM. Bioextract from hazelnut shell. Patent: *Industrial Property Bulletin (Baku)*, 2019; No 6: p 5. (in Azerbaijan).
- [19] Rollov AL. *Wild plants of the Caucasus, their distribution, properties and applications*. Tiflis: 1908, 599 p. (in Russian).
- [20] Burri J, Graf M, Lambelet P, Löliger J. Vanillin: More than a flavouring agent—a potent antioxidant. *Journal of the Science of Food and Agriculture*, 1989; 48(1): 49-56.
- [21] Yang J-F, Yang C-H, Liang M-T, Gao Z-J, Wu Y-W, Chuang L-Y. Chemical Composition, Antioxidant, and Antibacterial Activity of Wood Vinegar from Litchi chinensis. *Molecules*, 2016; 21(9): 1150 (10 p.).
- [22] Choi J-M, Lee E-O, Lee H-J, Kim K-H, Ahn K-S, Shim B-S, Kim N-I, Song MC, Baek N-I, Kim S-H. Identification of campesterol from *Chrysanthemum coronarium* L. and its antiangiogenic activities. *Phytotherapy Research*, 2007; 21(10): 954-959.
- [23] Sundarraj S, Thangam R, Sreevani V, Kaveri K, Gunasekaran P, Achiraman S, Kannan S. γ -Sitosterol from *Acacia nilotica* L. induces G2/M cell cycle arrest and apoptosis through c-Myc suppression in MCF-7 and A549 cells. *Journal of Ethnopharmacology*, 2012; 141(3): 803-809.
- [24] Saeidnia S, Manayi A, Gohari AR., Abdollahi M. The story of beta-sitosterol – A review. *European Journal of Medicinal Plants*, 2014; 4(5): 590-609.

- [25] Yang Y, Kinoshita K, Koyama K, Takahashi K, Tai T, Nunoura Y, Watanabe K. Anti-emetic principles of *Pogostemon cablin* (Blanco) Benth. *Phytomedicine*, 1999; 6(2): 89-93.
- [26] Bliss EL, Ailion J. Relationship of stress and activity to brain dopamine and homovanillic acid. *Life Sciences*, 1971; 10(20): 1161-1169.
- [27] Khatiwora E, Vaishali BA, Kulkarni M, Deshpande NR, Kashalkar RV. Antibacterial activity of Dibutyl Phthalate: A secondary metabolite isolated from *Ipomoea carnea* stem. *Journal of Pharmacy Research (India)*, 2012; 5(1): 150-152.