Biol. Stud. 2023; 17(1): 3–18 • DOI: https://doi.org/10.30970/sbi.1701.699
www.http://publications.lnu.edu.ua/journals/index.php/biology

UDC: 604.4:615.371:582.929.4:678.746.4:616.934

SCREENING OF ANTICANDIDAL ACTIVITY OF *VACCINIUM CORYMBOSUM* SHOOTS' EXTRACTS AND CONTENT OF POLYPHENOLIC COMPOUNDS DURING SEASONAL VARIATION

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Yavorska, H. V., Vorobets, N. M., Yavorska, N. Y., & Fafula, R. V. (2023). Screening of anticandidal activity of *Vaccinium corymbosum* shoots' extracts and content of polyphenolic compounds during seasonal variation. *Studia Biologica*, 17(1): 3–18. doi:10.30970/sbi.1701.699

Background. A comprehensive analysis of polyphenols (flavonoids and proanthocyanidins) content of aqueous and hydroethanolic shoots' extracts of *Vaccinium corymbosum* L. (highbush blueberry) (HB) cv. Elliott was performed.

Materials and Methods. In this study, water and various concentrations of aqueous-ethanol (AE) were used as extragents, and plant material – the shoots of *V. corymbosum* harvested at stages of flowering (I), fruiting (II), after fruiting (III), and at the beginning of winter dormancy (IV). The anticandidal activity of aqueous (A) and AE extracts was studied with five strains of fungi: *Candida pseudotropicalis* (*Kluyveromyces marxianus* ATCC 4922=VKM Y-922), *C. curvata* (*Cutaneotrichosporon curvatus* ATCC 10567=VKM Y-2230), *C. kefyr* (*Kluyveromyces marxianus* VKM Y-459), *C. parapsilosis* ATCC 22019=UKM Y-73т=VKM Y-58 and *C. tenuis* ATCC 10573=UKM Y-1525т (*Yamadazyma tenuis* ATCC 10573=VKM Y-70). These strains were treated with extracts to investigate their effect on the growth of these microorganisms *in vitro* and compare with commercially available herbal medicinal extracts and antiseptic drugs. Anticandidal activity has been compared with the content of total phenolic compounds (flavonoids and proanthocyanidins).

Results. Our results reveal that phenolic compounds concentration of *V. corymbosum* shoots' extracts were significantly dependent on extragents and the stage of growth. The total content of phenolic compounds in aqueous-ethanol extracts was generally higher than aqueous and depended on the concentration of aqueous-ethanol. The highest

extraction yield of total phenolic compounds was obtained using 40–80%-AE at all investigated stages. The highest content of flavonoids (105–123 mg·g^{-1} DW in quercetin equivalent) was observed at the stage of winter dormancy (IV). The content of proanthocyanidins was the highest at stages II and IV, and with 40–96% AEs as solvents; their contents varied within 178–239 mg·g^{-1} DW in catechin equivalent. Extracts prepared with 40–80% AE have pronounced inhibitory activities against all investigated *Candida* spp., but the maximum inhibition zone of a single strain may vary. High correlations indicate the determining effect of proanthocyanidins on the anticandidal activity of the extract.

Conclusions. The study results indicate that *V. corymbosum* shoots may have promising properties in supporting therapy as anticandidal drugs.

Keywords: *Vaccinium corymbosum* cv. Elliott shoot, phenolics, flavonoids, proanthocyanidins, anticandidal activity

INTRODUCTION

The 20th century breakthrough in the treatment of infectious diseases was largely due to the discovery and widespread use of antibiotics. However, their use did not in all cases cure the disease, which was often accompanied by allergic reactions. At the same time, the number of microorganisms resistant to antimicrobial drugs has increased (Service 1995; WHO 2020), including in Ukraine (Sklyar *et al.*, 2021). Since secondary plant metabolites are known to provide many benefits to the human body, numerous studies have been devoted to studying the chemistry of herbal antimicrobials and the mechanisms involved in suppressing microbial growth, due to their lower toxicity compared to synthesized ones. Our attention was attracted by the North American species of *Vaccinium corymbosum* L., varieties of which are widespread in European countries and known for the high nutritional value of fruits with a large number of secondary metabolites, mainly phenolic (Siddiq & Dolan, 2017; Wang *et al.*, 2017; Sun *et al*., 2018) with antimicrobial and other activities (Johnson *et al.*, 2013; Joshi *et al.*, 2016; Kelly *et al.*, 2017). Biologically active substances (BAS) of HB's aboveground organs is much less studied. Cultivated HB plants require pruning of shoots that contain various BAS, but in most cases, they are underutilized and/or treated as waste or byproducts and discarded (Piljac-Zegarac *et al.*, 2009; Cezarotto *et al.*, 2017). At the same time, well-grown shrubs with multiple shoots could produce more plant material and higher fruit yields were described in several species (Siefker & Hancock, 1986). Meanwhile, several species and cultivars of *Vaccinium* have been recognized as some of the best sources of phenolic compounds not only in fruits but in vegetative organs (Riihinen *et al.*, 2008; Kelly *et al.*, 2017). The above suggests the ability of HB' shoots to accumulate phenolic compounds. In recent decades, cultivation of highbush blueberry has significantly increased in the world and in Ukraine.

The content of biologically active substances in plants depends on the genotype and environmental conditions; therefore, it is important to assess the optimal time for their maximum accumulation. *V. corymbosum* cv. Elliott was bred in the US in 1948 and in 1973 recognized as industrial to produce fruit in Zone: 5 to 8 [Missouri Botanical Garden, missouribotanicalgarden.org, 2022]. The height of the highbush blueberry bush is 1.5–2.1 m; bloom time: May; fruit ripening time is very late season – from August; ovate, medium green leaves and stems turn yellow-orange to reddish and purple in fall. In Ukraine, cv. Elliott has been adapted and widely used in field crops to harvest berries.

Biochemical analysis of active BAS in raw materials and phytopreparations is considered an important step in studying their efficacy and therapeutic safety and mechanisms of action of their ingredients. It has been established that berries and their phenols, which are formed and accumulated in some species of the *Vaccinium*, have the ability to eliminate reactive oxygen species, thus, providing medicinal properties (Puupponen-Pimiä *et al.*, 2005). Leaf extracts of several species of *Vaccinium* showed a higher antioxidant effect than berry extracts due to the higher content of phenolic compounds in the leaf extracts. Previous studies have shown that the crude extract of highbush blueberry shoots contains phenolic compounds and has a high antioxidant activity (Yavorska *et al.*, 2020). The content of phenolic compounds in plants depends on environmental factors, such as light, temperature, humidity, precipitation, which are variable in Eastern Europe, especially during the year (Sharma *et al.*, 2019). Additionally, their accumulation depends on the activity of metabolic processes at different stages of plant development. The natural antioxidants present in plant materials are of considerable interest because of their presumed safety and potential therapeutic value. Antioxidant compounds, especially from agricultural waste, can be a source of valuable compounds for the medical and pharmaceutical industries and at the same time contribute to a fuller use of the crop. Since different antioxidants may or may not be soluble in different solvents, and the yield of extraction depends on the polarity of the solvent, it is important to choose the appropriate solvent to obtain reliable results of the study of phenolic compounds content in raw materials.

Highbush blueberry is a perennial plant that passes several phases of growth and development each year; during these periods the plant's nutritional needs change. Thus, the aim of this study was to investigate the content of phenolics in aqueous and hydroethanolic extracts of shoots of *V. corymbosum* cultivar Elliott during four stages of development. We also decided to screen and evaluate the anticandidal activity of these extracts and compare it with the content of phenols to assess their relative antimicrobial contribution. An *in vitro* disc diffusion methodology was employed, as well as statistical for these comparisons.

MATERIALS AND METHODS

Plant materials. The field-grown, highbush blueberry *V. corymbosum* cv. Elliott was planted in the nurseries of Berry Partner LLC in Lviv region of Ukraine. Plant raw materials – shoots of *V. corymbosum* cv. Elliott (l = 30 cm), were harvested in the seasons of 2018–2020 in the stages (phenological phases) of flowering (I), fruiting (II), post fruiting (III) and at the beginning of winter dormancy (IV); (May, July, August, December respectively). Growth stages were determined according to biologists from the University of Michigan (Blueberries. Machigan State University, canr.msu.edu, 2022).

Shoot materials were collected as a composite sample from the planting site at the appropriate time of each stage of development. The plant material was air-dried in the dark at a temperature of 22–24 °C and ground to powder before use.

Preparation of the extracts. Dried shoots were homogenized and the powders obtained were collected, passed through a sieve of 2 mm mesh and used for extraction. Aqueous extract was performed by suspending 2 g of material in 20 mL of distilled water (DW) under reflux conditions in a boiling water bath for 30 minutes.

Aqueous ethanol in various concentrations (20, 30, 40, 50, 60, 70, 80, 96%) was used to prepare extracts with air-dry shoots. The extracts were prepared by maceration methods according to State Pharmacopoea of Ukraine (1:10/weight: volume/g: mL,

14 days in darkness at 25 °C). After completing the extraction process, each extract was filtered through Whatman No.1 filter paper in order to obtain a clear crude extract solution. Subsequently, this crude extract was subjected to phytochemical screening and their anticandidal activity was tested.

Chemicals and reagents. Only analytical grade chemicals were used in the studies. Methanol, ethanol, ascorbic acid, gallic acid, quercetin, aluminum chloride, sodium carbonate, phenolic reagent Folin–Ciocalteu, sulfuric acid were purchased from Sphere Seven Co. (Lviv, Ukraine).

Spectrophotometric determination of total phenolic, total flavonoid and proanthocyanidins content

Estimation of total phenolic content (TPC). The content of total phenols in *V. corymbosum* extracts was determined with Folin–Ciocalteu reagents described in K. K. Chew *et al.*, (2011) with gallic acid as a standard with slight modifications (Yavorska&Vorobets, 2020). Crude extracts were diluted 15 times with deionized water prior to analysis. 1.5 mL of diluted extract was mixed with 1.5 mL of diluted Folin–Ciocalteu reagent (10 times diluted with deionized water). After incubating the mixture at room temperature for 4 min, 1.2 mL of 7.5% (w/v) sodium carbonate anhydrous solution was added into the mixture. The mixture was then immediately vortexed for 10 s and incubated in dark environment at room temperature for 2 h. Blank was prepared by replacing 1 mL of extract with 1 mL of deionized water. The absorbance of the mixture was measured against blank at 650 nm by using UV-light spectrophotometer (Model CF-46 LOMO, Russia). The concentration of total phenolics in the test sample was determined from the calibration curve. Gallic acid was used to calibrate the standard curve and the calibration equation for gallic acid was $y = 0.0025x + 1.5755$ ($R^2 = 0.9982$). We obtained the equation for the calibration curve of gallic acid in the range of 50–450 $\mu g \cdot mL^{-1}$. Each crude extract was analyzed in triplicate and the results were expressed in milligrams of gallic acid equivalents per gram of dry weight (mg $\cdot g^{-1}$ DW in gallic acid equivalent).

Estimation of total flavonoid content (TFC). Aluminium chloride colorimetric technique was used for flavonoids estimation as described in K. K. Chew *et al.*, (2011) with slight modifications. 0.25 mL of *V. corymbosum* shoot extract was firstly mixed with 1.25 mL of deionized water, followed by addition of 75 µL of 5% (w/v) sodium nitrite solution. After 6 min, 150 µL of 10% (w/v) aluminium chloride solution was added and the mixture was allowed to stay at room temperature for 5 min. Subsequently, 0.5 mL of 1 M sodium hydroxide was added into the mixture and followed by addition of 330 µL of deionized water. The mixture was then vortexed for 10 s and kept at room temperature for 30 min. The absorbance of the resulting solution was measured at 510 nm by using spectrophotometer. Blank was prepared by replacing 0.30 mL of *V. corymbosum* extract with 0.30 mL of deionized water. Quercetin was used to calibrate the standard curve and the calibration equation for quercetin was $y = 0.0004x–0.0243$ ($R^2 = 0.9871$). The quercetin standard solution was 50 to 600 $\mu g \cdot mL^{-1}$. The total flavonoids content was expressed as milligrams of quercetin equivalent per g dried weight (mg$\cdot g^{-1}$ DW in quercetin equivalent).

Determination of proanthocyanidins

Proanthocyanidins content was determined by vanillin-H_2SO_4 assay as described by H. Noorul *et al.*, 2017. Volumes of 1.0 mL aliquots of each extract were mixed with 2.5 mL of 1.0% vanillin in absolute methanol and then with 2.5 mL of 25% (v/v) sulfu-

ric acid in absolute methanol to undergo vanillin reaction with polyphenols in extract. The blank solution was prepared in the same procedure without vanillin. The vanillin reaction was carried out in 26 °C water bath for 15 minutes. The absorbance at 510 nm was read and the results were expressed as (+)- catechin equivalent by a calibration method, and the results were expressed in milligrams of catechin equivalent per g dry weight ($mg \cdot g^{-1}$ DW in catechin equivalent). The equation obtained for the catechin calibration curve: $y = 0.1141x - 0.0118$ ($R^2 = 0.998$) (Noorul *et al.*, 2017).

All experiments were conducted three times, and each crude extract was analyzed in triplicate.

Estimation of antimicrobial activity. The strains of fungi were used from the Microbial Culture Collection of the Department of Microbiology of Ivan Franko National University of Lviv. *Candida pseudotropicalis* (*Kluyveromyces marxianus* ATCC 4922=VKM Y-922)*, C. curvata* (*Cutaneotrichosporon curvatus* ATCC 10567=VKM Y-2230), *C. kefyr* (*Kluyveromyces marxianus* VKM Y-459), *C. parapsilosis* ATCC 22019=UKM Y-73т=VKM Y-58 and *C. tenuis* ATCC 10573=UKM Y-1525т (*Yamadazyma tenuis* ATCC 10573=VKM Y-70) were used as tested microorganisms.

Test for antifungal activities. The agar diffusion method, as adapted earlier using in modification by the wells, (Vorobets & Yavorska, 2016) was used. From the daily culture of microorganisms, a suspension was made in distilled sterilized water, and every suspension was adjusted to equal a 0.5 McFarland standard. Each cup with Sabouraud agar was filled with 0.2 mL of the microbial suspension. After 20–30 minutes, the wells were made on the surface of the seeded medium with a 6 mm stamp (4–5 pc). After that, in the wells, the sample of 0.2 mL of the substance was applied. Anticandidal activity was judged about by the presence and size of the growth zone of the studied microorganisms around the wells with the extract (Inhibition zone diameter). Stuffed Petri dishes were incubated in a thermostat at 28±1 ºC for 24–48 hours for all tested cultures of *Candida* spp. depending on the growth in the control medium. To determine the anticandidal activity of the examined samples, the following scale was used: diameter of the growth retardation zone more than 20 mm – highly sensitive; 10–20 mm – sensitive; up to 10 mm – moderately sensitive. Values ranging from 6 to 8 mm were considered as non-active against microorganisms. When the strain showed no activity, the value was considered equal to zero.

Aqueous ethanol in concentrations of 20, 30, 40, 50, 60, 70, 80, 96% and distilled water were used as solvent controls. Commercial herbal medicinal extracts and antiseptic drugs were tested as standard positive controls: Decasan (Solution of decamethoxine dihydrochloride 0.02% by weight in water with sodium chloride, Yuria–Pharm Ltd.), Rotokan (PJSC "Lubnypharm"), Fluconazole (150 mg) (dissolved in sterile water 1 capsule in 9 mL of sterile water to obtain a homogeneous suspension), Eucalyptus tincture (Tinctura Eucalypti LLC "Ternopharm" Ternopil' city), and Chlorophyllipt (chlorophyllipt solution in ethanol 1%; LLC "Galichpharm" Lviv' city). We dripped into the wells of control solutions: 0.2 mL of aqueous ethanol of appropriate concentration (solutions were prepared using sterile distilled water); one drop of Decasan, 0.2 mL of Fluconazole, 0.2 mL of Chlorophyllipt, 0.2 mL of Eucalyptus tincture.

Statistical analysis. All experimental data reported are mean ± standard deviation (SD). Correlation analysis were carried out using ANOVA. Statistical significance ($p < 0.05$) of the results was established by comparing the studied mean values of the sample and control mean values.

RESULTS

Phenolics. The results of the study of polyphenolic profiles in the shoots of *V. corymbosum* cv. Elliott are presented in **Fig. 1.** The content of total phenolics in the shoots indicates significant differences ($p<0.05$) between the stages of development and depend on the solvent. Under the experimental conditions, the total content of phenolics in aqueous extracts in the shoots was 74.64±4.05 mg GAE g^{-1} DW in the flowering stage, reached maximum values in the post–fruiting stage (189/40±5.50 mg GAE·g^{-1} DW) and decreased by the onset of winter dormancy stage (103.32 ±1.80 mg GAE·g^{-1} DW).

Aqueous ethanol in different concentrations extracted more phenolics compared to water as extragent (**Fig. 1**). At the flowering stage, the smallest amount of phenols was extracted with 20% aqueous ethanol (AE), higher concentrations of AE extracted more phenolics, and the highest concentration of phenolics was recorded when using 80% AE (213.36±3.60 mg GAE g^{-1} DW). At the stage of fruiting, the phenolics content increased compared to the flowering stage and reached the highest values in extracts prepared with 50% AE, although the differences in their content in the extracts prepared using AE in different concentrations did not exceed 30%. At the post-fruiting stage, the content of phenolics remained high and, depending on the concentration of AE, ranged within 46%. At the stage of the beginning of winter dormancy, the content of phenolics reached 192.06±2.91 mg of GAE g^{-1} DW only in the extract prepared with 70% AE.

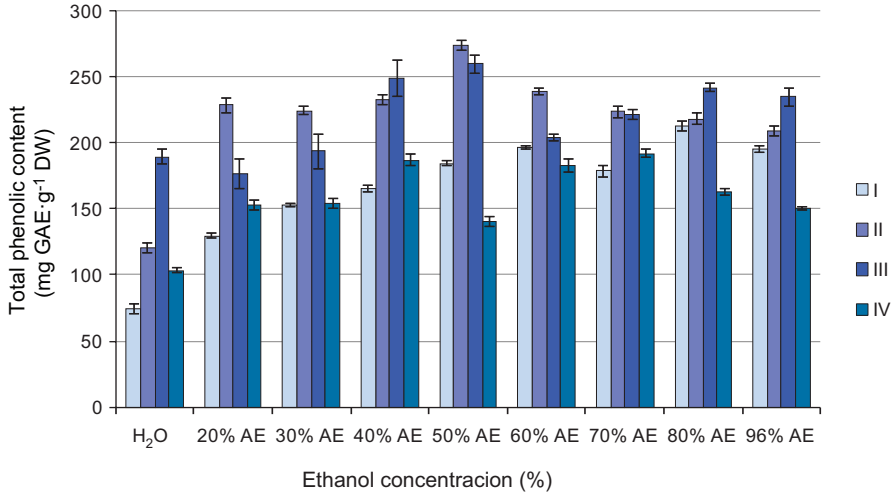

Fig. 1. Total phenolics content (mean ± SD) in the extracts of *Vaccinium corymbosum* cv.Elliott shoots at different stages of development (I–IV) prepared with H_2O and aqueous ethanol (AE) of various concentrations as a solvent. Y – Total phenolics content, mg GAE·g^{-1} DW; X – extragent

Flavonoids. The value of flavonoids in the shoots varied depending on the extragent, as well as on the stage of development (**Table 1**). The highest content of flavonoids in the shoots was found at the beginning of winter dormancy (stage IV), although at the stage of flowering and fruiting the content was high (**Table 1**). Comparing the stages, it was found that the total content of flavonoids at the stage of winter dormancy is higher compared to other stages: eg. ~1.4 times higher than at the stage of flowering and ~1.5 times higher than at the stage of fruiting in extracts with 20% AE; 1.5 times

Table 1. **The content of flavonoids and proanthocyanidins (mean ± SD) in the shoots of *Vaccinium corymbosum* cv. Elliott according to the harvest period**

Sample extragent	Flavonoid content (mgquercetin·g^{-1} DW)				Proanthocyanidins content (mgcatechin·g^{-1} DW)			
	The flowering stage	The fruiting stage	The stage after fruiting	The stage of winter dormancy	The flowering stage	The fruiting stage	The stage after fruiting	The stage of winter dormancy
H_2O	231.67±2.17	269.98±5.64**	32.12±1.62***	105.17±0.69***	40.91±2.35	74.90 ±2.20***	98.55±2.54***	172.06±1.22***
20% AE	77.33±3.60	71.89±1.79#	45.49±2.80***	107.97±1.74**	8.67±0.14	117.41±0.53***	47.46±1.83***	132.21±1.17***
30% AE	81.55±2.46	72.53±0.85*	48.93±4.55***	122.62±1.48***	20.06±0.86	161.17±1.34***	70.56±1.07***	165.51±1.36***
40% AE	86.59±1.32	67.70±7.59#	62.53±4.68**	114.55±1.20***	64.76±0.82	221.59±1.11***	120.44±1.01***	178.66±0.96***
50% AE	74.16±1.58	80.66±1.59*	60.85±5.54*	114.95±1.35***	75.74±0.96	194.02±3.17***	143.00±1.52***	194.71±2.19***
60% AE	80.66±1.84	75.41±1.10#	68.10±3.21*	112.32±1.34***	97.60±0.70	195.40±1.84***	119.14±3.10**	188.98±1.18***
70% AE	90.55±1.96	69.15±4.91*	79.01±3.53*	111.32±0.66***	58.82±1.00	227.36±2.81***	162.39±2.62***	182.03±1.21***
80% AE	76.74±1.47	70.24±3.18#	58.31±2.41**	121.75±3.87***	98.52±0.64	239.70±1.32***	147.15±6.31**	178.53±2.17***
96% AE	82.77±2.56	67.22±0.74**	52.35±2.28***	116.97±1.61***	128.03±0.91	238.12±5.82***	101.81±6.37*	166.07±1.30***

Note: # – p ≥ 0.1; * – p ≤ 0.05; ** – p <0.01; *** – p <0.001. AE – aqueous-ethanol

Table 2. **Anticandidal activity of *Vaccinium corymbosum* cv. Elliott shoots extracts**

Sample solvent		Diameter of inhibition zone, mm (mean±SD)				
		Candida pseudotropicalis	*Candida curvata*	*Candida kefyr*	*Candida parapsilosis*	*Candida tenuis*
1		2	3	4	5	6
–	H_2O	8.33±0.58^{abcd}	8.67±2.31^{a}	10.00±0.00^{cd}	12.33±2.52^{a}	9.67±0.58^{acd}
	20% AE	8.00±0.00^{abcd}	6.33±0.58^{acd}	10.33±1.53^{be}	8.00±0.00^{bcde}	8.67±0.58^{bcde}
	30% AE	6.67±0.58^{abcd}	7.33±1.15^{e}	11.67±0.58^{ace}	6.33±0.58^{abcd}	12.00±1.00^{abcde}
	40% AE	7.33±0.58^{abcd}	8.00±0.00^{b}	8.33±0.58^{acd}	7.33±0.58^{abcd}	12.67±1.15^{abcde}
	50% AE	11.67±0.57^{abcde}	10.00±0.00^{abcde}	16.33±3.79^{e}	15.67±1.15^{abcde}	18.67±1.15^{abcde}
	60% AE	14.67±2.31^{e}	20.33±0.58^{abcde}	17.33±2.08^{abcde}	17.00±1.73^{abcde}	17.00±2.65^{abcde}
	70% AE	9.67±2.52^{b}	16.33±1.15^{abcde}	11.33±2.31^{ac}	6.00±0.00^{abcd}	12.33±2.52^{abde}
	80% AE	10.33±1.54^{ce}	15.67±0.58^{abcde}	29.00±1.00^{abcde}	34.67±0.58^{abde}	24.33±2.08^{abcde}

End of Table 2

1		2	3	4	5	6
II	H_2O	7.67±1.53^{ab}	5.67± 0.58^{abd}	7.33±0.58^{abcd}	6.33±1.15^{abcd}	7.67±0.58^{acd}
	20% AE	10.33±1.53^{ae}	6.33±1.15^{a}	7.33±0.58^{abcde}	6.00±1.00^{abcde}	7.33±1.15^{e}
	30% AE	12.00±1.00^{ace}	20.00±0.00^{abcde}	13.33±1.53^{ace}	17.67±4.04^{ace}	12.00±1.73^{abcde}
	40% AE	18.33±1.54^{abcde}	14.00±1.00^{abcde}	13.33±1.53^{be}	11.33±2.89^{be}	11.33±2.31^{ae}
	50% AE	7.00±0.00^{bcd}	5.67±0.58^{ad}	6.00±0.00^{abcd}	6.00±1.00^{abcd}	7.33±0.58^{a}
	60% AE	6.67±0.59^{abcd}	20.67±0.58^{abcde}	5.67±0.58^{abcde}	10.33±0.58^{abcde}	7.00±0.00^{ae}
	70% AE	11.67±0.58^{abce}	14.33±1.15^{abcde}	19.00±1.73^{bde}	13.00±2.65^{bde}	7.67±2.08^{cd}
	80% AE	13.00±1.73^{e}	16.33±3.79^{bce}	13.67±1.15^{be}	14.67±2.31^{be}	19.00±1.73^{abcde}
III	H_2O	7.33±1.15^{abd}	14.00±3.46^{ac}	8.00±0.00^{abcd}	13.33±2.89^{acd}	10.33±0.58^{cd}
	20% AE	6.00±0.00^{abcd}	6.33±0.58^{acd}	8.67±2.31^{b}	13.33±2.89^{b}	9.33±1.15^{bcde}
	30% AE	6.00±0.00^{abcd}	7.00±1.00^{ce}	14.67±0.58^{abcde}	9.67±0.58^{abcde}	7.67±0.58^{abcde}
	40% AE	7.00±1.00^{abcde}	6.33±0.58^{abcd}	12.67±2.52^{e}	11.00±1.00^{be}	10.67±1.15^{acde}
	50% AE	6.00±0.00^{bcde}	6.33±0.58^{ad}	9.67±0.58^{bcd}	9.67±0.58^{bcd}	16.00±1.00^{abcde}
	60% AE	2.33±2.52^{abcde}	6.33±0.58^{abcd}	8.00±0.00^{bcd}	11.67±2.89^{bcd}	13.33±2.89^{bcde}
	70% AE	15.33±0.58^{abce}	6.67±1.15^{bd}	9.67±1.53^{ac}	18.67±3.21^{ac}	16.67±2.89^{abce}
	80% AE	8.67±0.57^{bce}	6.67±1.15^{cd}	18.00±2.65^{acde}	16.33±3.79^{acde}	18.67±4.04^{de}
IV	H_2O	6.67±1.15^{abcd}	8.33±0.58^{ac}	10.00±2.00^{c}	10.33±2.08^{a}	8.33±0.58^{acd}
	20% AE	7.67±1.15^{acd}	7.67±2.08^{e}	6.33±1.53^{bcd}	6.33±0.58^{abcd}	7.33±1.15^{de}
	30% AE	8.67±2.31^{e}	17.00±3.61^{abcde}	12.67±3.21^{ac}	12.33±3.21^{e}	14.33±3.79^{abe}
	40% AE	8.33±2.08^{b}	11.33±3.21^{e}	12.33± 3.05^{e}	12.00±3.61^{e}	11.67±1.53^{acde}
	50% AE	13.33±3.79^{ae}	15.00±4.36^{de}	8.33±2.08^{abc}	11.00±2.65^{a}	8.67±2.31^{a}
	60% AE	9.67±2.05^{ae}	11.67±3.51^{e}	14.00±1.73^{ae}	10.00±1.73^{e}	14.33±3.05^{bcde}
	70% AE	12.33±0.58^{abce}	13.33±2.89^{acde}	17.67±4.04^{be}	13.00±2.65^{e}	13.67±1.53^{abce}
	80% AE	11.67±0.58^{abde}	18.33±2.89^{abcde}	20.33±0.58^{acde}	15.67±0.58^{abcde}	15.00±2.65^{abe}

Note: # – p ≥0.1; *– p ≤0.05; ** – p <0.01; *** – p <0.001. AE – aqueous-ethanol; statistical significance (p <0.05) was established by comparing the studied mean values of the sample and control mean values, respectively: a – control Fluconazole, b – control Chlorophyllipt, c – control Eucalyptus tincture, d – control Decasan, e – control aqueous ethanol

and 1.69 times in extracts with 30% AE, 1.32 times and 1.69 times in 40% AE; 1.55 and 1.43 times in 50% AE; 1.39 and 1.49 times in 60% AE; 1.23 and 1.61 times in 70% AE; 1.59 and 1.73 times in 80% AE; 1.41 and 1.74 times in 95% aqueous ethanol, respectively (**Table 1**).

Proanthocyanidin. Shoots of highbush blueberry are clearly differentiated by the content of proanthocyanidins at different stages of development. Proanthocyanidin content in shoots at the stage of flowering was lower than at other ones (**Table 1**). Proanthocyanidins were better extracted using the highest concentration of AE. Our results indicate a significant content of proanthocyanidins in the shoots of Elliott at stages II, III and IV (**Table 1**).

Antimicrobial activity. The tested aqueous and aqueous ethanolic Elliott shoot extracts demonstrated various anticandidal activity. The studied aqueous and water-ethanol extracts of shoots collected at stage I with AE 20, 30, 40, 50% showed low anticandidal activity (**Table 2**). Extracts prepared with 60% AE and AE of higher concentrations using the same raw material were active in inhibiting the growth of all studied *Candida* spp. (**Table 2**). Extract prepared with 80% AE had the highest activity against *C. kefyr*, *C. tenuis* and *C. parapsilosis* (inhibition zone 29, 24 and 35 mm, respectively).

Inhibition of all strains of *Candida* spp. by *V. corymbosum* extracts dosed at 0.2 mg/mL was equal to or higher than that of Chlorophyllipt, Tinctura Eucalipti, Decasan and even Fluconazole (**Table 3**). All investigated *Candida* strains were non-sensitive to the used extragents.

Table 3. **The effect of control solutions on *Candida* spp.**

Solvent, drug	Inhibition zone diameter, (mean ± SD) mm				
	Candida pseudotropicalis	*Candida curvata*	*Candida kefyr*	*Candida parapsilosis*	*Candida tenuis*
20% AE	6.00±1.00	5.67±0.58	5.67±0.58	6.33±0.58	6.00±0.00
30% AE	6.00±0.00	6.33±0.58	6.33±0.58	5.67±0.58	6.33±0.58
40% AE	6.67±1.15	6.33±1.53	7.33±0.58	6.00±0.00	6.00±1.00
50% AE	6.33±0.58	6.67±0.58	7.67±1.15	7.67±1.15	6.67±1.15
60% AE	6.67±0.58	6.00±1.00	9.33±1.15	6.67±1.15	6.33±0.58
70% AE	6.67±1.15	6.00±0.00	8.33±0.58	6.67±0.58	6.67±1.15
80% AE	6.33±0.58	6.67±0.58	9.33±1.53	6.33±0.58	5.67±0.58
Tinctura Eucalypti	9.67±0.58	6.33±0.58	22.33±2.52	12.00±1.00	6.33±0.58
Decasan	10.33±0.58	7.67±0.58	11.67±0.58	11.33±0.58	6.33±0.58
Chlorophyllipt	14.33±0.58	9.33 ±0.58	8.67±0.58	9.33±0.58	9.00±0.00
Fluconazole	30.00±0.00	27.67±7.02	30.33±8.74	31.67±2.89	12.33±1.15

Note: AE – aqueous ethanol

Candida strains were insensitive to aqueous and 20%-aqueous-ethanol extracts prepared with raw material of shoots harvested at all investigated stages. Extracts prepared

with AE of higher concentrations showed higher anticandidal activity. *C. pseudotropicalis* strain was sensitive to the extract prepared with 40%-AE and raw material harvested at stage II. *C. curvata* strain was sensitive to the extracts prepared with 60%-AE and raw material harvested at stages I and II. *C. kefyr* strain was sensitive to the extracts prepared with 80%-AE and raw material harvested at stages I, III and IV, as well as with 70%-AE and raw material harvested at stage II. *C. parapsilosis* strain was the most sensitive to the extract prepared with 80%-AE and raw material harvested at stage I. *C. tenuis* strain was sensitive to the extract prepared with 50%- and 60%-AE and raw material harvested at stage I, 80%-AE and raw material harvested at stages II, III and IV.

Correlation analysis was used to explore the relationships between the total phenolics, flavonoids, proantocyanidins and anticandidal activity measured for all shoot extracts of raw material harvested at four phenological stages (**Table 4**).

Table 4. **Correlation coefficient (r) between the content of BAS and anticandidal activity of extracts from the shoots of *Vaccinium corymbosum* cv. Elliott**

BAS, phenological stage		*Candida pseudotropicalis*	*Candida curvata*	*Candida kefyr*	*Candida parapsilosis*	*Candida tenuis*
Total phenolic content	I	0.551	0.641	0.663	0.495	0.795
	II	0.107	0.243	0.019	0.130	0.010
	III	-0.082	-0.382	0.377	-0.034	0.654
	IV	0.359	0.243	0.506	0.264	0.619
Total flavonoids content	I	-0.039	0.283	-0.143	-0.330	-0.007
	II	-0.617	-0.096	-0.568	-0.278	-0.299
	III	0.607	-0.696	0.061	0.324	0.604
	IV	0.507	0.847	0.456	0.546	0.663
Total proanthocyanidins content	I	0.776	0.784	0.709	0.797	0.847
	II	-0.640	0.329	0.029	0.079	0.308
	III	0.330	-0.714	0.515	0.254	0.675
	IV	0.607	0.444	0.418	0.557	0.406

A high correlation coefficient (r = 0.709–0.847) was found between the total content of proanthocyanidins in extracts made using raw materials collected at the stage of flowering and anticandidal activity against all studied *Candida* species. High correlations indicate the determinig effect of proanthocyanidins on the anticandidal activity of the extract.

DISCUSSION

A number of studies have shown that the concentration of phenolic compounds in plant tissues depends on the season and can also vary at different stages of growth and development (Lynn & Chang, 1990). Changes in the place where plants grow force them to adapt. Phenolic compounds are produced by plants mainly in tissues that help

protect against various types of stress, and obviously, they are especially needed in organs that do not die in winter. We can use this property for our own purposes. The total content of phenols in many species (including the genus *Vaccinium*) is consistently higher in the leaves than in berries (Tian *et al.*, 2016). The obtained results confirm the changes in the content of phenolics at different physiological phases in the shoots of *V. corymbosum*, including at low temperatures in winter.

Activated under low temperatures (like under other stress conditions), phenylpropanoid biosynthetic pathway results in accumulation of various phenolic compounds which, among other roles, have the potential to scavenge harmful reactive oxygen species (Sharma *et al.*, 2019). Plants increase synthesis of polyphenols such as flavonoids under abiotic stress (e.g. low temperature) conditions too, which helps the plant to cope with environmental constraints (Sharma *et al.*, 2019). Flavonoids are important for plant resistance to pathogenic bacteria and fungi, partly due to their antioxidant properties (Mierziak *et al.*, 2014). Flavonoids are known to serve many functions for the plants themselves, especially during the flowering and fruiting period. That is, the plant itself needs them constantly in greater or lesser quantities. We observed a fairly high content of flavonoids in the shoots of highbush blueberry cv. Elliott at all stages of development (**Table 1**). Differences in flavonoid content at the same stage of development, which we observed, may be due to different polarity and viscosity of the extracts, as well as their interaction with different natural compounds, as has been shown with other species (Kajdžanoska *et al.*, 2011). Proanthocyanidins are also important for plants (Yu *et al.*, 2020).

Flavonoids are found in numerous plants, fruits, vegetables and are known as the most common phytochemicals which possess a range of multiple pharmacological effects. These secondary metabolites have been described as potent antioxidants, free radical scavengers, and metal chelators. The detected biological effects of proanthocyanidins were due to their ability to bind proteins, as well as antioxidant, antiradical, and antibacterial activity. Previous studies showed that leaves of several species of *Vaccinium* are obviously poorer in proanthocyanidins than fruits (Riihinen *et al*., 2008). Genetic background and environmental factors (temperature and light) are the main determinants of their content in plants grown in nature and field experimental conditions. Apparently, the mentioned factors account for the accumulation of proanthocyanidins in highbush blueberry too (as our results showed).

The content of polyphenolic compounds (flavonoids and proanthocyanidins) is associated with the value of edible and medicinal products, since they are not synthesized in the human body and at the same time fulfill vital functions in it. In human systems, habitual intake of polyphenols, as well as flavonoids and proanthocyanidins has been associated with many health benefits, especially a reduced incidence of cardiovascular diseases and with regard to chronic diseases (Fraga *et al.*, 2019; Ruskovska *et al.*, 2020). The pathogenesis of these and other diseases is closely linked to the excessive formation and action of reactive oxygen species, thus the possibility of using antioxidants in food and medicine is important.

In our opinion, the high content of polyphenols in shoots of *V. corymbosum* cultivar and the high anticandidal activity of their extracts offer the prospects of using them for human needs. In each case, a preliminary careful study of the content of different groups of polyphenols as well as pharmacological properties remains necessary.

CONCLUSION

Shoots of *V. corymbosum* of the Elliott variety contain a high content of polyphenols (flavonoids, proanthocyanidins) during the growing season. Aqueous and hydroethanolic extracts of *V. corymbosum* cv. Elliott shoot affected the growth of the different *Candida* species. The best anticandidal activity has been shown by *V. corymbosum* shoot extracts prepared with 50–80% AE as extragents. The highest content of flavonoids (105–123 mg·g^{-1} DW in quercetine quivalent) was observed for AE of winter dormancy (IV) when the highest content of proanthocyanidins (varied within 178–239 mg·g-1 DW in catechine quivalent) has been observed for 40–96% AEs at vegetation stages II and IV. High correlations indicate the determining effect of proanthocyanidins on the anticandidal activity of the extracts. Thus, the optimal phases of physiological development of *Vaccinium corymbosum* L. have been identified during which the largest amount of biologically active compounds of phenolic nature accumulates in their shoots, and the extracts obtained from them have high anti-candidal activity. Studies on the effect of these extracts on biofilm formation by various *Candida* strains in the oral cavity and vagina will apparently be promising, since the users of implants and vaginal coils change their microbial ecosystems, and proanthocyanidins reduce the risks of biofilm formation. It is obvious that such studies should be preceded by the determination of the composition of various groups of phenolics in extracts with application of high-performance liquid chromatography coupled with diode array detector and mass spectrometry as well as high-performance-thin-layer-chromatography. In a broader sense, the use of *V. corymbosum* shoots expands the raw material base for the creation of pharmaceutical preparations.

ACKNOWLEDGEMENTS AND FUNDING SOURCES

The authors received no financial support for the research, authorship, and publication of this article.

COMPLIANCE WITH ETHICAL STANDARDS

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Animal Rights: This article does not contain any studies with animal subjects performed by the any of the authors.

AUTHORS CONTRIBUTIONS

Conceptualization, [V.N.M.; Y.H.V.]; methodology, [V.N.M.; Y.H.V.]; validation, [V.N.M.; Y.H.V.]; formal analysis, [F.R.V.; Y.N.Y.]; investigation, [V.N.M.; Y.H.V.; F.R.V.; Y.N.Y.]; resources [V.N.M.; Y.H.V.; F.R.V.; Y.N.Y.]; data curation [V.N.M.; Y.H.V.; F.R.V.; Y.N.Y.]; writing original draft preparation [V.N.M.]; writing [V.N.M.]; visualization [Y.H.V.; F.R.V.; Y.N.Y.]; supervision [V.N.M.]; project administration [V.N.M.].

All authors have read and agreed to the published version of the manuscript.

REFERENCES

Cezarotto, V., Giacomelli, S., Vendruscolo, M., Vestena, A., Cezarotto, C., da Cruz, R., Maurer, L., Ferreira, L., Emanuelli, T., & Cruz, L. (2017). Influence of harvest season and cultivar on the variation of phenolic compounds composition and antioxidant properties in *Vaccinium ashei* leaves. *Molecules*, 22(10), 1603. doi:10.3390/molecules22101603
Crossref ● PubMed ● PMC ● Google Scholar

Chew, K. K., Ng, S. Y., Thoo, Y. Y., Khoo, M. Z., Wan Aida, W. M., & Ho, C. W. (2011). Effect of ethanol concentration, extraction time and extraction temperature on the recovery of phenolic compounds and antioxidant capacity of *Centella asiatica* extracts. *International Food Research Journal*, 18(2), 571–578.
Google Scholar

Fraga, C. G., Croft, K. D., Kennedy, D. O., & Tomás-Barberán, F. A. (2019). The effects of polyphenols and other bioactives on human health. *Food & Function*, 10(2), 514–528. doi:10.1039/c8fo01997e
Crossref ● PubMed ● Google Scholar

Growth Stages. Blueberries. Michigan State University. (n. d.). Available at: https://www.canr.msu.edu/blueberries/growing_blueberries/growth-stages

Johnson, S., & Arjmandi, B. (2013). Evidence for anti-cancer properties of blueberries: a mini-review. *Anti-Cancer Agents in Medicinal Chemistry*, 13(8), 1142–1148. doi:10.2174/18715206113139990137
Crossref ● PubMed ● Google Scholar

Joshi, S. S., Howell, A. B., & D'Souza, D. H. (2016). Reduction of enteric viruses by blueberry juice and blueberry proanthocyanidins. *Food and Environmental Virology*, 8(4), 235–243. doi:10.1007/s12560-016-9247-3
Crossref ● PubMed ● Google Scholar

Kajdžanoska, M., Petreska, J., & Stefova, M. (2011). Comparison of different extraction solvent mixtures for characterization of phenolic compounds in strawberries. *Journal of Agricultural and Food Chemistry*, 59(10), 5272–5278. doi:10.1021/jf2007826
Crossref ● PubMed ● Google Scholar

Kelly, E., Vyas, P., & Weber, J. (2017). Biochemical properties and neuroprotective effects of compounds in various species of berries. *Molecules*, 23(1), 26. doi:10.3390/molecules23010026
Crossref ● PubMed ● PMC ● Google Scholar

Lynn, D. G., & Chang, M. (1990). Phenolic signals in cohabitation: implications for plant development. *Annual Review of Plant Physiology and Plant Molecular Biology*, 41(1), 497–526. doi:10.1146/annurev.pp.41.060190.002433
Crossref ● Google Scholar

Mierziak, J., Kostyn, K., & Kulma, A. (2014). Flavonoids as important molecules of plant interactions with the environment. *Molecules*, 19(10), 16240–16265. doi:10.3390/molecules191016240
Crossref ● PubMed ● PMC ● Google Scholar

Missouri Botanical Garden. (2022). Available at: https://www.missouribotanicalgarden.org/PlantFinder/PlantFinderDetails.aspx?taxonid=264361&isprofile=0&

Noorul, H., Mujahid, M., Badruddeen, Khalid, M., Vartika, S., Nesar, A., Zafar, K., & Zohrameena, S. (2017). Physico-phytochemical analysis & Estimation of total phenolic, flavonoids and proanthocyanidin content of *Persea americana* (avocado) seed extracts. *World Journal of Pharmaceutical Sciences*, 5(4), 70–77.
Google Scholar

Piljac-Žegarac, J., Belščak, A., & Piljac, A. (2009). Antioxidant capacity and polyphenolic content of blueberry (*Vaccinium corymbosum* L.) leaf infusions. *Journal of Medicinal Food*, 12(3), 608–614. doi:10.1089/jmf.2008.0081
Crossref ● PubMed ● Google Scholar

Puupponen-Pimiä, R., Nohynek, L., Hartmann-Schmidlin, S., Kähkönen, M., Heinonen, M., Määttä-Riihinen, K., & Oksman-Caldentey, K.-M. (2005). Berry phenolics selectively inhibit the growth of intestinal pathogens. *Journal of Applied Microbiology*, 98(4), 991–1000. doi:10.1111/j.1365-2672.2005.02547.x
Crossref ● PubMed ● Google Scholar

Riihinen, K., Jaakola, L., Kärenlampi, S., & Hohtola, A. (2008). Organ-specific distribution of phenolic compounds in bilberry (*Vaccinium myrtillus*) and 'northblue' blueberry (*Vaccinium corymbosum* x *V. angustifolium*). *Food Chemistry*, 110(1), 156–160. doi:10.1016/j.foodchem.2008.01.057
Crossref ● PubMed ● Google Scholar

Ruskovska, T., Maksimova, V., & Milenkovic, D. (2020). Polyphenols in human nutrition: from the *in vitro* antioxidant capacity to the beneficial effects on cardiometabolic health and related inter-individual variability – an overview and perspective. *British Journal of Nutrition*, 123(3), 241–254. doi:10.1017/s0007114519002733
Crossref ● PubMed ● Google Scholar

Sharma, A., Shahzad, B., Rehman, A., Bhardwaj, R., Landi, M., & Zheng, B. (2019). Response of phenylpropanoid pathway and the role of polyphenols in plants under abiotic stress. *Molecules*, 24(13), 2452. doi:10.3390/molecules24132452
Crossref ● PubMed ● PMC ● Google Scholar

Siddiq, M., & Dolan, K. D. (2017). Characterization of polyphenol oxidase from blueberry (*Vaccinium corymbosum* L.). *Food Chemistry*, 218, 216–220. doi:10.1016/j.foodchem.2016.09.061
Crossref ● PubMed ● Google Scholar

Siefker, J. H., & Hancock, J. F. (1986). Yield component interactions in cultivars of the highbush blueberry. *Journal of the American Society for Horticultural Science*, 111(4), 606–608. doi:10.21273/jashs.111.4.606
Crossref ● Google Scholar

Sklyar, T., Gavryliuk, V., Lavrentieva, K., Kurahina, N., Lykholat, T., Zaichenko, K., Papiashvili, M., Lykholat, O., & Stepansky, D. (2021). Monitoring of distribution of antibiotic-resistant strains of microorganisms in patients with dysbiosis of the urogenital tract. *Regulatory Mechanisms in Biosystems*, 12(2), 199–205. doi:10.15421/022128
Crossref ● Google Scholar

Sun, Y., Li, M., Mitra, S., Hafiz Muhammad, R., Debnath, B., Lu, X., Jian, H., & Qiu, D. (2018). Comparative phytochemical profiles and antioxidant enzyme activity analyses of the southern highbush blueberry (*Vaccinium corymbosum*) at different developmental stages. *Molecules*, 23(9), 2209. doi:10.3390/molecules23092209
Crossref ● PubMed ● PMC ● Google Scholar

Tian, Y., Liimatainen, J., Alanne, A.-L., Lindstedt, A., Liu, P., Sinkkonen, J., Kallio, H., & Yang, B. (2017). Phenolic compounds extracted by acidic aqueous ethanol from berries and leaves of different berry plants. *Food Chemistry*, 220, 266–281. doi:10.1016/j.foodchem.2016.09.145
Crossref ● PubMed ● Google Scholar

Vorobets, N. M., & Yavorska, H. V. (2016). Modifications of agar diffusion method to determination of the antimicrobial effect of the herbal medicinal products. *Ukraïns'kij Biofarmacevtičnij Žurnal*, 2(43), 80–84. doi:10.24959/ubphj.16.30
Crossref ● Google Scholar

Wang, H., Guo, X., Hu, X., Li, T., Fu, X., & Liu, R. H. (2017). Comparison of phytochemical profiles, antioxidant and cellular antioxidant activities of different varieties of blueberry (*Vaccinium* spp.). Food Chemistry, 217, 773–781. doi:10.1016/j.foodchem.2016.09.002
Crossref ● PubMed ● Google Scholar

WHO Antibiotic resistance. (2020). Available at: https://www.who.int/news-room/fact-sheets/detail/antibiotic-resistance

Yavorska, N. Y., Vorobets, N. M., Salyha, Yu. T., & Vishchur, O. I. (2020). Preliminary comparative phytochemical screening and antioxidant activity of varieties *Vaccinium corymbosum* L. (Ericaceae) shoot' extracts. *The Animal Biology*, 22(4), 3–8. doi:10.15407/animbiol22.04.003
Crossref ● Google Scholar

Yavorska, N., & Vorobets, N. (2020). Seasonal variation in the polyphenols and flavonoids content in shoots of highbush blueberry cultivars during vegetation stages. *Bulletin of Problems in Biology and Medicine*, 3(157), 70–75. doi:10.29254/2077-4214-2020-3-157-70-75 (In Ukrainian)
Crossref ● Google Scholar

Yu, D., Huang, T., Tian, B., & Zhan, J. (2020). Advances in biosynthesis and biological functions of proanthocyanidins in horticultural plants. *Foods*, 9(12), 1774. doi:10.3390/foods9121774
Crossref ● PubMed ● PMC ● Google Scholar

СКРИНІНГ АНТИКАНДИДОЗНОЇ АКТИВНОСТІ ЕКСТРАКТІВ ПАГОНІВ *VACCINIUM CORYMBOSUM* ТА ВМІСТУ ПОЛІФЕНОЛЬНИХ СПОЛУК УПРОДОВЖ ВЕГЕТАЦІЙНОГО ПЕРІОДУ

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Обґрунтування. Комплексний аналіз вмісту поліфенолів (флавоноїдів і проантоціанідинів) було виконано у водних та водно-етанольних екстрактах пагонів *Vaccinium corymbosum* L. (лохини високорослої) сорту Елліот.

Матеріали та методи. В цьому дослідженні як екстрагенти використовували воду та водний етанол (ВЕ) різних концентрацій, а рослинну сировину – пагони лохини високорослої (*V. corymbosum*), зібрані у фазах цвітіння (I), плодоношення (II), після плодоношення (III), початку зимового спокою (IV).

Антикандидозну активність водних і ВЕ екстрактів вивчали на п'яти штамах грибів: *Candida pseudotropicalis* (*Kluyveromyces marxianus* ATCC 4922= VKMY-922), *C. curvata* (*Cutaneotrichosporon curvatus* ATCC 10567=VKMY-2230), *C. kefyr* (*Kluyveromyces marxianus* VKM Y-459), *C. parapsilosis* ATCC 22019=UKMY-73т=VKMY-58 і *C. tenuis* ATCC 10573=UKMY-1525т (*Yamadazyma tenuis* ATCC 10573=VKM Y-70*).* Обробляли екстрактами, щоб дослідити їхній вплив на ріст цих мікроорганізмів *in vitro* та порівняти з комерційно доступними рослинними лікарськими екстрактами й антисептичними препаратами. Антикандидозну активність порівнювали зі загальним вмістом фенольних сполук (флавоноїдів і проантоціанідинів).

Результати. Встановлено, що концентрація фенольних сполук в екстрактах пагонів *V. corymbosum* суттєво залежала від екстрагентів і стадії росту рослин. Сумарний вміст фенольних сполук у водно-етанольних екстрактах був загалом вищим, ніж у водних, і залежав від концентрації ВЕ. Найвищий вихід фенольних сполук отримано у разі використання 40–80%-ВЕ, причому на всіх досліджуваних

стадіях. Найбільший вміст флавоноїдів (105,2–121,8 мг·г$^{-1}$сухої маси у перерахунку на кверцетин) зафіксовано на стадії зимового спокою (IV). Вміст проантоціанідинів був найвищим на II та IV стадіях і з 40–96% ВЕ як екстрагентів, а їхній вміст коливався в межах 178–239 мг·г$^{-1}$ сухої маси в перерахунку на катехін. Екстракти, які були виготовлені з 40–80% ВЕ, мають виражену інгібіторну дію щодо всіх досліджених видів *Candida*, але максимальна зона інгібування окремого штаму може бути різною. Високі кореляції свідчать про визначальний вплив проантоціанідинів на антикандидозну активність екстракту.

Висновки. За результатами дослідження, пагони *Vaccinium corymbosum* можуть мати перспективні властивості в підтримуючій терапії як антикандидозні.

Ключові слова: пагони *Vaccinium corymbosum* сорту Елліот, фенольні речовини, флавоноїди, проантоціанідини, антикандидозна активність

Received / Одержано 15 December, 2022 | Revision / Доопрацьовано 04 January, 2023 | Accepted / Прийнято 22 March, 2023 | Published / Опубліковано 29 March, 2023