Фармакологічні дослідження біологічно активних речовин

ФАРМАЦЕВТИЧНИЙ ЧАСОПИС

http://ojs.tdmu.edu.ua/index.php/pharm-chas

DOI https://doi.org/10.11603/2312-0967.2024.2.14759
УДК 615.322:615.074:582.929.4

ASSESSMENT OF *GLECHOMA HEDERACEA* L. EXTRACTS INFLUENCE ON *ESCHERICHIA COLI, BACILLUS SUBTILIS* AND *CANDIDA PARAPSILOSIS*

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INFORMATION

Надійшла до редакції / Received: 20.03.2024
Після доопрацювання / Revised: 30.04.2024
Прийнято до друку / Accepted: 14.05.2024

Key words:
Glechoma hederacea L.*;*
total phenols content;
total hydroxycinnamic acids content;
antimicrobial activity.

ABSTRACT

The aim of the work. To investigate the interdependence of the total phenols content (TPC), the total hydroxycinnamic acids content (THC) in the extracts of *G. hederacea* grass and their antimicrobial activity.
Materials and Methods. Extraction under reflux conditions and maceration for *G. hederacea* extracts preparation; spectrophotometry for TPC and THC determination; method of diffusion in agar for antimicrobial investigation; correlational analysis, namely, Pearson's linear pairwise correlation.
Results and Discussion. The content of polyphenolic compounds in the studied aquatic ethanol (AE) extracts varied between 2.890 and 17.076 mg·g^{-1}DW in gallic acid equivalent. Extracts with AE of various concentrations exhibited a diameter of the growth zone retardation (ZR) of 8.67–15.67 mm, 8.67–15.00 mm, and 17.00–21.00 mm with *Escherichia coli*, *Bacillus subtilis* and *Candida parapsilosis*, respectively. A close relationship was established between the zones of inhibition and the biologically active substances (BAS) of the extract with 95% AE of *G. hederacea* (correlation matrix 1). A negative correlation was noted between the ZR of *C. parapsilosis* and TPC (in terms of gallic acid) with r≥-0.806 (p<0.053), THC (in terms of chlorogenic acid) r≥-0.747 (p<0.088) and a positive correlation with THC (in terms of caffeic acid) r≥+0.856 (p<0.03). Correlations between other ZR of microorganisms and the content of studied BASs were not found.
Conclusions. The phytochemical screening of hydroalcoholic extracts of *G. hederacea* showed the presence of pharmacologically active substances such as polyphenols, in particular hydroxycinnamic acids (HCA) in significant quantities. It is obvious that the species *G.hederacea* has excellent antimicrobial properties against *E. coli*, *B. subtilis* and *C. parapsilosis,* and can also be used as a potential source of compounds with antibacterial activity, even though close relationships were established with a positive correlation between the diameter of growth ZR of *C. parapsilosis* with THC (in equivalent of caffeic acid) of the extract prepared with 95 % AE only.

Funding. **The performance of the work did not have any financial support.**

Introduction. The experience of folk medicine with the use of medicinal plants is still a reliable source of the modern research using various methods, the results of which allow expanding the list of medicinal plants that can be used to create medicines. The species *G. hederacea* (Ground-ivy in Engl., "розхідник звичай-

ний" in Ukr.) is a perennial herbaceous plant of the family Lamiaceae, distributed throughout the territory of Ukraine, as well as in various regions of Eurasia. The species grows in deciduous and mixed forests, on meadows, waterlogged areas, is found in swampy, shady places, among bushes, on wet open meadows, on flooded meadows throughout Ukraine. It blooms in April-September, and commonly harvested during flowering [1, 2]. The species can be cultivated [3, 4]. It often used in folk medicine of Ukraine and other countries. *G. hederacea* is used as a source of powerful therapeutic agents with wound-healing, expectorant properties [1], for the treatment of gallstones, cholecystitis, jaundice, urinary tract stones [5], in treatments for asthma, diabetes, bronchopneumonia, colds and inflammation [1, 6, 7], diseases of the throat and thyroid gland, liver cancer, lung catarrh and bronchitis [1], in the etiology of which microorganisms are often involved. The main compounds identified in polar solvent extracts of *G. hederacea* aerial part were phenolic acids, as well as flavonoids [4]. Hot water *G. hederacea* extracts indicated that rosmarinic acid, chlorogenic acid, caffeic acid, rutin, genistin, and ferulic acid were the most abundant phytochemicals [8]. The content and activity of many BASs in the composition of *G. hederacea* changed during the season [8–11].

The antimicrobial properties of *G. hederacea* against *Staphylococcus aureus, Pseudomonas aeruginosa, Salmonella typhi, Bacterium proteus, Klebsiella pneumoniae* [12]; *Escherichia coli, Candida albicans* [13] have been revealed. The need to study the antimicrobial activity of herbal preparations is increasing, especially in view of the increase in multi-resistance of many microorganisms, the increase in cases of nosocomial infections, as well as contamination of patients with implants.

Despite the long-known healing properties of *G. hederacea*, there are no universally accepted standards for the raw material and drug quality of ground ivy in Europe [9], and the species is missing from the State Pharmacopoeia of Ukraine [14]. In order to determine the mode of antimicrobial action, the *G. hederacea* upground parts were prepared as aqueous and aqueous-ethanolic extracts and tested for their effects on several microbial strains.

This study aimed to analyze the content of polyphenols and hydroxycinnamic acids, antibacterial and anti-candidal activity of *G. hederacea* extracts and their interdependence.

Materials and Methods. The aerial parts of *G. hederacea* were collected from neighborhoods of Lviv in August-September 2023 and identified according to the their description [2]. Flowering shoots were harvested, dried to air-dry state and stored till investigation. Distilled water and 20 %, 60 % and 96 % AE were used as extractants.

Aqueous extract of air-dried herbs was prepared by suspending the plant material in distilled water (1:10/ mass:volume/g:mL) under reflux conditions in a water bath for 30 minutes. To obtain extracts with AE, the infusion method combined with maceration (extraction time 14 days, extraction temperature 20–25 °C) was used; the ratio of sample: extractant was 1:10 (mass: volume/ g: mL). The obtained extracts were filtered through Whatman No. 1 filter paper and then the extracts were kept at 4°C and used for analyses. TPC and THC was determined in the obtained extracts, as well as antibacterial and anticandidal activity.

The TPC and THC were studied by spectrophotometric method. The TPC in extracts was determined with a Folin-Ciocalteu reagents as described in [15] and with gallic acid as standard with slight modifications [16]. Crude extracts were diluted 15 times with deionized water before 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 seconds and incubated in a dark environment at room temperature for 1 h. Blank was prepared by replacing 1 mL of extract with 1 mL of deionized water. The absorbance of the mixture was measured against a blank at 650 nm by using a UV-light spectrophotometer (Model Ulab 102, 102UV). The concentration of TPC in the test sample was determined from the calibration curve. Gallic acid was used to calibrate the standard curve. Each crude extract was analysed in triplicate and the results were expressed in milligrams of gallic acid equivalents per gram of dry weight (mg g^{-1} DW in gallic acid equivalent).

Estimation of the THC was carried out as described in [17]. 1 ml of the extract was added to a 50 ml volumetric flask and brought up to the mark with 20% AE. The optical density of the obtained solution was measured at a wavelength of 325 nm, which is analytical for caffeic acid and of 327 nm for chlorogenic acid. The reference solution is 20% BE. The THC (X) in percent (%) was calculated in terms of caffeic or chlorogenic acid and absolutely dry raw materials according to the formula:

$$X = A \cdot 50 \cdot V \cdot 100 / E1\% \cdot m \cdot V \cdot (100-W),$$

where A is the optical density of the solution under study; V (mL) is the volume of the test solution; E is the specific absorption index for caffeic acid (at 325 nm = 782) or chlorogenic acid (at 327 nm = 531); m (g) is the weight of the tested raw material; Va (mL) – aliquot volume; W (%) is humidity.

Estimation of antimicrobial activity

The strains of microbes were used from the Microbial Culture Collection of the Department of Microbiology of Ivan Franko National University of Lviv. Reference strains of bacteria: *Escherichia coli* ATCC 25922, *Bacillus subtilis* VKM B-408, *C. parapsilosis* ATCC 22019=UKM Y-73t=VKM Y-58. To determine the inhibitory effect of the extracts, the generally accepted

method of diffusion in agar was used. Petri dishes were filled with up to 20 ml of sterile medium: meat-peptone agar – for bacteria and Sabouraud's medium – for *Candida*. 0.2 ml of a suspension of microorganisms was applied to the surface of a dense nutrient medium to obtain continuous growth (lawn).

Suspensions were prepared in separate test tubes in sterile distilled water from one- or two-day cultures of bacteria or fungi of the genus *Candida*. The concentration of microorganisms in the suspension was determined on a photoelectrocalorimeter at the appropriate wavelengths in a cuvette with an optical path of 3 mm. A suspension with biomass from 0.1 to 0.5 mg·mL^{-1} was used for sowing. After 20-30 minutes, holes with a diameter of 6 mm (4-5 pieces) were made on the surface of the seeded medium with a flambéed stamp, into which the test sample of the water or aqueous ethanol extract in the volume of 0.2 mL, as well as the control, was introduced. The seeded Petri dishes were incubated in a thermostat at +28±2 °C for 24 hours for bacteria and 48 hours for *Candida* fungi. The diameter of the growth ZR of the test cultures was measured in mm after one or two days, including the diameter of the hole. The following scale was used to assess the antimicrobial activity [18]: the diameter of the growth ZR over 13 mm is highly sensitive; 11–13 mm – sensitive; up to 10 mm - not sensitive. The measurements were carried out in three replications.

Statistical analysis

Parametric data are described by means (M) and standard deviation (SD). The statistical program Jamovi 2.3.21 was used to process the data. The data were checked for consistency with a normal distribution. The scales are aligned with a normal distribution. Parametric methods, namely Pearson's linear pairwise correlation, were used to test the hypothesis of a relationship between the diameter of inhibition zones and Biologically Active Substances content.

Results and Discussion. Extracts with various polarities were selected for experiments. Table 1 shows the results obtained for TPC and THC investigation.

The results obtained in this study showed a significant level of polyphenolics in the ethanolic extracts of *G. hederacea* flowering aerial parts, and the values varied according to the extractant. HCAs are the main intermediates in the biosynthetic pathways of polyphenols. They have been recognized as important antioxidants in the composition of plants and play an influential role in their therapeutic activity [19], and as cosmeceutical ingredients [20]. Often, the antimicrobial activity of plants is related to the content of hydroxycinnamic acids in them [20–24]. It is believed that the antimicrobial ability of hydroxycinnamic acids in the plants helps them to resist infectious agents [23,24]. We tested the ability of two bacterial and one *Candida* strain to resist *G. hederacea* extracts (Table 2).

Extracts with AE of various concentrations exhibited a ZR of 8.67–15.67 mm with *E. coli;* 8.67–15.00 mm with *B. subtilis; and* 17.00–21.00 mm with *C. parapsilosis*. Reference antimicrobial compounds caused a several times stronger effect on the tested microorganisms (Table 2). Therefore, *C. parapsilosis* was highly sensitive to all applied AE extracts. Aqueous extract inhibited growth of *B. subtilis* only.

According to the results of the correlation analysis between the zones of inhibition and investigated BAS of *G. hederacea* extracts, close relationships were established with a negative correlation between the diameter of growth ZR of *C. parapsilosis* and polyphenols (in terms of gallic acid) with r≥-0.806 (p<0.053), hydroxycinnamic acids (in equivalent of chlorogenic acid) r≥-0.747 (p<0.088), and positive with hydroxycinnamic acids (in equivalent of caffeic acid) r≥+0.856 (p<0.03) of the extract prepared with 95% AE (correlation matrix 1) (Table 3). No correlations were found between the other studied ZR of microorganisms and BAS content.

Conclusions. The phytochemical screening of the hydroalcoholic extract of *G. hederacea* shown the presence of pharmacologically active substances such as polyphenolics, in particular hydroxycinnamic acids in significant quantities. It is clear that the species *G.hederacea* has excellent antimicrobial properties against *E. coli*, *B. subtilis* and *C. parapsilosis*, and can also be used as a potential source of compounds with antimicrobial activity, even though correlations were

Table 1
The content of TPC and THC in extracts of *G. hederacea,* M±σ, n=6

Extract with extractant	TPC, mg·g^{-1} of DW, in terms of gallic acid	THC content, % of dry weight, in equivalent of	
		chlorogenic acid	caffeic acid
H_2O	14.32±0.81	5.482±0.226	12.795±0.023
20 % AE	2.89±0.11	2.061±0.167	5.205±0.432
60 % AE	7.84±0.20	4.328±0.014	10.810±0.065
96 % AE	17.08±0.04	5.354±0.027	12.564±0.057

Note. AE – aqueous ethanol.

Table 2
Antibacterial activity of *G. hederacea* herbal extracts, n=6

Active substance or extract	Test cultures, diameter of growth retardation zone, mm		
	E. coli	*B. subtilis*	*C. parapsilosis*
Control, ciprofloxacin, 0.3 % (0.2ml/well)	50.7±0,5	60.0±0,8	–
Control, Fluconazole (150 mg, 0,2 ml/well)	–	–	50.3±0,5
Aqueous extract	10.66±0.27	20.53±0.24	6.00±0.0
Extract with 20 % AE	8.67±0.58	8.67±0.58	17.00±0.17
Extract with 60 % AE	11.33±1.53	15.00±3.00	19.00±0.00
Extract with 96 % AE	15.67±0.58	13.33±1.53	21.00±1.00

Table 3
Correlation matrix 1. Correlation between the diameter of growth retardation zone and TPC and THC of *G. hederacea*

Correlation matrix 1					
		Candida parapsilosis (96 %)	TPC/ in Gallic acid equivalent	THC/in Chlorogenic acid equivalent	THC/in Caffeic acid equivalent
Candida parapsilosis (with 96 % AE)	r Pearson	–			
	df (degrees of freedom)	–			
	p-value	–			
TPC/in Gallic acid equivalent	r Pearson	-0.806	–		
	df (degrees of freedom)	4	–		
	p- value	0.053	–		
THC/in Chlorogenic acid equivalent	r Pearson	-0.747	0.217	–	
	df (degrees of freedom)	4	4	–	
	p- value	0.088	0.680	–	
THC/in Caffeic acid equivalent	r Pearson	0.856	-0.404	-0.930	–
	df (degrees of freedom)	4	4	4	–
	p- value	0.030	0.427	0.007	–

established only between zones of inhibition *C. parapsilosis* and TPC and THC of the extract with 95 % AE.

Conflicts of interest: authors have no conflict of interest.

Конфлікт інтересів: відсутній.

ОЦІНКА ВПЛИВУ ЕКСТРАКТІВ *GLECHOMA HEDERACEA* L. НА *ESCHERICHIA COLI*, *BACILLUS SUBTILIS* ТА *CANDIDA PARAPSILOSIS*

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Мета роботи. Дослідити взаємозалежність між загальним вмістом поліфенолів (ЗВП), загальним вмістом гідроксикоричних кислот (ЗВГ) в екстрактах трави *Glechoma hederacea* L. та їх антимікробною активністю.
Матеріали і методи. У дослідженні застосовано екстракцію зі зворотним холодильником і мацерацію для приготування екстрактів *Glechoma hederacea* L.; спектрофотометрію для визначення ЗВП та ЗВГ; метод дифузії в агар для антимікробного дослідження; кореляційний аналіз, а саме, лінійну попарну кореляцію Пірсона.
Результати й обговорення. ЗВП у досліджуваних водно-етанолових екстрактах коливався від 2,890 до 17,076 мг·г$^{-1}$ сухої маси в еквіваленті до галової кислоти. Екстракти з водним етанолом (ВЕ) різної концентрації демонстрували зону затримки росту діаметром 8,67–15,67 мм, 8,67–15,00 мм і 17,00–21,00 мм для *Escherichia coli, Bacillus subtilis* і *Candida parapsilosis* відповідно. Згідно з результатами кореляційного аналізу, між зонами інгібування і біологічно активними речовинами (БАР) екстракту з 95 % ВЕ *Glechoma hederacea* L. встановлено тісні зв'язки (кореляційна матриця 1). Відзначено негативну кореляцію між зоною інгібування (ЗІ) *Candida parapsilosis* і ЗВП (в перерахунку на галову кислоту) з r≥-0,806 (p<0,053), ЗВГ (в перерахунку на хлорогенову кислоту) r≥-0,747 (p<0,088) та позитивну кореляцію з гідроксикоричними кислотами (в перерахунку на кавову) r≥+0,856 (p<0,03). Кореляцій між іншими дослідженими ЗІ мікроорганізмів та вмістом досліджених БАР не виявлено.
Висновки. Результати фітохімічного скринінгу водно-спиртових екстрактів *Glechoma hederacea* L. показали наявність у значних кількостях таких фармакологічно активних речовин, як поліфенольні сполуки, зокрема, гідроксикоричні кислоти. Очевидно, що вид *Glechoma hederacea* L. має відмінні антимікробні властивості проти *Escherichia coli, Bacillus subtilis* і *Candida parapsilosis*, а також може бути використаний як потенційне джерело сполук з антимікробною активністю, незважаючи на те, що встановлено тісний зв'язок із позитивними кореляціями між діаметром зони затримки росту і *Candida parapsilosis* та ЗВГ (в еквіваленті до кавової кислоти) екстракту, приготовленого лише з 95 % ВЕ.

Ключові слова: *Glechoma hederacea* L.; загальний вміст поліфенолів; загальний вміст гідроксикоричних кислот; антимікробна активність.

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