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EFFECTIVENESS OF THE USE OF ESSENTIAL OILS IN THE FIGHT AGAINST ANTIBIOTIC RESISTANCE

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INTRODUCTION

The indiscriminate use of antimicrobials has led to the emergence of a number of drug-resistant bacteria, fungi, and viruses. Research results, according to the literature, indicate that in 2019, about 4.95 million deaths in our world were related to bacterial resistance to antimicrobial agents. Of these, about 1.27 million people died from an infection caused by bacterial antibiotic resistance, more deaths than malaria and HIV/AIDS combined. The scientists also identified six major pathogens, each responsible for more than 250,000 resistance-related deaths. These are *Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae, Streptococcus pneumoniae, Acinetobacter baumannii, and Pseudomonas aeruginosa.*

To reduce the growing resistance of pathogenic microbes, it is necessary to develop more effective drugs. Medicinal plants used in traditional medicine for the treatment of infectious diseases are rich in new biologically active secondary metabolites.

Scientists are constantly searching for new active compounds of rposline origin that can be used as antimicrobial drugs. Currently, about 80% of medicinal products obtained from plant raw materials are very rarely used as antimicrobial agents. At the same time, plants contain a wide range of biologically active compounds with potential antimicrobial properties. Therefore, in the last few years, a significant number of plant extracts have been studied for their antimicrobial activity.

Essential oils obtained from medicinal plants (for example, fennel (*Foeniculum vulgare*), peppermint (*Mentha piperita*), and thyme (*Thymus vulgaris*)) have been found to have antimicrobial activity against gram-positive and gram-negative bacteria, as well as against yeast, fungi, and viruses.

There is a constant search for new antimicrobial agents, in particular among medicinal plants that are known for their action in medicine, have a sufficient raw material base and minimal side effects on the body, but contain biologically active substances that have a powerful antibacterial effect.

An urgent issue is the complex use of known and unknown medicinal plants and the search among them for sources for obtaining antimicrobial drugs. In this regard, the plants of the *Ranunculus* are promising, in particular the *Ranunculus acris*, which contains valuable biologically active substances with a potential antibacterial effect. The effect of the plant as an antibiotic is used in medicine of various peoples of the world.

1. General information about essential oils and their production methods

Essential oils are a complex of substances, the composition of which mainly includes C10– and C15-terpenes and terpenoids, which are in a free state, in the form of complex esters or glycosides. In addition to terpenes, essential oils contain hydrocarbons, alcohols, simple and complex ethers, aldehydes, ketones, aliphatic and cyclic acids. The natural essential oil contains from 200 to 800 components (depending on the type of plant from which it is extracted). Essential oils, depending on the method of extraction, are divided into natural, naturalized, and synthetic. The only natural essential oil has healing properties. Synthetic essential oil is a product of a fraction of petroleum or coal tar[1].

Chemical composition of essential oils. As mentioned earlier, essential oils are a complex of substances, the composition of which mainly includes C10– and C15-terpenes

and terpenoids, which are in a free state, in the form of complex esters or glycosides. In addition, their chemical composition is represented by the following compounds:

• among saturated aliphatic aldehydes – decanal;

• from terpene compounds – citral, hydroxycitronellal;

• from aromatics – vanillin, heliotropin; from fatty and aromatic – phenylacetaldehyde, cinnamic aldehyde.

• among ketones, the most widely used are alicyclic compounds that contain a keto group in the ring (vethion, jasmone) or in the side chain.

• The class of alcohols includes the following aroma-forming substances: monoatomic terpenes (linalool) and aromatics (benzyl alcohol).

Classification of essential oils. According to the main component, essential oils are classified into three groups:

1) monoterpenes;

2) sesquiterpenes;

3) aromatic compounds.

Monoterpenes have the general molecular formula $C_{10}H_{16}$. They can be acyclic, monocyclic, and bicyclic. Sesquiterpenes consist of three isoprene units and have the general molecular formula $C_{15}H_{24}$. They can also be acyclic, monocyclic, and bicyclic, tricyclic forms are also known [2].

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[1] Войткевич С. А. Эфирные масла, ароматизаторы, консерванты. Москва, 2000. 70 с.

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Depending on the part of the plant from which the oil is obtained, the raw materials are divided into groups:

– grains (fruits and seeds) – coriander, anise;

– herbaceous part (leaves, ground part of herbaceous plants, young branches of woody plants) – mint, basil, patchouli, eucalyptus, wormwood;

– floral part (flowers, inflorescences, flower buds) – rose, clary sage, lavender, jasmine, tobacco, white lily;

– root (roots, rhizomes) – airwort, vetiver, iris.

Depending on the family, essential oils can be produced and accumulated in special secretory structures such as glands (*Lamiaceae* and *Asteraceae*), modified parenchyma cells (*Lauraceae* and *Piperaceae*), secretory ducts or tubules (*Apiaceae*), and internal receptacles (*Pinaceae* and *Rutaceae*).

The composition of essential oils depends on the type of plant, its chemotype, the ecological situation in the area of plant germination, weather conditions during harvesting, storage conditions of raw materials, the method of oil preparation, and also, in many cases, on the duration and conditions of storage[3].

The role of essential oils in the plant. It is assumed that essential oils primarily perform a protective function: they protect plants from diseases, pests, eating by animals, protect them from temperature fluctuations, regulate transpiration, and tighten wounds in the bark and wood. Essential oils help attract pollinating insects. Many components of essential oils act as allelopathic agents. It is believed that essential oils, changing the surface tension, accelerate the movement of water in the plant. In addition, they affect certain enzymatic processes.

Some essential oil plants can release a lot of volatile substances into the air. For example, *Dictamnus albus* emits so much essential oil that it can catch fire if you hold a lit match close to it, which is why it is called «unburnt».

Methods of obtaining. Common methods of obtaining essential oils include: steam distillation, pressing, maceration, and extraction with organic solvents.

Steam distillation. Essential oils are usually poorly soluble in water, so distillation of essential oil with water vapor is considered one of the cases of distillation of two mutually insoluble and chemically non-reactive liquids. In practice, essential oils are often distilled in two ways: hydrodistillation and steam distillation.

Pressing. Cold pressing. It is mainly used to obtain essential oil from the peel of fruits. This is how the essential oil of bergamot, grapefruit, orange, and lemon are obtained. The highest yield of the product is given by cold pressing. This method is used in the production of essential oils from citrus fruits.

[3] Танасиенко Ф. С. Эфирные масла. Содержание и состав в растениях. *Киев: Наукова думка.* 1985.

Pressing is carried out on hydraulic presses from the peel remaining after squeezing the juice from the fruits. The oil obtained in this case is inferior in quality to pressed essential oil. It can be used as a flavoring agent for food products and household chemicals.

Enfleurage (maceration). The oil obtained by this method is called «absolute». Absolut is usually a highly concentrated viscous liquid, but sometimes it has solid or semi-solid consistency, such as rose absolute. It hardens at room temperature, and if you hold the bottle of absolute in your hand for a while, it becomes liquid as it heats up. Absolute has a strong smell and strong therapeutic properties.

Extraction with organic solvents. Solvent extraction is used in those cases when the plant raw material yields too little oil during distillation or when distillation produces oil of unsuitable quality (high temperatures during steam distillation can distort the aroma and contribute to the formation of decomposition products).

Volatile organic solvents of a high degree of purification are used for this method: petroleum ether, hexane, pentane, and diethyl ether.

Physico-chemical properties. Although essential oils differ significantly in their chemical composition, they share a number of common physical properties. It can be said that, with rare exceptions, essential oils are colorless liquids, insoluble in water, and capable of being distilled with water vapor. They are characterized by a pleasant smell and are optically active[4].

The use of essential oils has been known to mankind for a long time. Plants that are often used for the treatment of various diseases and contain essential oils are: common thyme (*Thymus vulgaris)*, chinese cinnamon (*Cinnamomum cassia)*, peppermint, wormwood (*Artemisia absinthium)*, tea tree (*Camellia sinensis*), and others.

Thyme essential oil contains both carvacrol and thymol, which ensure its use as an antimicrobial agent against gram-negative and gram-positive bacteria, fungi, and yeast. Although carvacrol and thymol have several target sites in bacterial cells, the biosynthetic machinery of bacterial cell walls is their main target site[5]. First, carvacrol and thymol can sensitize cell walls (including membranes) and cause significant membrane damage, which leads to the breakdown of the integrity of the bacterial cytoplasmic membrane, the leakage of vital intracellular contents, and ultimately the death of bacterial cells. Leakage often occurs due to cell wall damage, cytoplasmic membrane damage, cytoplasmic coagulation, and membrane protein disruption, and a

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reduction in proton motive force. Second, due to their lipophilic structure, carvacrol and thymol can easily penetrate bacterial membranes between fatty acid chains and cause the membranes to expand and become more fluid. With these properties, carvacrol and thymol are considered promising alternatives to antibiotics[6]. Thymol and carvacrol can damage the outer membrane of *Salmonella typhimurium* and *Escherichia coli*. The essential oil is highly active against pathogenic fungi and trichocephalus[7].

Cinnamon essential oil. Cinnamon, like other plants, has a wide range of secondary metabolites that exhibit antibacterial properties. Secondary metabolites, unlike primary ones, are not essential for plant survival; instead, they are defense compounds against pathogens. These compounds include cinnamaldehyde, cinnamic acid, and a wide range of essential oils such as trans-cinnamaldehyde, cinnamic acetate, eugenol, L-borneol, camphor, caryophyllene oxide, b-caryophyllene, L-bornyl acetate, E-nerolidol, α-cubebene, α– terpineol, terpinolene, and α-thujene. The amount and presence of each in the composition vary depending on the part of the plant. Eugenol and cinnamic aldehyde have a phenolic functional group and their antimicrobial action is related to the membrane. Cinnamaldehyde and eugenol can effectively inhibit the histidine decarboxylase activity of Enterococcus aerogenes at sublethal levels. The hydroxyl group of eugenol and the carbonyl group of cinnamic aldehyde bind to proteins, inhibiting the action of amino acid decarboxylases in Enterococcus aerogenes. Cinnamon bark oil and cinnamic aldehyde could potentially be active natural compounds for the treatment of multidrug-resistant *Pseudomonas aeruginosa, Escherichia coli and Staphylococcus aureus, Acinetobacter baumannii, Acinetobacter* spp A-06 infection[8].

Peppermint leaves contain 0.5–4% essential oil, the main component of which is menthol (30–80%), menthol esters (in particular, acetate and isovalerate), menthone, menthofuran and other monoterpenes, sesquiterpenes (3,4– 4.5%), tannins, rosmarinic acid and caffeic acid derivatives, triterpenoids. The study of the effect of peppermint essential oil on standard strains of *Staphylococcus aureus, Pseudomonas aeruginosa*, and *Essherichia coli* (the causative agents of purulent-inflammatory diseases) showed high antibacterial activity. The obtained data allowed us to make an assumption that peppermint essential oil affects the bacterial cell wall. Some scientists

[6] Salgueiro LR, Pinto E, Goncalves MJ, Pina-Vaz C, Cavaleiro C, Rodrigues AG, Palmeira A, Costa-de-Oliveira S, Martinez-de-Oliveira J. Chemical composition and antifungal activity of the essential oil of Thymbra capitata. Planta Med, 2004.

[7] Omonijo, F. A., Ni, L., Gong, J., Wang, Q., Lahaye, L., & Yang, C. Essential oils as alternatives to antibiotics in swine production. Animal Nutrition, 4(2). 2018. 126–136 p.

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have found that peppermint oil and its extracts show a strong barrier against the growth of various microbes, such as *Escherichia coli, Salmonella pullorum, Comamon asterrigena, Streptococcus faecalis, Acinetobacter sp, Streptococcus thermophiles, Lactobacillus bulgaricuscurecus Stadium, Streptococcus bulgaricuscus, Streptococcus asterrigena, Streptococcus faecalis. Serratiamarcescens, Mycobacterium avium, Salmonella typhi, Salmonella paratyphi A/B, Proteus vulgaris, Enterobacteraerogenes, Yersinia enterocolitica* and *Shigella dysenteriae*[9].

Sage leaves. Its main components are essential oil (1–2.8%) and tannins. The composition of the essential oil includes α– and β-thujone, 1,8-cineole, borneol, camphor, caryophyllene, linalyl acetate, and other terpenes. Sage leaves have antibacterial activity against *Bacillus subtilis, Staphylococcus aureus, Escherichia coli,* and *Salmonella enteritidis*, as well as antifungal activity against *Aspergillus niger*. Carriers of antimicrobial activity of sage oil include α-thujone and camphor[10].

Wormwood contains essential oil, which is rich in mono– and sesquiterpenes and is a by-product with medicinal properties. The main components are camphor (up to 48%), germacrene D (up to 18.9%), artemisia ketone (up to 68%) and 1.8 cineole (up to 51.5%). Effective against gram-positive bacteria (*Enterococcus, Streptococcus, Staphylococcus, Bacillus*, and *Listeria spp*.), gram-negative bacteria (*Escherichia, Shigella, Salmonella, Haemophilus, Klebsiella*, and *Pseudomonas spp*.) and other microorganisms (*Candida, Saccharomyces*, and *Aspergillus spp*.)[11,12].

Tea tree. The main components of tea tree oil are terpinen-4-ol, γ-terpinene, α-terpinene, 1,8-cineole, α-terpineol, α-terpinolene, p-cymene, α-pinene, and limonene. The sesquiterpene fraction includes aromatendrene, viridiflorene, δ-cadinene, globulol, and viridiflorol. It exhibits a broad antimicrobial effect, the result of which is the ability to break the permeability barrier of microbial membrane structures. It acts against the gram-negative

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bacterium *Escherichia coli*, the gram-positive bacterium *Staphylococcus aureus*, and the yeast *Candida albicans*[13].

Ranunculus acris is a medicinal plant of the *Ranunculaceae* family of the *Ranunculidae* subclass. The plant has been used for a long time in folk medicine of various countries and exhibits a wide range of medicinal properties, but it is insufficiently studied from a phytochemical and pharmacological point of view.

Ranunculus acris essential oil is characterized by a high content of fatty acids, the dominant acid being octadienoic acid. A high content of phytol was also found in the essential oil of *Ranunculus acris*.

Experimental and clinical studies revealed that the plant has antibacterial, anti-inflammatory, anti-toxic, epithelizing and anti-tuberculosis properties. *Ranunculus acris* is used mainly as an external remedy for the treatment of wounds, infected dermatoses and tuberculosis of the skin. *Ranunculus acris* was used by indigenous peoples of America for oral candidiasis. In Tibetan medicine, flowers are used to raise body temperature. Also used to treat disorders caused by purulent wounds. The plant as part of phytocompositions is used as a cleaning antimicrobial mixture for disinfection[14].

It is advisable to conduct a more detailed study of both the chemical composition and pharmacological properties of *Ranunculus acris*. The study of its antibacterial properties, in particular the essential oil, which can be used as a single agent or as a component of the composition, is particularly relevant today. Combining the essential oil of *Ranunculus acris* with other essential oils or active components will enhance the action and obtain a more powerful effect.

Antibiotic resistance is considered one of the main threats today. According to research, more than 5 million people died in 2019 due to this problem. If we do not find a solution to this problem, over time these indicators will increase on a large scale[15].

The challenges associated with bacterial infection and comorbidities are related to the current shortage of effective treatments, the lack of successful preventive measures, and the lack of new antibiotics, which challenges the development of new treatment regimens and the use of alternative antimicrobial treatments or agents.

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Antibiotic resistance of microorganisms occurs as a result of cross-resistance, which increases the resistance of antibiotics with a similar mechanism of action. Another important reason is the spread of the resistance factor, the consequence of which is the acquisition of resistance simultaneously to several substances with antibacterial properties. The last but no less important factor is the human factor[16].

In connection with the urgency of the problem, scientists began to look for new antimicrobial drugs of biological origin. Bacteriophages, bacteriocins, microbial surfactants, lectins, and essential oils began to be considered as potential drugs against pathogenic microorganisms.

2. Study of the antimicrobial action of the essential oil of *Ranunculus acris*

Procurement of raw materials. *Ranunculus acris* grass was harvested during the flowering period of the plant in dry weather, morning time in 2021. It was crushed to a particle size of about 5 mm.

The extraction method was used to obtain the essential oil. To do this, we assembled the Soxhlet apparatus. Raw materials were ground in a mortar by hand. The first portion of the product was discarded, as the oil released during grinding is used for oiling the working surfaces. All subsequent portions of the crushed product were placed in a glass with a capacity of 250 ml and mixed with a spatula. Cartridges for the nozzle of the Soxhlet extractor were prepared from filter paper 110×500 mm in size, degreased with petroleum ether.

From the mixed mass of the crushed product, a weight of 5-10 g was taken into a cartridge prepared for extraction, a second piece of cotton wool was placed on top and the upper edges of the cartridges were bent inward. The cartridges were placed in the extractor with the aim. A defatted, pre-dried to constant weight at a temperature of 102-105°C and a weighed flask were attached to the extractor. The solvent was poured into the extractor so that the cartridge in it was completely covered with a layer of ether. Ether was poured into the flask to 1/3 of its volume. After connecting all parts of the apparatus, cold water was fed into the refrigerator and the flask was heated using a water bath. Ether trickled down to the cartridges. In the siphon, the ether turned into steam, which again rose into the refrigerator, condensed and flowed into the extractor.

The essential oil solution was collected in a flask. The final removal of the ether and drying of the essential oil was carried out in an electric oven at a temperature of 102-105°C to a constant weight.

The antimicrobial and antifungal effect of the obtained essential oil of *Ranunculus acris* was determined by the method of diffusion in agar by the method of serial dilutions (resazurin cleavage in broth) using 10 reference

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cultures and 4 clinical isolates of microorganisms isolated from patients with infections associated with the provision medical assistance. The following reference cultures were used*: Staphylococcus aureus* ATCC 26923 (F-49), *Staphylococcus epidermidis* 191, *Escherichia coli* ATCC 25922, *Bacillus licheniformis* VKPM-7038, *Pseudomonas aeruginosa* ATCC 27853 (F-51), *Candida albicans* ATCC 885/653, *Candida albicans* ATCC 668-853*; clinical isolates: Staphylococcus aureus* № 142, *Escherichia coli* № 5, *Proteus vulgaris* 165, *Candida albicans* № 60, *Candida membranifaciens* 117.

These clinical isolates were multiple drug resistance (MDR), in accordance with the European recommendations for the assessment of the degree of antibiotic resistance, from the museum of cultures of pathogens of infectious diseases of the Department of Microbiology of the Lviv National Medical University named after Danylo Halytskyi. 5 strains of each type of clinical strains of microorganisms were used. *Candida albicans* resistant to nystatin (nis*)* and *Candida non-albicans* resistant to azoles (ketoconazole – ket).

The agar diffusion method involved adding 50 µl of the studied essential oil (ethanol solution) into a hole with a diameter of 5.5 ± 0.5 mm, with a microorganism culture suspension (McFarland 2.0) previously applied to an agar plate (MPA, Saburo for fungi). The method of serial dilutions (Resazurin Reduction-Based Assay) involved adding 50 µl of a nutrient medium (Muller-Hinton broth, glucose MPA for fungi), 100 µl of the studied extract and 50 ml of a microorganism suspension (McFarland 2.0) to a 96-well plate, with the addition of 15 µl of 0.02% resazurin in each well. As the culture of microorganisms grew in the broth, resazurin was split and the well changed its color from blue to transparent. In the wells where the growth of microorganisms was inhibited by essential oil, the color of the indicator remained blue. From each well, after 24 hours of incubation, inoculation was carried out on a solid nutrient medium in order to approximately determine the minimum bactericidal concentration.

This experiment was carried out three times, the assessment of the antimicrobial activity of essential oils was carried out taking into account the bactericidal effect of ethyl alcohol.

Statistical processing was performed using the Microsoft Excel 2019 statistical functions package computer program. The arithmetic mean M, the error of the arithmetic mean m, the number of observations n, and Student's t-test were determined.

The essential oil showed activity against gram-positive and gram-negative microorganisms. The greatest activity against gram-positive microorganisms (*Table 1*, *Table 3*).

Table 1

Antimicrobial activity of *Ranunculus acris* essential oil (agar diffusion method), p<0,05

Diameter	**Control**		**7,0 ± 0,2**	**8,0 ± 0,3**	**9,6 ± 0,2**	**10,0 ± 0,3**	**8,0 ± 0,4**		**7,0 ± 0,3**	**8,5 ± 0,1**	**10,0 ± 0,2**
	Essential oil		**15,5 ± 0,2**	**15,0 ± 0,1**	**10,4 ± 0,2**	**12,8 ± 0,1**	**14,1 ± 0,3**		**14,5 ± 0,15**	**10,0 ± 0,4**	**11,0 ± 0,3**
Strains of microorganisms		Standard strains	*Staphylococcus aureus* ATCC 25923 (F-49)	*Staphylococcus epidermidis* 191	*Escherichia coli* ATCC 25922	*Bacillus licheniformis* ВКПМ-7038	*Pseudomonas aeruginosa* ATCC 27853 (F-51)	Clinical strains	*Staphylococcus aureus* № 142	*Escherichia coli* № 5	*Proteus vulgaris* 165

Table 2

Antifungal activity of *Ranunculus acris* essential oil (agar diffusion method), p<0,05

***Candida albicans* 60 (nis)**	***Candida membranifaciens* 117 (ket)**	**Clinical strains**	***Candida albicans* ATCC 885-653**	***Candida albicans* ATCC 668-853**	**Standard strains**	**Strains of microorganisms**	
12,0 ± 0,1	11,0 ± 0,3		13,0 ± 0,1	12,0 ± 0,1		Essential oil	The diameter of the retardation zone
11,0 ± 0,3	9,0 ± 0,7		11,0 ± 0,2	10,0 ± 0,4		Control	

Table 3

Indicators of antimicrobial and antifungal action of *Ranunculus acris* essential oil (serial dilution method), p<0.05

Standard strains microorganisms	Dilution		
	Essential oil		
	1:1	1:2	1:4
Candida albicans ATCC 668653	++	+	–
Staphylococcus aureus ATCC 25923(F-49)	+	+	–
Staphylococcus epidermidis 191	++	+	–
Escherichia coli ATCC 25922	++	+	–
Bacillus licheniformis ВКПМ-7038	++	+	–
Pseudomonas aeruginosa ATCC 27853 (F-51)	+	–	–

Note: the presence of bactericidal properties – «++», the presence of bacteriostatic properties – «+», the absence of bactericidal and bacteriostatic properties – «-».

Also, the essential oil of *Ranunculus acris* showed an antifungal effect against museum and clinical strains of *Candida* fungi (*Table 2*). When applying the method of serial dilutions, it was established that the essential oil of *Ranunculus acris* in a 1:1 dilution has a bactericidal effect (*Table 3)*[17,18,19].

Within the framework of this work, based on the obtained research results, we developed and proposed 2 compositions that have a potential antibacterial effect. In order to develop a technology for obtaining aroma compositions based on base oils, it was proposed to use the following algorithm for the preparation of an aroma agent:

1) Weigh the essential oils that are part of the composition, as well as the base oil – *Ranunculus acris*;

2) Mix these ingredients;

3) Keep the mixture for 2 weeks;

4) Filter and check the quality of the received product.

The compositions were made according to the following recipe:

Composition № 1. 75% of the total mass was taken as the basis of the essential oil of *Ranunculus acris*. *Eucalyptus* oil 7%, *Zagrava peppermint* 6%, and *Lavender* essential oil 2% were added alternately.

Composition № 2. 70% of the total weight of the essential oil of *Ranunculus acris*, 15% of a mixture of *peppermint* oils, 7% of *Lavender essential oil*, 6% of *Juniper oil*, 2% of *Lavender* oil.

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It is worth noting that the creation of antiseptic compositions based on essential oils is in the process of development and research of their pharmacological properties.

CONCLUSION

The researched essential oil of *Ranunculus acris* was obtained and investigated as an antimicrobial agent for the first time.

As a result of this study, the essential oil of *Ranunculus acris* was obtained and its antibacterial properties were determined using the method of diffusion in agar and serial dilutions against a number of standard and clinical strains of microorganisms. The greatest antibacterial effect was shown by the essential oil of calendula caustic in relation to standard strains of *Candida albicans, Staphylococcus epidermidi, Escherichia coli, Bacillus licheniformis*.

The composition of compositions based on the essential oil of *Ranunculus acris*, which can be used to overcome antibiotic resistance, has been developed.

SUMMARY

The indiscriminate use of antimicrobial agents has led to the emergence of a number of drug-resistant bacteria, fungi, and viruses. To overcome the growing resistance of pathogenic microbes, more effective drugs must be developed. Therefore, in the last few years, a large number of plant extracts have been tested for their antimicrobial activity. Essential oils obtained from medicinal plants have been found to have antimicrobial activity against gram-positive and gram-negative bacteria, as well as against yeasts, fungi and viruses.

The efect of the essential oil of the *Ranunculus acris* on microorganisms was studied and compositions based on this essential oil that could overcome antibiotic resistance were developed.

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