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HYDROGEL CARRIERS FOR CONTROLLED RELEASE OF BIOACTIVE SUBSTANCES

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Abstract. In recent years, interest in natural products in cosmetics and pharmacy has significantly increased. Consumers are preferring products based on plant materials that combine efficacy, safety and support for maintaining healthy skin. The demand for such products continues to rise, partly because establishing clear criteria for "skin quality" remains challenging and partly due to the consumers' growing interest in maintaining optimal skin condition. It is important that cosmetic and pharmaceutical products not only provide aesthetic effects but also exert a comprehensive influence on physiological skin processes by enhancing protective and regenerative properties, maintaining optimal hydration levels and reducing inflammatory responses. Therefore, the development of innovative polymeric delivery systems for naturally derived biologically active compounds is a relevant research direction. In this study, the integration of medicinal plant extracts *Calendula officinalis*, *Eucalyptus viminalis*, *Hypericum perforatum* and their blend into a hydrogel matrix based on poly(2-hydroxyethyl methacrylate) and polyvinylpyrrolidone (HEMA/PVP) was investigated to create functional systems for delivering biologically active compounds for pharmaceutical and cosmetic applications. The study included a comparative evaluation of plant extraction conditions (solvent type, concentration, and plant-to-solvent ratio), determination of flavonoid and phenolic content in each extract and their combinations, as well as assessment of antioxidant activity and their effect on oxidative stress parameters, based on the content of thiobarbituric acid reactive substances (TBARS) products and the determination of ketone groups (KG) in proteins. It was found that optimal extraction conditions ensured a higher yield of biologically active compounds, indicating the potential of the obtained plant extracts to serve as antioxidant components for further immobilization in polymeric systems. The obtained extracts were incorporated into the HEMA/PVP hydrogel matrix and their effect on the physicochemical properties of the hydrogels, including electrical conductivity, was evaluated. The resulting hydrogel complexes demonstrated pronounced antibacterial and antifungal activity against the tested strains, namely *Escherichia coli*, *Staphylococcus aureus*, *Candida tenuis* and *Aspergillus niger*. Thus, the developed complexes combine the biological activity of plant-derived components with the stability and functionality hydrogel matrix, providing opportunities for their application in modern pharmaceutical and cosmeceutical products for targeted delivery of active substances.

Keywords: hydrogel, plant extracts, polyvinylpyrrolidone (PVP), 2-hydroxyethyl methacrylate (HEMA).

Introduction. Formulation of the problem

"*The identification of beauty is intuitive, whereas its definition is subjective, variable, and difficult to formulate*," - psychologist Nancy Etcoff. Every person strives to have beautiful and healthy skin, but establishing precise criteria for its condition remains a complex task. Despite centuries of attempts to understand the "*phenomenon of beauty"*, universal standards cannot be defined, as they are depend on biological, topographical, psychological and individual factors. At the same time, flawless skin is one of the most desired attributes linked to the concept of "*skin quality"*, which is gaining increasing attention in the

fields of medicine, dermatology, pharmacy, cosmetics and cosmeceuticals worldwide.

Anti-aging procedures, cosmeceutical products and minimally invasive injection therapies are becoming increasingly popular, as they aim not only to correct age-related changes but also to improve the overall quality of the skin. Recent years have been marked by growing consumer demand for natural components in cosmetic products, which stimulates the development of innovative approaches to creating effective and safe skincare formulations. Among these, particular attention is drawn to hydrogel masks and patches, which combine high biocompatibility, moisturizing effects and the ability to deliver active substances of natural origin.

The main objective of this study is to investigate the integration of medicinal plant extracts (*Calendula officinalis*, *Eucalyptus viminalis*, *Hypericum perforatum* and their blend) into a hydrogel matrix based on poly(2-hydroxyethyl methacrylate) and polyvinylpyrrolidone (HEMA/PVP) with the aim of creating functional delivery systems of biologically active compounds for pharmaceutical and cosmetic applications. The research focuses on optimizing the extraction conditions of plant materials and determining the content of flavonoids and phenolic compounds; evaluating the antioxidant activity of the extracts and their influence on oxidative stress indicators; incorporating the extracts into the hydrogel matrix and studying its physicochemical and functional properties; as well as assessing the antimicrobial and antifungal activity of the obtained complexes.

Thus, this work aims to develop functional complexes that combine the biological activity of plant extracts with the functional properties of a polymeric matrix, making them promising for applications in pharmaceutical, dermatological and cosmeceutical products.

Analysis of recent research and publications

The skin is an essential, complex and at the same time the largest organ of the human body, performing a wide range of vital functions. It maintains the body's homeostasis, protects againts external damage, regulates body temperature, water balance and transmits sensory information. To effectively carry out its numerous and complex functions, the skin has developed a high degree of plasticity in response to environmental changes while preserving its structural integrity. The skin participates in maintaining water-salt balance (through the function of the epidermal barrier and sweet glands), regulates thermoregulation (via receptors in the dermis) and plays a crucial role in the body's immune response. At the same time, it performs an aesthetic function: the appearance, condition and health of the skin are closely associated with a person's psychoemotional well-being. Facial skin defects, such as acne, angioma, rosacea, hyperpigmentation and other dermatological disorders can cause significant psychological distress. Such disorders can significantly affect quality of life, social interactions, self-esteem and self-perception, can lead to the development of depressive and anxiety disorders [1-4].

Today, the concept of "*skin quality*" is becoming increasingly important. Despite the growing interest in this concept across fields such as evolutionary studies, psychology, aesthetic medicine and clinical research, the scientific literature still lacks a consistent definition. Terminology varies across sources and parameters are often described differently with freqesnt overlaps or contradictions. This creates challenges for the standardization of methods used to evaluate the effectiveness of cosmetic products and procedures. Existing studies focus on skin aging processes, whereas a systematic definition of skin quality remains unclear and varies among researchers and regions. Therefore, it is essential to establish scientifically based criteria and measurement methods that would enable objective assessment and support the development of effective treatment and prevention strategies. A conceptual model has been proposed that comprises three main categories of attributes that define healthy skin quality: visual, mechanical and topographical. These parameters may overlap, for instance, hydration or redness can have both visual and mechanical manifestations. Scars, however, are excluded, as they represent secondary lesions rather than intrinsic characteristics of the skin.

Visual attributes include uneven pigmentation associated with variations in melanin content, photodamage (hypo- or hyperpigmentation), redness (erythema), dullness, yellowish tone, loss of radiance (glow), oiliness and dryness. Topographical characteristics describe the surface relief of the skin, its smoothness or roughness. These parameters are key indicators of age-related or photostructural changes and include wrinkles, enlarged pores, reduced turgor and crepiness. Mechanical attributes comprise elasticity, firmness, thickness and tension. Elasticity refers to the skin's ability to recover its shape after deformation, whereas firmness reflects its flexibility. Excessive looseness or thickness may result from morphological changes in the dermis due to aging or ultraviolet exposure. These parameters are commonly used to evaluate the effectiveness of aesthetic procedures.

Modern methods for assessing skin quality ivolve a wide range of tools and technologies. Approaches to improving skin quality include both invasive and non-invasive procedures, such as chemical peels, laser treatments, microneedling, ultrasound, fillers and botulinum toxin injection, as well as the use of **cosmeceuticals** and **nutraceuticals** [5,6].

In contemporary society, cosmetic products have become an integral part of daily facial skincare routines. Cosmetic formulations feature diverse compositions and functionalities, enabling them to effectively address various skin concerns [7]. International studies of

skincare products primaly focus on consumer purchasing behavior and the factors influencing the choice of cosmetic items. Today, the global cosmetic industry is characterized by steady growth and high competitiveness, motivating manufacturers to pursue continuous innovation. Consumers' primary expectations include product safety, quality, efficacy and accessibility [8].

Among the wide range of cosmetic products, cosmetic masks, particularly hydrogel masks, occupy a special place. These products adhere closely to the skin, become saturated with active ingredients and ensure deep penetration [9]. Hydrogel masks are used for moisturizing, soothing and anti-inflammatory care, as well as in dermatological and cosmetic treatments, for example, after sunburns, phototherapy or dermatitis. Hydrogel patches represent an innovative form of targeted cosmetic care. Owing to their unique structure, they effectively reduce puffiness and dark circles under the eyes, diminish inflammation, accelerate wound healing, support the skin's barrier function and help to prevent premature aging [10,11].

Hydrogels are three-dimensional polymer networks capable of absorbing water in their dry state and swelling without dissolving or undergoing changes in their chemical structure. The presence of crosslinking points (junction nodes) enable hydrogels to retain their three-dimensional form during swelling. Upon contact with water, hydrogels become soft and highly flexible. These points represent physical or chemical crosslinks that create a network structure and prevent the complete dissolution of the polymer matrix [12].

Hydrogels are synthesized by chemical or physical methods using hydrophilic monomers, with the optional incorporation of hydrophobic monomers to adjust their properties. The methods of hydrogel preparation include crosslinking polymerization, radiation crosslinking and polymerization in bulk, solution or suspension. The essential components of hydrogel synthesis are the monomer, initiator and crosslinking agent, while diluents, such as water or aqueous solution are used to control the final characteristics of the material. Advances in modern technology have enabled the creation of hydrogels with specific, customizable properties, making them versatile and efficient materials for applications in cosmetology, medicine, pharmacy, biotechnology and related fields [13,14].

Hydrogels can be classified according to several criteria. One common classification is based on the type of crosslinking, which may be covalent or non-covalent. Depending on the polymer source, hydrogels are categorized as natural, semi-synthetic or synthetic. According to the method of preparation, polymer chains may form homopolymers, copolymers, block copolymers or interpenetrating polymer networks (IPNs). Hydrogels can also be classified as biodegradable and non-biodegradable, as well as conventional (non-responsive) or smart (stimuli-responsive) hydrogels [12,14].

Hydrogels are used in various fields, including tissue engineering, implant development, drug delivery systems, scaffold fabrication. One of their most promising applications is as wound dressings, owing to their ability to absorb wound exudate and effectively treat necrotic lesions. As mentioned, hydrogels are also widely used in cosmetics, particularly in the masks and patches, which have become "must-have" products in skincare routines.

A key advantage of hydrogel patches is their ability to be efficiently loaded with active components and biologically active substances. Due to to their three-dimensional network structure, water molecules and dissolved ingredients can easily penetrate the polymer matrix, ensuring uniform and controlled release onto the skin. This property underlies their widespread use as carriers of bioactive compounds in cosmetic formulations. In particular, the incorporation of medicinal plant extracts into hydrogel matrices allows the development of products that provide targeted effects for symptom relief and overall enhacement of skin quality [15-17].

The use of bioactive extracts or phytochemical compounds derived from medicinal plants in cosmetic formulations serves two main functions: body care and modulation of the skin's biological functions by supplying essential nutrients required for maintaining healthy condition. Plant extracts are rich sources of biologically active compounds that exhibit a wide range of properties, both therapeutic (for certain skin disorders, particularly inflammatory ones such as acne, psoriasis or atopic dermatitis) and cosmetic (antioxidant, antibacterial, regenerative, cleansing, softening or brightening).

The composition and properties of plant extracts depend on several factors, including cultivation and harvesting conditions, the degree of raw material grinding, drying methods and extraction techniques. Plant extracts may be obtained from either the whole plant or specific parts (leaves, roots, stems, seeds or flowers) using appropriately selected solvents, such as water, ethanol or glycerol [18-20].

Among the medicinal plants of particular interest in cosmetology are *Calendula officinalis*, *Hypericum perforatum* and *Eucalyptus viminalis*.

Calendula officinalis L. is one of the most valuable medicinal plants, widely used in cosmetic, pharmaceutical and dermatological applications because of its rich phytochemical composition and strong biological activity. Numerous studies have shown that *Calendula officinalis* contains saponins, flavonoids, triterpenoids, triterpene alcohol esters, phenolic compounds, organic acids and carotenoids which give its flowers their characteristic orange color. These compounds contribute to a broad spectrum of pharmacological and cosmetic properties, including

anti-inflammatory, antioxidant, antimicrobial and wound-healing effects. *Calendula officinalis* is included in the Worls Health Organization (WHO) monographs owing to its proven effectiveness in wound healing and inflammation reduction. In modern cosmetology, calendula extracts are primarily incorporated into products for sensitive and irritated skin care. Formulations containing calendula extract help alleviate dermatitis, promote epithelialization, reduce transepidermal water loss, restore the skin's barrier function and enhance elasticity. The antioxidant activity of calendula flower extracts protects cells from damage caused by ultraviolet radiation and oxidative stress, while inhibition of matrix metalloproteinases contributes to anti-aging effects. Due to its mild yet effective action, calendula extract is among the most promising ingredients for the development of soothing, moisturizing and regenerating cosmetic formulations [21-23].

Hypericum perforatum L. is a medicinal plant with an exceptionally complex and diverse chemical composition, which includes naphthodianthrones (hypericin, pseudohypericin), acylphloroglucinol derivatives (hyperforin), biflavones, phenolic acids and flavonoid glycosides, such as rutin, hyperoside, quercetin, isoquercitrin and quercitrin. This combination of constituents determines the wide range of biological activities of *Hypericum perforatum*, including antioxidant, anti-inflammatory, antimicrobial, antiviral, wound-healing and regenerative effects. Due to the presence of hypericin and hyperforin, *Hypericum perforatum* extracts exhibit photosensitizing, antiseptic and neuroprotective properties, which explain their extensive use in phytotherapy, pharmaceuticals and cosmetics. In the cosmetic field, *Hypericum perforatum* extract is particularly valued for its ability to reduce inflammation, irritation and to promote wound healing. Its flavonoid content allows it to effectively neutralize free radicals, thereby preventing oxidative stress and premature skin aging. Furthermore, *Hypericum perforatum* stimulates epidermal cell regeneration, improves microcirculation, enhances skin firmness, tone and normalizes sebaceous gland activity, thus reducing breakouts. Several studies have shown that *Hypericum perforatum* extracts accelerate the healing of wounds, burns and exhibit pronounced antibacterial activity against *Staphylococcus aureus, Candida albicans* and other pathogens, making this plant a promising ingredient in formulations designed for problem or sensitive skin care [24-27].

Eucalyptus viminalis is another valuable source of bioactive compounds, particularly phenolic compounds, flavonoids and tannins, which determine its pharmacological and cosmetic potential. The chemical profile of *Eucalyptus viminalis* leaves includes significant amounts of phenolic acids (mainly gallic acid and its derivatives), flavonoids (derivatives of quercetin, isorhamnetin and myricetin) and hydrolyzable tannins. *Eucalyptus viminalis* extracts exhibit a broad spectrum of antimicrobial activity against both gram-positive and gram-negative bacteria, as well as certain fungal species. The high content of phenolic compounds and flavonoids provides *Eucalyptus viminalis* extracts pronounced antioxidant, anti-inflammatory and antimicrobial properties, making then a promising ingredient for cosmetic products with soothing and protective effects [28-30].

Purpose and objectives of the study. The aim of this study is to investigate the potential use of hydrogel materials as effective carriers for plant extracts and to develop hydrogel-extract complexes for application in the pharmaceutical and cosmetic industries. To achieve this aim, the following research objectives were set:

1. To evaluate medicinal plant raw materials and hydrogel matrices.
2. To obtain plant extracts under optimized extraction conditions that ensure the maximum recovery of biologically active compounds.
3. To determine the content of phenolic compounds and flavonoids in the obtained extracts.
4. To assess the antioxidant properties of the extracts and evaluate their extracts on key indicators of oxidative stress.
5. To develop hydrogel-extract complexes and study their physicochemical characteristics.
6. To analyze the antibacterial and antifungal activity of the developed complexes.

Materials and methods.

The quality of raw plant materials *Eucalyptus viminalis, Hypericum perforatum* and *Calendula officinalis* was assessed based on appearance, color, odor and presence of impurities. When selecting extraction solvents, their polarity, chemical compatibility with target bioactive compounds, safety and extraction efficiency were taken into account. Based on the literature, aqueous-ethanolic solutions (40% and 70%) were identified as optimal solvents for *Eucalyptus viminalis, Hypericum perforatum* and *Calendula officinalis*.

Plant extracts were obtained by maceration at raw material-to-solvent ratios of 1:10 and 1:20. Specifically, 5 g of dried plant material was extracted with 50 ml or 100 ml of 40% or 70% ethanol. The extraction process was carried out for 7 days at 18±5 °C in the dark to prevent degradation of sensitive compounds. After maceration, the extracts were filtered through a folded paper filter to remove residual plant particles.

Hydrogel films were synthesized using 2-hydroxyethyl methacrylate (HEMA), polyvinylpyrrolidone (PVP) and potassium persulfate ($K_2S_2O_8$) as a polymerization initiator. Polymerization was conducted under a stepwise temperature regime, followed by washing and stabilization in distilled water to remove unreacted monomers and by-products. The resulting hydrogel films were stored in distilled water at room temperature (18±2 °C) until saturation with plant

extracts of *Calendula officinalis, Eucalyptus viminalis, Hypericum perforatum* and their blend.

The flavonoid content of the extracts was determined spectrophotometrically using the aluminum chloride ($AlCl_3$) complexation method at a wavelength of 420 nm. The quantitative results were expressed as milligrams of rutin equivalent per gram of extract.

The total phenolic content was measured by the Folin-Ciocalteu method at a wavelength of 760 nm, with the results expressed in milligrams of gallic acid equivalent per gram of extract.

The antioxidant capacity was evaluated by the DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging assay at λ = 517 nm and the results were expressed as a percentage of radical inhibition.

Indicators of oxidative stress were determined by measuring thiobarbituric acid reactive substances (TBARS, expressed as malondialdehyde, MDA) spectrophotometrically at λ = 532 nm following the reaction with thiobarbituric acid and by assessing the level of protein oxidative modification (carbonyl groups, CG) using the 2,4-dinitrophenylhydrazine (DNPH) assay at λ = 370 nm [30].

Hydrogel-extract complexes were prepared by immersing HEMA:PVP hydrogel samples in the plant extracts (*Calendula officinalis, Eucalyptus viminalis, Hypericum perforatum* and their blend) at a ratio of 1:5 (hydrogel:extract) and incubating them at 18±5 °C until equilibrium swelling and saturation were achieved.

The electrical conductivity of hydrogel films saturated with *Calendula officinalis, Eucalyptus viminalis, Hypericum perforatum* and blend extracts was measured in the frequency range up to 50 kHz by determining the complex impedance.

The antibacterial and antifungal activity of the hydrogel:extract complexes was evaluated by the disk diffusion method. The test microorganisms included *Escherichia coli, Staphylococcus aureus, Candida tenuis* and *Aspergillus niger*. Nutrient media used were meat-peptone agar for bacteria and wort-agar for fungi. Incubation was performed at 37 °C for 24 h for bacterial strains and at 30 °C for 48 h for fungal strains. Antimicrobial activity was assessed by measuring the diameter of the inhibition zones around the disks.

Results of the research and their discussion

During the quality assessment of the medicinal plant raw materials, the packaging and labeling were verified to ensure compliance with standard requirements. The packaging was found to be intact and free from damage and the plant material was in satisfactory condition. An initial visual inspection confirmed that the raw materials met established standards for appearance and organoleptic properties.

The study utilized properly prepared plant materials: *Calendula officinalis* - whole and crushed flowers; *Eucalyptus viminalis* - crushed leaves; *Hypericum perforatum* - crushed herb. For extraction, analytical-grade ethanol (96%) and distilled water were used to obtain solvent concentrations of 40% and 70%. The extraction was performed by maceration using two plant material-to-solvent ratios: 1:10 (5 g of plant material per 50 ml of solvent) and 1:20 (5 g of plant material per 100 ml of solvent).

Based on previously reported findings and analysis [31], a hydrogel with a HEMA:PVP ratio of 80:20 and a film thickness of 1 mm was selected for the preparation of complexes containing plant extracts of *Calendula officinalis, Eucalyptus viminalis, Hypericum perforatum* and their blend.

Spectrophotometric analysis revealed that the content of active compounds in the investigated extracts depended on several factors, namely the type of plant raw material, the concentration of the solvent (ethanol) and the plant material-to-solvent ratio. When determining the total phenolic and flavonoid content, a clear trend was observed, as the plant material-to-solvent ratio decreased from 1:20 to 1:10, the concentration of these bioactive compounds increased in all extracts. This indicates a more efficient extraction process at higher plant material concentrations, as a larger amount of target compounds was transferred into the solvent phase. The results of the quantitative analysis of phenolic compounds and flavonoids in the obtained extracts are summarized in Table 1.

The highest flavonoid content was detected in the *Hypericum perforatum* extracts, where values ranging from 0.36% to 0.54%. *Calendula officinalis* showed a moderate flavonoid level (0.20-0.48%), whereas *Eucalyptus viminalis* demonstrated the lowest content (0.04-0.11%), which is consistent with literature data indicating the predominance of essential oils in its composition. For the blend extracts (*Calendula officinalis, Eucalyptus viminalis, Hypericum perforatum*), the flavonoid content ranged from 0.20% to 0.38%, occupying an intermediate position between the individual plants. This indicates a balanced composition and a potentially synergistic effect.

The highest content of phenolic compounds was found in *Eucalyptus viminalis* extracts, in agreement with literature reports on the high polyphenol content of eucalyptus leaves. The lowest phenolic content was recorded in *Hypericum perforatum*, indicating a predominance of other bioactive substances in its composition. In the case of *Calendula officinalis*, it was observed that grinding the flowers increases the yield of phenolic compounds by enlarging the contact surface between the raw material and the solvent, thus facilitating more intensive diffusion. Particularly notable are the results obtained for the blend of *Calendula officinalis, Eucalyptus viminalis* and *Hypericum perforatum* extracts, compared to single-component extracts. This finding indicates a synergistic effect among the components, which may enhance the solubility or stability of phenolic compounds within the mixture.

Table 1 – Results of the quantitative analysis of phenolic compounds and flavonoids

Досліджуваний екстракт	**Flavonoids, %**	**Phenolic compounds, mg/ml**
Calendula officinalis (whole flowers) (1:10 ethanol 40%)	0,48	1,505
Calendula officinalis (whole flowers) (1:20 ethanol 40%)	0,24	0,860
Calendula officinalis (whole flowers) (1:10 ethanol 70%)	0,38	1,562
Calendula officinalis (whole flowers) (1:20 ethanol 70%)	0,20	1
Calendula officinalis (crushed flowers) (1:10 ethanol 40%)	0,20	1,730
Calendula officinalis (crushed flowers) (1:20 ethanol 40%)	0,21	1,364
Calendula officinalis (crushed flowers) (1:10 ethanol 70%)	0,39	1,727
Calendula officinalis (crushed flowers) (1:20 ethanol 70%)	0,35	1,242
Eucalyptus viminalis (1:10 ethanol 40%)	0,09	4,162
Eucalyptus viminalis (1:20 ethanol 40%)	0,08	2,759
Eucalyptus viminalis (1:10 ethanol 70%)	0,11	4,175
Eucalyptus viminalis (1:20 ethanol 70%)	0,04	2,676
Hypericum perforatum (1:10 ethanol 40%)	0,53	1,427
Hypericum perforatum (1:20 ethanol 40%)	0,46	0,403
Hypericum perforatum (1:10 ethanol 70%)	0,54	0,947
Hypericum perforatum (1:20 ethanol 70%)	0,36	0,619
Blend: *Calendula officinalis*, *Eucalyptus viminalis*, *Hypericum perforatum* (1:10 ethanol 40%)	0,38	2,233
Blend: *Calendula officinalis*, *Eucalyptus viminalis*, *Hypericum perforatum* (1:20 ethanol 40%)	0,21	1,282
Blend: *Calendula officinalis*, *Eucalyptus viminalis*, *Hypericum perforatum* (1:10 ethanol 70%)	0,36	1,258
Blend: *Calendula officinalis*, *Eucalyptus viminalis*, *Hypericum perforatum* (1:20 ethanol 70%)	0,20	1,091

Given the results of quantitative analysis of total phenolic compounds and flavonid content, extracts at a 1:10 plant-to-solvent ration, which showed the highest concentration of bioactive compounds, were selected for further antioxidant assessment, including the DPPH radical scavenging method and the evaluation of oxidative stress markers (TBARS and protein carbonyls).

Based on the results of the antioxidant activity assessment of the medicinal plant extracts using the DPPH radical scavenging method, several conclusions can be drawn. All tested extracts, obtained at the 1:10 plant-to-solvent ratio, demonstrated pronounced antioxidant activity, confirming their high potential as natural sources of antioxidants. The ethanol concentration influenced the radical-scavening activity: extracts prepared with 70% ethanol generally exhibited slightly higher activity compared to those prepared with 40% ethanol, which justified selecting these extracts for subsequent oxidative stress analyses. This observation indicates that antioxidant potential depends not only on the total quantity of active compounds but also on their functional availability and reactivity in assay. The *Calendula officinalis* extract demonstrated a moderate level of antioxidant activity, which increased from 82% (at 40% ethanol) to 87% (at 70% ethanol). The *Hypericum perforatum* extract demonstrated higher antioxidant activity (88%), which was close to the values of the positive control (BHT - 88.50%). This result indicates the presence of a considerable amount

of effective antioxidant compounds, primarily flavonoids and phenolic derivatives. The *Eucalyptus viminalis* extract showed the highest antioxidant activity (89%) among single-component extracts, even exceeding the control (BHT). The blend of *Calendula officinalis, Eucalyptus viminalis* and *Hypericum perforatum* extracts exhibited the maximum antioxidant activity at both ethanol concentrations (90%), exceeding all individual extracts and the reference antioxidant BHT. This result highlights a pronounced synergistic effect, where the interaction of various bioactive constituents enhances the overall antioxidant action.

An additional assessment of the antioxidant properties of the studied extracts was performed by analyzing thiobarbituric acid-reactive substances (TBARS) and protein carbonyl (PC) group levels. Extract samples for this stage were selected based of the results of DPPH assay; therefore, extracts obtained at the 1:10 plant-to-solvent ratio by using 70% ethanol were used. All tested extracts *Calendula officinalis, Hypericum perforatum* and the blend extract *(Calendula officinalis, Eucalyptus viminalis, Hypericum perforatum*) exhibited marked antioxidant activity, demonstrated by a significant (>50%) reduction in lipid peroxidation products (TBARS) and oxidative modification of proteins (PC) compared to the control (70% ethanol). The highest antioxidant effectiveness was observed for the blend extract, which reduced oxidative stress markers by 73.9-86.5%, indicating a pronounced synergistic effect that enhances overall antioxidant potential. The *Hypericum perforatum* extract showed a moderate antioxidant effect, decreasing TBARS content by 65.0% ($p \leq 0.01$) and protein carbonyls by 81.0% ($p \leq 0.001$). The *Calendula officinalis* extract demonstrated the lowest, yet still significant, antioxidant activity, reducing TBARS levels to 44.7±5.6% and protein carbonyls to 35.5±11.5% relative to the control. These results are consistent with the DPPH assay data, confirming that the blend extract exhibits the greatest potential among the studied samples.

Subsequently, studies were conducted on the hydrogel-extract complexes. For preparation, hydrogel film samples were cut into various shapes, including squares (0.5 × 0.5 mm) and disks (d = 0.5 mm). The samples were weighed and then impregnated with the plant extracts at a ratio of 1:10.

The incorporation of plant extracts (*Calendula officinalis, Eucalyptus viminalis, Hypericum* perforatum and the blend) into the hydrogel films led to cnahges in appearance and an increase in electrical conductivity within the polymer matrix. This effect is attributed to the presence of biologically active components in the extracts, including trace elements (iron, copper, etc.), which create additional conductive pathways within the hydrogel. The most pronounced increase in electrical conductivity was observed in samples saturated with the blend of extracts, which can be explained by the synergistic effect of the components and the higher concentration of ionized particles in the system. The observed enhacement of electrical conductivity may have practical significance, potentially improving the therapeutic properties of the hydrogels for transdermal delivery of active substances via electrophoresis.

The antibacterial and antifungal properties of the hydrogel-extracts complexes were evaluated against test cultures *Escherichia coli, Staphylococcus aureus, Candida tenuis* and *Aspergillus niger*, and classified as fungicidal (FC), fungistatic (FS), bactericidal (BC), bacteriostatic (BS) or no activity (n/a). For the antimicrobial assessment, hydrogel-extracts complexes were selected based on two criteria: extracts obtained using 70% ethanol, which demonstrated the highest antioxidant activity in the assays and literature reports indicating significant antimicrobial potential of these. The results are summerized in Table 2. As controls, pure HEMA/PVP hydrogel and hydrogel saturated with 70% ethanol were used.

Table 2 – Resulys of the antibacterial and antifungal properties of the complexes

Tested samples	Diameter of growth inhobotion zones, mm			
	Escherichia coli	*Staphylococcus aureus*	*Candida tenuis*	*Aspergillus niger*
Hydrogel HEMA/PVP - distilled water	n/a	n/a	n/a	n/a
Hydrogel HEMA/PVP - ethanol (70%)	n/a	n/a	FS (11)	n/a
Hydrogel HEMA/PVP - extract *Eucalyptus viminalis*	BC (17,3)	BC (18)	FC (11)	n/a
Hydrogel HEMA/PVP -extract *Hypericum perforatum*	BS (8,5)	BS(11,7)	FS (5,5)	n/a
Hydrogel HEMA/PVP - extract blend *(Calendula officinalis, Eucalyptus viminalis, Hypericum perforatum)*	BC (7,3)	BC (7,3)	FC (10,3)	n/a

The control HEMA/PVP hydrogel itself did not show any antimicrobial activity against the test-cultures, confirming the absence of biocidal or biostatic properties in its polymer matrix. Hydrogel saturated with ethanol exhibited fungistatic activity against *Aspergillus niger*, but did not affect the other microorganisms, likely due to their greater resistance to alcohol. The hydrogel HEMA/PVP - *Eucalyptus viminalis* extract complex demostrated pronounced bactericidal activity against *Escherichia coli* and *Staphylococcus aureus*, indicating the sensitivity of these bacterial strains to eucalyptus extract. A fungicidal effect, though less pronounced, was observed against *Candida tenuis*, while no activity was detected against *Aspergillus niger*. The hydrogel HEMA/PVP - *Hypericum perforatum* extract complex exhibited bacteriostatic and fungistatic effects, which were insufficient to completely inhibit microbial growth, possibly due to the lower content or reduced activity of antimicrobial compounds in this extract. The lowest antimicrobial activity was recorded for the complex based on the blend of plant extracts (*Calendula officinalis, Eucalyptus viminalis, Hypericum perforatum*), which showed a reduction in the inhibition zones against *Escherichia coli, Staphylococcus aureus* and *Candida tenuis* compared with the individual *Eucalyptus viminalis* extract. It should be noted that *Calendula officinalis* was included in the blend but was not evaluated as a separate hydrogel-extract complex in this study; however its contribution to the antioxidant and potential synergistic effects within the blend cannot be excluded. This approach ensures that the observed antimicrobal effects reflect the combined action of the extracts, while also highlighting the need for future studies to explore the individual contribution of *Calendula officinalis.*

Approbation of research results. The obtained results can be applied in the industrial production of pharmaceutical and cosmetic products following additional research and clinical trials. In particular, HEMA/PVP hydrogel matrices containing plant extracts may serve as a basis for functional facial masks or patches with controlled release of active components. The observed increase in electricial conductivity upon incorporation of plant extracts has practical significance, as it can facilitate more effective transdermal delivery of active compounds through electrophoretic mechanisms, potentially enhancing the therapeutic and cosmetic effectiveness of the hydrogel complexes. Further *in vitro* and *in vivo* studies will allow assessment of the safety, efficacy and stability of these delivery systems. In the long term, the developed systems may be implemented into pharmaceutical manufacturing processes for the creation of innovative topical formulations with antioxidant, anti-inflammatory and antimicrobial properties, as well as into the cosmetic industry for the development of high-performance skincare products.

Conclusion

In this study, medicinal plant materials *Calendula officinalis, Eucalyptus viminalis* and *Hypericum perforatum* were utilized, along with a hydrogel material composed of HEMA/PVP. Evaluation of the raw materials and hydrogel samples was performed, forming the basis for the development of hydrogel-extract complexes to further investigate their antioxidant, physicochemical and antimicrobial properties. The extraction process was optimized by varying ethanol concentration (40% and 70%) and the plant material-to-solvent ratio. It was established that at a ratio of 1:10 provided the most efficient extraction of biologically active compounds. Both ethanol concentrations yielded extracts with significant phenolic compounds and flavonoids content. The highest content of phenolic compounds was observed in *Eucalyptus viminalis* extracts, while the highest flavonoid content was found in *Hypericum perforatum* and in the blend extract (*Calendula officinalis, Eucalyptus viminalis, Hypericum perforatum*). All investigated extracts exhibited antioxidant activity, confirmed by the DPPH assay and measurement of oxidative stress markers (TBARS and protein carbonyl groups). Extracts prepared with 70% ethanol generally demonstrated slightly higher radical-scavening activity than those with 40%, indicating that antioxidants effectiveness depends on both compound concentration and fuctional reactivity. Among the individual extracts, *Calendula officinalis* exhibited the lowest, though still significant antioxidant activity, while the blend extract demonstrated the strongest activity, suggesting a possible synergistic effect among its bioactive compounds. Based on these extracts, hydrogel HEMA/PVP-extract complexes were developed. Incorporation of plant extracts into the hydrogel matrix led to increased electrical conductivity, likely due to the trace elements in the extracts forming conductive pathways within the hydrogel structure. This enhacement may improve the efficiency of transdermal delivery of active compounds via electrophoresis, supporting the functional performance of the developed hydrogel systems. Assessment of antibacterial and antifungal properties showed that the pure HEMA/PVP hydrogel had no antimicrobial activity. However, upon loading with plant extracts, the complexes acquired bactericidal or bacteriostatic and fungicidal or fungistatic properties. The highest activity was observed for the hydroglel HEMA/PVP - *Eucalyptus viminalis* extract complex, which effectively inhibited the growth of *Escherichia coli*, *Staphylococcus aureus* and *Candida tenuis*. Complexes containing *Hypericum perforatum* extract and the blend extract exhibited less pronounced activity, which may be associated with differences in the concentration and interactions of active compounds. Although *Calendula officinalis* was not tested individually for antimicrobial activity, its

presence in the blend may contribute to synergistic effects. Future studies could focus on optimizing its extraction parameters, solvent composition and concentration, particle size, and its proportion, to enhance antioxidant activity and further evaluate antimicrobial performance. Overall, the developed HEMA/PVP hydrogel complexes containing plant extracts are characterized by a high content of biologically active compounds, pronounced antioxidant activity and the ability to exhibit antimicrobial properties. These results confirm the potential for using such systems in cosmetic and dermatological products with prolonged action. Future research should focus on evaluating the stability, safety and efficacy of these complexes under conditions of long-term use.

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ГІДРОГЕЛЕВІ НОСІЇ ДЛЯ КОНТРОЛЬОВАНОГО ВИВІЛЬНЕННЯ БІОЛОГІЧНО АКТИВНИХ РЕЧОВИН

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Анотація. Останніми роками зацікавленість до натуральних засобів у косметиці та фармації значно зросла. Споживачі все частіше надають перевагу продуктам на основі рослинної сировини, які поєднують ефективність, безпечність та сприяють підтриманню здорового стану шкіри. Попит на такі засоби зростає також через складність встановлення чітких критеріїв "якості шкіри" та прагнення споживачів підтримувати її оптимальний стан. Важливо, щоб косметичні та фармацевтичні продукти не лише забезпечували естетичний ефект, але й комплексно впливали на фізіологічні процеси шкіри, покращували захисні та відновлювальні властивості, підтримували оптимальний рівень зволоження, а також сприяли зниженню запальних процесів. Тому актуальною темою є створення інноваційних полімерних систем доставки біологічно активних речовин природного походження. У даній роботі досліджено інтеграцію екстрактів лікарських рослин *Calendula officinalis, Eucalyptus viminalis, Hypericum perforatum* та їх комбінації у гідрогелеву матрицю на основі полі(2-гідроксиетилметакрилату) та полівінілпіролідону (*HEMA/PVP*) з метою створення функціональних систем доставки біологічно активних речовин для фармацевтичного та косметичного застосування. В ході досліджень, проведено порівняльне вивчення умов екстрагування рослинної сировини (тип розчинника, його концентрації та співвідношення сировини до екстрагента), визначено вміст флавоноїдів та фенольних сполук у кожному з екстрактів та їх комбінації, а також антиоксидантну активність та їх вплив на показники оксидативного стресу, на основі вмісту ТБК-активних продуктів та визначення концентрації кетонних груп (КГ) в білках. Встановлено, що оптимальні умови екстрагування забезпечують підвищений вихід біологічно активних речовин і вказують на потенціал отриманих рослинних екстрактів як антиоксидантних компонентів для подальшої іммобілізації у полімерні системи. Отримані екстракти були інтегровані у гідрогелеву матрицю складу HEMA/PVP та досліджено їх вплив на фізико-хімічні характеристики гідрогелів, зокрема електропровідність. Отримані гідрогелеві комплекси проявляли виражену антибактеріальну та протигрибкову дію щодо використаних тест-культур: *Escherichia coli, Staphylococcus aureus, Candida tenuis* та *Aspergillus niger*. Таким чином, розроблені комплекси поєднують високу біологічну активність рослинних компонентів із стабільною та функціональною гідрогелевою матрицею, що відкриває можливості їх застосування у сучасних фармацевтичних і косметичних продуктах для цілеспрямованої доставки активних речовин.

Ключові слова: гідрогель, екстракти, полівінілпіролідон (ПВП), 2-гідроксиетилметакрилат (ГЕМА).