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***THE DEVELOPMENT AND CHARACTERIZATION
OF SOME TOPICAL PREPARATIONS THAT
CONTAIN EXTRACTIVE PRODUCTS OF
LEVISTICUM OFFICINALE L. AND ROSMARINUS
OFFICINALIS L.***

Summary of PhD Thesis

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INTRODUCTION

Rosemary (*Rosmarinus officinalis* L.) and lovage (*Levisticum officinale* L.) with their rich bioactive profiles fit perfectly into this trend. As consumers increasingly seek multifunctional, eco-friendly and effective products, the incorporation of rosemary and lovage into dermatocosmetics offers both therapeutic benefits and sustainability, responding to consumer preferences for clean beauty products that support skin health and the environment.

Rosemary (*Rosmarinus officinalis* L.) is a well-known aromatic plant from the Lamiaceae family. It is widely used in gastronomy, medicine and the cosmetic industry due to its high concentration of bioactive compounds, especially polyphenols and essential oils [1-7]. These constituents contribute to antioxidant, antimicrobial and anti-inflammatory activities, which have stimulated a growing scientific interest in rosemary-based applications, especially in dermatocosmetic formulations [8-12].

The main bioactive components of rosemary include carnosic acid, carnosol, rosmarinic acid, and essential oils such as eucalyptol, camphor, and bornyl acetate [4, 10-12]. These compounds are known to be influenced by several factors, including geographical origin, climatic conditions, and extraction methods used during processing.

Levisticum officinale L., traditionally known as lovage, is an aromatic and medicinal plant widely used in both gastronomy and traditional European and Asian medicine.

It is valued not only for its distinctive aroma, but also for its multiple therapeutic properties, documented in numerous scientific studies [13,14]. The phytochemical composition of lovage is complex, including flavonoids, phenolic acids, coumarins, phthalides, and essential oils, compounds with antioxidant, anti-inflammatory, antimicrobial, and diuretic effects [14,15].

Recent research on *Levisticum officinale* L. has highlighted its therapeutic potential through phytochemical, pharmacological and clinical studies, in addition to consolidating the position of lovage as a source of antioxidant substances, essential for reducing oxidative stress, a factor implicated in numerous chronic diseases [16-19]. Despite the established potential of rosemary, comparative studies focusing on regional variations in its bioactive composition, as well as the impact of extraction methods on its potency, remain scarce.

Current research focuses predominantly on the broad applications of rosemary, but there is a lack of comprehensive studies examining the geographical influence on its chemical profile and biological activity, especially in relation to dermatocosmetic formulations.

The Dobrogea region of Romania, with its unique climatic and pedological conditions, has not been thoroughly studied in the context of the potential of rosemary for skin care applications, especially in comparison with Bulgarian rosemary samples.

There is an obvious research gap in understanding how different extraction solvents, such as ethanol concentrations, affect the antioxidant, antimicrobial and anti-inflammatory properties of rosemary and how these properties influence the formulation of effective dermatocosmetic products. The influence of mineral composition on the biological activity of rosemary also remains underexplored, despite the fact that minerals such as calcium, zinc and iron could improve skin health and contribute to the efficacy of rosemary-based skin care products.

The studies conducted within the framework of this doctoral thesis provide updated data on rosemary extracts, addressing the gaps related to regional variations, extraction efficiency and dermatocosmetic applications. By integrating this information into product development, this thesis supports the optimization of rosemary-based skin care formulations with enhanced efficacy and stability.

This study compares the antioxidant activity, mineral composition and phytochemical profile of rosemary from two distinct geographical regions: Dobrogea (Romania) and the coastal area of Bulgaria, where differences in soil and climate are expected to influence the bioactive properties. In addition, the study examines the effects of ethanol maceration at 96%, 70% and 40% to optimize the extraction of bioactive compounds and evaluate the antimicrobial activity of the extracts against Gram-positive and Gram-negative bacteria.

The findings provide valuable information on the impact of geographical, extraction and microbial factors on the chemical composition and biological activity of rosemary. The extracts with the highest concentrations of bioactive compounds were further incorporated into hydrogels and dermatocosmetic creams, demonstrating their potential for applications in skin care.

The development and comparative evaluation of new dermatocosmetic preparations based on hydroalcoholic macerates of rosemary (*Rosmarinus officinalis* L.) was also investigated,

focusing on their antioxidant, antimicrobial and anti-inflammatory properties. To this end, the hydroalcoholic macerates of rosemary were analyzed by evaluating the content of biologically active compounds, determining their antioxidant and antimicrobial capacity.

At the same time, the present study contributes to the expansion of knowledge about *Levisticum officinale* L. through a detailed investigation of alcoholic extracts and their integration into carbopol-based hydrogels with therapeutic and cosmetic potential.

The present study aims to compare hydroalcoholic extracts (70% ethanol) obtained from the root, leaves and whole plant of *Levisticum officinale* L. by determining the total content of phenolic compounds, characterizing the polyphenolic profile and evaluating antioxidant activity. In addition, the extracts obtained were incorporated into carbopol-based hydrogels, which were characterized from a rheological and physicochemical point of view, and their antioxidant activity was evaluated to determine their stability and efficiency as potential pharmaceutical or dermato-cosmetic forms with antioxidant action.

Through these innovative approaches, the proposed study will contribute to the optimization of the use of *Levisticum officinale* L. in pharmaceutical and cosmetic products, opening new perspectives for the development of effective formulations with extended therapeutic applicability.

I. GENERAL PART

1. Topical pharmaceutical systems – formulations and characteristics

1.1. Formulation of topical therapeutic products

For the formulation of a topical drug product, simplicity is essential; a short ingredient list is preferable. It is preferable to eliminate redundant components. However, to achieve effective drug release and consumer acceptance, a complex combination of excipients is required. It is crucial to avoid undesirable interactions between the ingredients in the formulation. For example, an anionic surfactant may react with a positively charged drug or an anionic emulsifier may be inactivated by multivalent counterions, such as Ca^{2+} or Mg^{2+} [20].

1.2. Evaluation of topical semi-solid products

To ensure the quality, efficacy, purity and safety of topical drug products, they are evaluated through various compendial and non-compendial tests. USP, F.Eur. monographs and other

regulatory recommendations provide guidance for testing and specifications regarding product processing, release and stability.

2. Use of plant extracts in topical products

Plants and plant constituents have been used for skin treatment and care for centuries, and the interest in their use in the formulation of pharmaceutical and cosmetic products has recently increased due to their safety and efficacy. Nowadays, they have become increasingly widespread in modern cosmetic formulations, especially due to consumer concerns about the safety of synthetic ingredients.

Given the inherent economic potential of exploiting natural resources in ecosystems, plant extracts can be used in cosmetic science to beautify and maintain the physiological balance of human skin. Compared to synthetic cosmetic ingredients, plant-based products are mild and biodegradable, presenting low toxicity.

Furthermore, the food industry and other plant processing industries generate numerous by-products that usually pose a disposal problem. However, some of these by-products can also be a promising source of compounds with favorable biological properties for cutaneous application. Thus, natural plant extracts, whether from naturally occurring plants or industrially processed plant waste, can be used to obtain new natural topical antioxidants, bleaching agents and preservatives, maximizing the usefulness of products that are currently underexploited or discarded.

Many plant extracts, once properly studied, can represent a safe, effective and cost-effective alternative to synthetic products. Integrating these extracts into cosmetic formulations not only provides innovative and sustainable solutions for skin care, but also promotes eco-friendly and environmentally responsible practices [21].

Continuous research and evaluation are essential to maximize the use of these natural resources, providing innovative solutions for skin care and the prevention of premature aging.

II. PERSONAL CONTRIBUTIONS

3. Working hypothesis and general objectives

The *novelty* of the research lies in the following approaches:

1. *Comparison of the phytochemical profile* of leaf, root and whole plant extracts, providing comparative data on the distribution of bioactive compounds;
2. *Use of hydrogels* as a release matrix for lovage extracts, optimizing their bioavailability

and opening new directions for pharmaceutical and cosmetic applicability;

3. **Correlation of phytochemical composition** with antioxidant activity, highlighting the potential of lovage as a source of new active ingredients for the pharmaceutical and food supplement industries.

The **general objectives** pursued in the doctoral thesis are:

1. Preparation of rosemary and lovage extractive products
2. Analysis of the content of biologically active compounds in the obtained products
3. Investigation of the antioxidant and antimicrobial properties of the extractive products
4. Formulation and obtaining of topically applied pharmaceutical forms incorporating the studied extractive products
5. Evaluation of the physicochemical and antioxidant characteristics of the topical preparations

4. General research methodology

4.1. Materials

The working samples included the root, stem and leaves of the species *Levisticum officinale* L., harvested from the Lunca Mare area, Prahova County (coordinates: 45°11'57" N 25°44'41" E), Romania.

For rosemary products, fresh leaves of *Rosmarinus officinalis* L. were collected in June 2023 from two specific locations: Dobrogea Region, Romania, near Constanța (44°10' N, 28°38' E), from a semi-wild habitat in the coastal area, and the coastal area of Bulgaria, near Varna (43°12' N, 27°55' E), from a cultivated site.

4.2. Preparation of plant extractive products

4.2.1. Preparation of hydroalcoholic extracts from lovage

The crushed plant material was left to macerate for 14 days, in a cool place and away from light, according to the method in the Romanian Pharmacopoeia, 10th Edition [22]. During this period, the samples were shaken daily for 30 minutes to ensure optimal extraction of the bioactive compounds. After 14 days, the hydroalcoholic extracts were filtered at normal pressure, using Whatman quantitative filter paper with blue band, to remove impurities and obtain clear solutions.

4.2.2. Preparation of hydroalcoholic macerates from rosemary

For this study, hydroalcoholic macerates of rosemary were prepared using ethanol at 96%, 70% and 40%, with samples from both Dobrogea (Romania) and Bulgaria. The Dobrogean

rosemary macerates were labeled as RDS1 (ethanol 96%), RDS2 (ethanol 70%) and RDS3 (ethanol 40%), while the Bulgarian rosemary macerates were designated as RBS1 (ethanol 96%), RBS2 (ethanol 70%) and RBS3 (ethanol 40%).

4.3. Investigation of the phytochemical composition of extractive products

4.3.1. Determination of total phenol content (Folin–Ciocâlțeu)

The total phenolic compound content is expressed in mg gallic acid equivalents/g extract (mg GAE/g) [23].

4.3.2. Determination of total flavonoids by the colorimetric method with AlCl₃

The results were expressed in mg QE/100 g fresh weight.

4.3.3. Determination of total condensed tannins content - Vanillin-HCl method

Condensed tannins (also known as proanthocyanidins) are polyphenols that can be quantified by spectrophotometric methods, using the vanillin-HCl reagent or the butanol-HCl method. These methods are based on the interaction of tannins with specific chemical reagents, resulting in the formation of colored complexes that can be measured spectrophotometrically.

4.3.4. Polyphenol profile analysis by HPLC-DAD

The identification and quantitative determination of the active principles in the solutions to be analyzed was carried out by comparing the retention times and purity of the peaks of the standard compounds used with the corresponding ones on the chromatograms of the solutions to be analyzed.

4.3.5. Analysis of metal concentrations

Metal concentrations were determined using a ContrAA® 700 atomic absorption spectrometer (Analytik Jena GmbH+Co. KG, Jena, Germany) with flame atomization.

4.4. Evaluation of antioxidant activity

4.4.1. Determination of antioxidant activity by ABTS

The results were expressed in μmol Trolox equivalents/g extract (TEAC).

4.4.2. Determination of antioxidant activity by DPPH

The IC₅₀ value was calculated, representing the concentration required to reduce the DPPH radical by 50%.

4.5. Testing of antimicrobial properties

The antimicrobial activity of rosemary macerates was tested against three reference strains: *Staphylococcus aureus* ATCC 25923 (Gram-positive cocci), *Escherichia coli* ATCC 25922 (Gram-negative bacilli) and *Candida albicans* ATCC 10231 (yeast).

4.6. Formulation and preparation of topical preparations with extractive product

4.6.1. Formulation and preparation of hydrogels with hydroalcoholic extracts of lovage

3 hydrogel formulas based on carbopol 940 2% were made, which included hydroalcoholic extracts in a concentration of 5% according to the data presented in table I.

Table I. Hydrogel formulas with hydroalcoholic extracts of lovage

Ingredients	Formula 1	Formula 2	Formula 3
Carbopol 940	2 g	2 g	2 g
Glycerin	5 g	5 g	5 g
Triethanolamine	q.s.	q.s.	q.s.
Hydroalcoholic extract from leaves	-	-	5 g
Hydroalcoholic extract from root	5 g	-	-
Hydroalcoholic extract from whole plant	-	5 g	-
Distilled water	q.s. to 100 g	q.s. to 100 g	q.s. to 100 g

q.s. = *quantum satis*

4.6.2. Formulation and preparation of dermatocosmetic products with rosemary macerates

Two hydrogel formulations (Formula A and Formula B) were prepared with the composition shown in Table II. Carbopol 940, corresponding to a final concentration of 1.5%, was hydrated using purified water for at least 24 hours in the presence of glycerin as a dispersing agent (purity > 99%; glycerin from Merck, Darmstadt, Germany). Triethanolamine (purity > 99%; triethanolamine from Carl Roth GmbH + Co. KG., Karlsruhe, Germany) was used for neutralization at the end of 24 hours in the cold and added to the semisolid matrix generated by hydration of the hydrophilic polymer under intensive stirring (2000 rpm for 10 minutes, using a turbine stirrer in a Heidolph RZR 2020, Heidolph Instruments GmbH & Co. KG, Schwabach, Germany).

Finally, the rosemary macerate and the volatile oil (rosemary essential oil) were added to the semi-solid matrix under stirring until complete homogenization. The volatile oil used for the preparation of the gels was an organic product from Mayam, with a quality certificate (certified by Ecocert Greenlife according to the Ecocert/Cosmos standard).

Table II. Composition of the hydrogels with rosemary macerates in 70% ethanol

Components	Quantity (g)	
	Formula A	Formula B
Carbopol 940	1.5 g	1.5 g
Glycerin	5 g	5 g
Triethanolamine	q.s	q.s
Rosemary essential oil	1 g	1 g
RDS2	2.5 g	-
RBS2	-	2,5 g
Purified water	q.s. 100 g	q.s. 100 g

Two cosmetic emulsion formulas (Formula C and Formula D) were prepared with the composition shown in Table III.

Table III. Composition of cosmetic emulsions with rosemary macerates in 70% ethanol

Components	Quantity (g)	
	Formula C	Formula D
Cetyl alcohol	1.5 g	1.5 g
Beeswax	4 g	4 g
Cocoa butter	10 g	10 g
Anhydrous lanolin	2 g	2 g
Sesame oil	32 g	32 g
Rosemary essential oil	2 g	2 g
RDS2	5 g	-
RBS2	-	5 g
Purified water	q.s.100 g	q.s. 100 g

4.7.Characterization of topical pharmaceutical preparations

4.7.1. pH determination

The pH of all formulations (emulsions and gels) was measured using a digital pH meter (Hanna Instruments, Woonsocket, RI, USA).

4.7.2. Determination of tensile capacity

The tensile capacity was evaluated 30 hours after preparation by placing 1 g of sample between two 20 × 20 cm glass plates for 1 minute, following the Ojeda-Arbussa extensiometric method.

4.7.3. Analysis of rheological characteristics

The rheological properties were evaluated at variable rotational speeds (ω) between 4 and 200 rpm. The measurements were performed with a rotational viscometer ST-2020 R, manufactured by Laboquimia, Spain, using 10-second intervals for each determination. Viscosity evaluations were performed with spindles R5 and R6, which were chosen to match the viscosity range of the samples. These spindles facilitated the calculation of the shear rate (D) in relation to the rotational speed (ω).

4.7.4. Determination of antioxidant capacity

The antioxidant activity of the hydrogel formulations was evaluated using the DPPH radical scavenging assay, using gallic acid (GAE) as a standard for plotting calibration curves [24].

4.7.5. Evaluation of anti-inflammatory action

This preclinical study was approved by the Scientific Research Ethics Committee of the "Carol Davila" University of Medicine and Pharmacy, Bucharest, according to Notification 6485/12 March 2024 and complied with the regulations in force regarding preclinical testing on laboratory animals. The tests were performed using two experimental methods of acute inflammation: induced edema in the rat paw with 10% kaolin suspension and with 6% dextran solution.

4.7.6. Stability assessment

The stability of the products was monitored over a period of time (60 days), evaluating changes in texture and visual appearance. Thermal and pH stability tests were performed to ensure that the product maintained its characteristics over time, without undergoing significant changes.

4.7.7. Statistical analysis

All experiments were performed in triplicate, and results were expressed as mean \pm standard deviation (SD), along with 95% confidence intervals (CI) for key measurements. A power analysis was performed using G*Power 3.1 to determine the appropriate sample size, ensuring a significance level (α) of 0.05, a power ($1-\beta$) of 0.80, and an estimated effect size (Cohen's d) derived from the pilot data. Based on this analysis, a minimum of 15 samples per ethanol concentration group was required for robust statistical comparisons. Statistical analyses were performed using IBM SPSS Statistics 27 and GraphPad Prism 9. ANOVA analysis was used to assess significant differences in total polyphenol content, flavonoid content, antioxidant activity, and mineral composition across ethanol concentrations. Post hoc comparisons were performed using the Tukey HSD test to identify pairwise differences. Independent t-tests were used to compare differences in mineral content between samples from Dobrogea and Bulgaria.

5. Characterization of extractive preparations obtained from *Levisticum officinale* L. and *Rosmarinus officinalis* L

5.1. Characterization of hydroalcoholic extracts from *Levisticum officinale* L

5.1.1. Total content of polyphenolic compounds

The results indicate that the lovage leaf extract presented the highest concentration of polyphenols (20.84 ± 1.18 mg GAE/g), suggesting a richer presence of flavonoids and phenolic acids. In contrast, the whole plant extract contained the lowest amount of polyphenols (18.26 ± 1.61 mg GAE/g), highlighting the variation in the distribution of bioactive compounds in different parts of the plant. These findings highlight the superior antioxidant potential of leaf extracts and their possible applications in pharmaceutical and cosmetic formulations [25].

5.1.2. Phenolic acid content

Analysis of phenolic acid content revealed the highest content in the hydroalcoholic extract of the whole plant (18.26 ± 1.65 mg GAE/g) and the lowest content in the alcoholic extract of the leaves (8.08 ± 0.33 mg GAE/g).

5.1.3. Total flavones content

The highest content of flavones was recorded in the hydroalcoholic extract of lovage leaves (11.39 ± 1.48 mg QE/g), and the lowest in the alcoholic extract of the root (6.6 ± 0.25 mg QE/g).

5.1.4. Condensed tannin content

The highest content of condensed tannins (1.98 ± 0.55 mg CE/g) was presented in the hydroalcoholic extract of lovage leaves, and the lowest in the alcoholic extract of the root (0.92 ± 0.12 mg CE/g).

5.1.5. Phenolic profile of lovage hydroalcoholic extracts

The analysis reveals a higher concentration of flavonoids, such as quercetin, kaempferol and rutin, in the leaves, while the roots show high levels of phenolic acids, including ferulic, caffeic and vanillic acids.

5.1.6. Antioxidant activity of hydroalcoholic extracts of lovage

The hydroalcoholic extract of the leaves showed the highest antioxidant activity, with values of 276.2 ± 3.4 μ mol TE/g by the ABTS method and 246.4 ± 3.6 μ mol TE/g by the DPPH method. These results can be correlated with the high content of flavonoids and phenolic acids identified in the extract, especially quercetin, rutin, luteolin and chlorogenic acid, known for their ability to donate electrons and neutralize reactive oxygen species.

5.2.Characterization of hydroalcoholic macerates of *Rosmarinus officinalis* L.

5.2.1. Total content of polyphenolic compounds (TPC)

The total phenolic compounds (TPC) content and antioxidant activity of hydroalcoholic macerates of *Rosmarinus officinalis* were evaluated to determine their potential for use in dermatocosmetic formulations. The results, expressed in mg gallic acid equivalents per 100 g fresh material (mg EGA/100 g body weight), are presented in Figure 1.

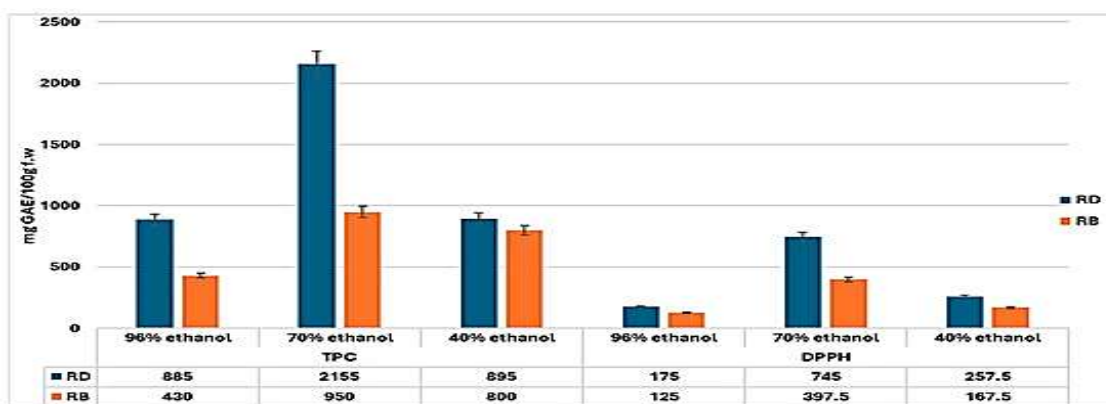


Fig. 1. Total phenolic content (TPC) and antioxidant activity evaluated by DPPH assay in *Rosmarinus officinalis* samples from Dobrogea (RD) and Bulgaria (RB).

The results confirm the essential role of solvent polarity in the extraction of phenolic compounds, demonstrating the superior efficacy of 70% ethanol. Significant variations in total phenolic compound (TPC) content and antioxidant activity were observed within the samples.

5.2.2. Antioxidant activity

Dobrogean rosemary macerate (RDS2) presented the highest radical scavenging activity (745.0 ± 2.33 mg GAE/100 g body weight), while its Bulgarian counterpart (RBS2) demonstrated significantly lower activity (397.5 ± 1.76 mg GAE/100 g body weight).

5.2.3. Activity of total flavonoid content (TFC)

The highest TFC value was also observed in the Dobrogea sample macerated with 70% ethanol (RDS2), with a value of 283.6 ± 1.52 mg QE/100 g fresh weight (g), which strongly correlates with its higher total phenolic content and antioxidant activity.

5.2.4. The mineral content of rosemary hydroalcoholic macerates

Rosemary samples from Dobrogea (RD) consistently demonstrated higher concentrations of essential minerals compared to Bulgarian samples (RB), which could be attributed to regional environmental factors such as soil composition and climate.

5.2.5. Antimicrobial activity

The results confirm that the RDS2 macerate exhibits superior antimicrobial activity compared to RBS2, especially against Gram-positive bacteria and yeast. This difference can be attributed to the higher content of polyphenolic compounds, such as carnosic acid and rosmarinic acid, in RDS2, which are known for their potent antimicrobial properties.

6. Characterization of topical pharmaceutical preparations

6.1. Characterization of hydrogels with hydroalcoholic extracts from *Levisticum officinale* L.



Figure 2. Hydrogels with hydroalcoholic extracts of lovage: 1- hydroalcoholic extract from the root; 2 – hydroalcoholic extract from the whole plant; 3- hydroalcoholic extract from the leaves

The results of the control tests performed on hydrogels with hydroalcoholic extracts of lovage are presented in Table IV.

Table IV. Characteristics of hydrogels with hydroalcoholic extracts of lovage

Characteristics	Formula 1	Formula 2	Formula 3
Initial organoleptic evaluation	<i>appearance:</i> homogeneous; <i>color:</i> pale yellow; <i>odor:</i> specific	<i>appearance:</i> homogeneous; <i>color:</i> yellow-green; <i>odor:</i> specific	<i>appearance:</i> homogeneous; <i>color:</i> green; <i>odor:</i> specific
Organoleptic evaluation after 30 days	maintaining the original characteristics unchanged	maintaining the original characteristics unchanged	maintaining the original characteristics unchanged
Organoleptic evaluation after 60 days	maintaining the original characteristics unchanged	maintaining the original characteristics unchanged	maintaining the original characteristics unchanged
pH – initial	4.5 -5	4.7 - 5.2	5 - 5.5
pH – after 30 days	4.5 -5	4.7 - 5.2	5 - 5.5
pH – after 60 days	5 – 5.2	5.3 – 5.5	5.5 – 5.8
Viscosity – inițială	824 ± 0.35 Pa·s	812 ± 0.25 Pa·s	780 ± 0.33 Pa·s
Viscosity – after 30 days	808 ± 0.65 Pa·s	796 ± 0.66 Pa·s	766 ± 0.45 Pa·s
Viscosity – after 60 days	782 ± 0.53 Pa·s	774 ± 0.50 Pa·s	758 ± 0.25 Pa·s

Table V. Antioxidant activity of hydrogels with hydroalcoholic extracts of lovage.

Sample	DPPH inhibition at 100 µg/mL	ABTS inhibition at 100 µg/mL
Hydrogel with hydroalcoholic leaf extract	77.6 ± 2.4 %	69.4 ± 1.6 %
Hydrogel with hydroalcoholic root extract	63.8 ± 1.2 %	61.2 ± 2.2 %

Hydrogel with hydroalcoholic extract from the whole plant	69.2 ± 1.6 %	65.8 ± 1.4 %
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It is observed that the hydrogel with lovage leaf extract exhibits the highest free radical neutralization capacities, both in the case of the ABTS method (69.4%) and the DPPH method (77.6%). These results are consistent with the high content of flavonoids identified in the leaf extract, especially quercetin, rutin and apigenin, which are compounds recognized for their powerful antioxidant effects.

6.1. Characterization of dermatocosmetic preparations based on hydroalcoholic macerates with *Rosmarinus officinalis* L.

The characteristics of the analyzed hydrogels are presented in Table VI and Figure 3.

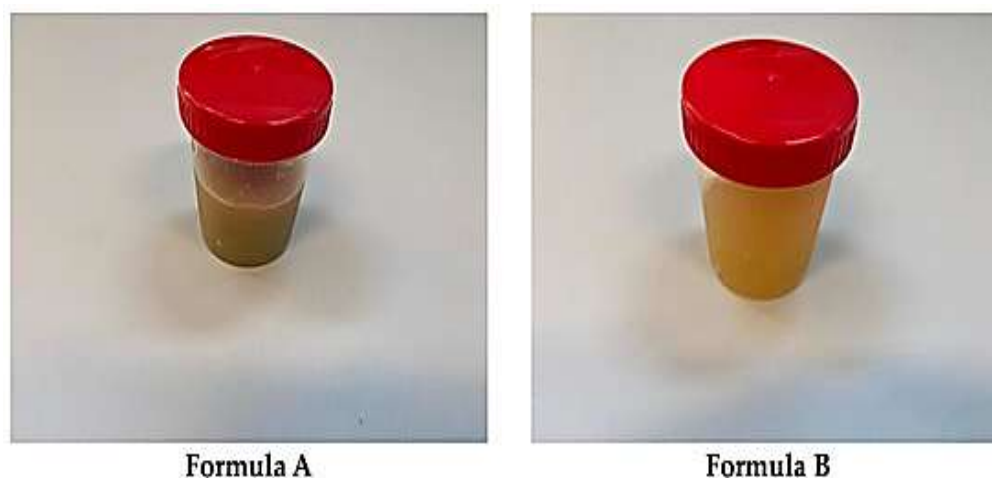


Fig. 3. Hydrogels based on rosemary macerates

Table VI. Characteristics of hydrogels based on rosemary macerates.

Characteristics	Formula A	Formula B
Initial organoleptic evaluation	<i>appearance:</i> homogeneous; <i>color:</i> green; <i>odor:</i> specific	<i>appearance:</i> homogeneous; <i>color:</i> yellow-green; <i>odor:</i> specific
Organoleptic evaluation after 30 days	maintaining the original characteristics unchanged	maintaining the original characteristics unchanged
Organoleptic evaluation after 60 days	maintaining the original characteristics unchanged	maintaining the original characteristics unchanged
pH – initial	4.8 – 5.0	4.7 – 4.9
pH – after 30 days	5.0 – 5.2	5.1 – 5.3
pH – after 60 days	5.4	5.5
Viscosity – inițială	680 ± 0.66 mPa·s	655 ± 0.25 mPa·s
Viscosity – after 30 days	662 ± 0.75 mPa·s	633 ± 0.66 mPa·s
Viscosity – after 60 days	634 ± 0.36 mPa·s	610 ± 0.52 mPa·s

The characteristics of the dermatocosmetic creams analyzed are presented in Table VII. and Figure 4.

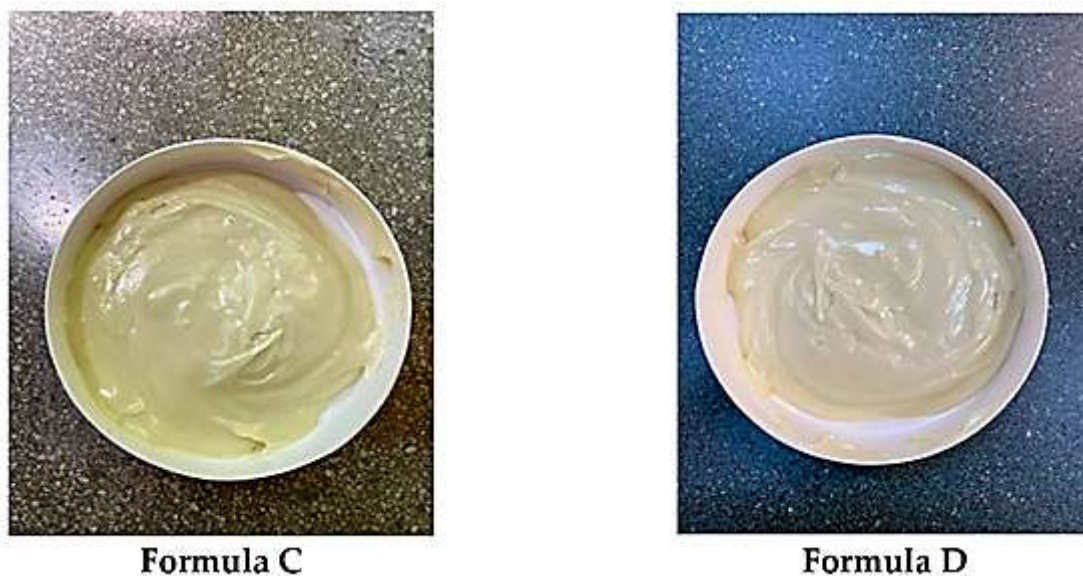


Fig. 4. Rosemary macerate-based creams

Table VII. Characteristics of rosemary macerate-based creams.

Characteristics	Formula C	Formula D
Initial organoleptic evaluation	<i>appearance:</i> homogeneous; <i>color:</i> green; <i>odor:</i> specific	<i>appearance:</i> homogeneous; <i>color:</i> yellow-green; <i>odor:</i> specific
Organoleptic evaluation after 30 days	maintaining the original characteristics unchanged	maintaining the original characteristics unchanged
Organoleptic evaluation after 60 days	maintaining the original characteristics unchanged	maintaining the original characteristics unchanged
pH – initial	5.0 – 5.2	5.3 – 5.4
pH – after 30 days	5.2 – 5.4	5.4 – 5.5
pH – after 60 days	5.5	5.6
Viscosity – inițială	978 ± 0.36 mPa·s	956 ± 0.25 mPa·s
Viscosity – after 30 days	956 ± 0.45 mPa·s	923 ± 0.55 mPa·s
Viscosity – after 60 days	930 ± 0.33 mPa·s	902 ± 0.66 mPa·s

Table VIII. Antioxidant activity of dermatocosmetic preparations.

No	Sample / dilution / volume	Maximum inhibition of free radicals	Total antioxidant capacity (nM TE/ μ L)	TEAC (mg TE/100 g sample)
1.	Formula A / stock solution / 5 μ L;	0.965	-3.504	-
2.	Formula B / stock solution / 5 μ L;	0.645	-2.304	-
3.	Formula C stock solution / 5 μ L;	0.874	-3.849	-
4.	Formula D / stock solution / 5 μ L;	0.704	-2.756	-

According to the presented results, the highest antioxidant activities were demonstrated by Formula C, followed by Formula A.

The experimental results demonstrate a significantly higher anti-inflammatory effect for dermatocosmetic creams compared to hydrogels, as evidenced by their ability to substantially reduce post-treatment inflammation levels [26].

Among all the tested formulations, Formula C exhibited the most pronounced anti-inflammatory activity. This was particularly evident in the reduction of kaolin-induced edema at 4 hours after induction and in the suppression of dextran-induced edema at 90 minutes after inflammation induction. The edema inhibition (E%) for inflammation induced by dextran solution is 49.2% for Formula C after 90 minutes and 62.3% for the reference group, and in the case of inflammation induced by kaolin suspension it is 49.63% for Formula C after 4 hours and 60.66% for the reference group, the data indicating a significant anti-inflammatory effect for Formula C.

CONCLUSIONS AND PERSONAL CONTRIBUTIONS

In this thesis, we aimed to obtain and evaluate extractive products from *Levisticum officinale* L. and *Rosmarinus officinalis* L., as well as to develop and characterize topical preparations with them. The extractive products were characterized from a physicochemical and bioactive point of view, focusing on their antioxidant, antimicrobial and anti-inflammatory properties, then they were incorporated into different pharmaceutical forms for topical application (hydrogels and emulsions). The pharmaceutical systems were evaluated from a pharmacotechnical and biological point of view, in order to establish their performance after application to the skin.

Regarding the composition of extractive products from *Levisticum officinale* L., the results indicate a differentiated distribution of polyphenolic compounds depending on the part of the plant used for extraction, which can be correlated with the metabolic variability of *Levisticum officinale*. Lovage leaves have a significantly higher content of phenolic compounds compared to roots,

which can be explained by the physiological role of these secondary metabolites in protection against oxidative stress and environmental factors, such as UV radiation or pathogens.

In addition, the chemical composition of the extracts is also influenced by the differential solubility of these metabolites in the solvent used, 70% ethanol being known for its efficiency in the extraction of flavonoids and phenolic acids, but also for its variable selectivity towards different classes of polyphenols.

Analysis of the phenolic acid content revealed the highest content in the hydroalcoholic extract of the whole plant (18.26 ± 1.65 mg GAE/g) and the lowest content in the alcoholic extract of the leaves (8.08 ± 0.33 mg GAE/g).

The results obtained regarding the content of condensed tannins indicate a significantly higher accumulation of these compounds in the hydroalcoholic extract of lovage leaves, compared to the extracts obtained from the root and the whole plant.

The analysis of the phenolic profile highlights a higher concentration of flavonoids, such as quercetin, kaempferol and rutin, in the leaves, while the roots present high levels of phenolic acids, including ferulic, caffeic and vanillic acids.

The hydroalcoholic extract of the leaves presented the highest antioxidant activity, with values of 276.2 ± 3.4 $\mu\text{mol TE/g}$ by the ABTS method and 246.4 ± 3.6 $\mu\text{mol TE/g}$ by the DPPH method. These results can be correlated with the high content of flavonoids and phenolic acids identified in the extract, especially quercetin, rutin, luteolin and chlorogenic acid, known for their ability to donate electrons and neutralize reactive oxygen species.

In the case of extractive products from *Rosmarinus officinalis* L., the highest total tocopherol concentration (TPC) was recorded in Dobrogean rosemary macerated with 70% ethanol (RDS2), reaching 2155 ± 2.45 mg GAE/100 g body weight, while the lowest was found in Bulgarian rosemary extracted with 96% ethanol (RBS1) (430 ± 1.25 mg GAE/100 g body weight). These findings highlight the preferential solubilization of phenolic compounds in 70% ethanol, attributed to its balanced polarity, which facilitates the extraction of both hydrophilic and lipophilic phenolic compounds.

The Dobrogean rosemary macerate (RDS2) showed the highest radical scavenging activity (745.0 ± 2.33 mg GAE/100 g b.w.), while its Bulgarian counterpart (RBS2) demonstrated a significantly lower activity (397.5 ± 1.76 mg GAE/100 g b.w.).

The highest TFC value was also observed in the Dobrogean sample macerated with 70% ethanol (RDS2), with a value of 283.6 ± 1.52 mg QE/100 g fresh weight (g), which strongly correlates with its higher total phenolic content and antioxidant activity. This suggests that the 70% ethanol extraction effectively solubilizes flavonoids, which play a key role in enhancing the free radical scavenging potential of rosemary.

The results confirm that the RDS2 macerate exhibits superior antimicrobial activity compared to RBS2, especially against Gram-positive bacteria and yeast. This difference can be attributed to the higher content of polyphenolic compounds, such as carnosic acid and rosmarinic acid, in RDS2, which are known for their potent antimicrobial properties.

The hydrogels prepared with the hydroalcoholic extracts of *Levisticum officinale* L. exhibit good physicochemical stability, maintaining their essential properties throughout the testing period. The pH parameter was stable in the range of 4.5–5.5, making them suitable for topical application, being compatible with the physiological pH of the skin. The lack of significant variations suggests that the bioactive extracts did not undergo major degradation and that the hydrogel matrix ensured adequate stability.

Comparing the three types of hydrogels, it is observed that the hydrogel with lovage leaf extract presents the lowest initial viscosity, which can be attributed to the interaction of flavonoids and tannins with the hydrogel structure, modifying the polymer network and increasing its flexibility.

From a macroscopic perspective, all four preparations containing hydroalcoholic macerates of *Rosmarinus officinalis* L. exhibit homogeneity, ensuring uniform distribution of the active ingredients in all formulations. The stability of these preparations is noteworthy, as no phase separation, sedimentation or visible changes in texture were observed over time, highlighting their robustness under standard storage conditions. In addition, their pH values are compatible with the physiological pH of the skin, minimizing the risk of irritation and making them suitable for long-term dermal application.

The rheological attributes of the hydrogels with Formula A and Formula B, developed using a hydroalcoholic extract of rosemary, demonstrate the key characteristics of well-structured formulations. Both formulas exhibited favorable viscosity profiles, ensuring ease of application and stable adhesion to the skin surface.

According to the presented results, the highest antioxidant activities were demonstrated by Formula C, followed by Formula A.

The experimental results demonstrate a significantly greater anti-inflammatory effect for dermatocosmetic creams compared to hydrogels, evidenced by their ability to substantially reduce post-treatment inflammation levels.

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