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Research paper

Comparative study of different gel bases with herbal and synthetic active substance

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Abstract

This study compares two gel bases in which either natural or synthetic active substances are incorporated: *Philadelphus coronarius* flower extract and BGP-15. The preparations were evaluated for texture analysis, *in vitro* drug release and pH characteristics. Gels were formulated using Carbopol 940 or hydroxypropyl methylcellulose (HPMC) as gelling agents. Texture analysis revealed comparable mechanical properties with slight increases in firmness upon incorporation of active substances. *In vitro* release studies demonstrated rapid early release for both gel bases, with *Philadelphus coronarius* reaching approximately 27% release at 180 minutes and BGP-15 achieving ~26% release. The findings support the dermal applicability of both agents and highlight their potential roles in natural and synthetic therapeutic skin preparations.

Keywords: gels, BGP-15. Philadelphus coronarius

1.Introduction

Topical preparations are applied directly to the skin or mucous membrane to treat various conditions. They are available in multiple forms, such as creams, ointments, gels, lotions, powders or patches. Commonly used for issues like skin infections, inflammation and localized conditions, these medications deliver targeted relief without significant systemic effects (1,2).

Nowadays gels are one of the most popular topical preparations due to their advantages (3). Creams, especially thicker ones, often leave a greasy or oily finish on the skin, while gels are lighter and absorb faster(4). Gels are typically designed to penetrate the skin more quickly than creams, making them ideal for products intended to deliver active ingredients directly (5). Moreover, gels are especially preferred for people with oily or acne-prone skin, as they don't contribute to excess oil buildup. Many patients find the cool, refreshing sensation of gels more appealing, particularly in hot weather or as part of post-workout routines (6).

Philadelphus coronarius (P. coronarius), commonly known as sweet mock-orange or syringa, is a deciduous shrub in the family Hydrangeaceae. *P. coronarius* has a long history of use in traditional medicine, although it lacks extensive scientific research compared to other herbs utilized in medicine. Its primary reported effects and applications include antimicrobial, antioxidant and anti-inflammatory properties thus potential benefits in topical formulations. Both the flower and the leaf of the herb possesses beneficial properties (7–9).

BGP-15 is a Hungarian developed drug candidate. It's a nicotinic amid-oxime derivate with various benefits including insulin sensitizing effect, cardioprotective effect and anti-inflammatory effect as well. The mechanism of action is not fully understood yet, BGP-15 is able to induce heat shock protein synthesis, which is crucial for protecting cells from stress-induced damage and maintaining cellular integrity under various environmental conditions. BGP-15 is also known for its antioxidant properties, which significantly contribute to its skin-protective effects (10–12).

The aim of our research was to formulate gels with either BGP-15 or *P. coronarius* leaf. Two gel bases were chosen for the research: carbopol 940 and hydroypropyl-methylcellulose (HPMC). In total four gels were formulated and tested from the aspect of texture, active ingredient release as well as pH.

2. Materials and methods

2.1 Materials

As gelling agent Carbopol 940 NF and HPMC was chosen. These materials were purchased from Sigma Aldrich (St. Louis, Missouri, United States) as well as Triethanolamine. BGP-15 was purchased from SONEAS Chemicals Ltd. (formerly known as Ubichem Pharma Services, Budapest, Hungary). *P. coronarius* flower extract

was utilized in lyophilized form which was obtained from the University of Oradea (Oradea, Romania).

2.2 Methods

2.2.1. Formulation

The composition of the formulated gels are summarized in Table 1. Powders were accurately measured on centigram quick balance. All weighing procedures were performed using a centigram-precision balance (readability: 0.01 g). The balance used in this research was a digital precision balance (Kern ABT PNJ 3000-2M, Balingen, Germany). The instrument was calibrated prior to use according to the manufacturer's instructions to ensure measurement accuracy and reproducibility.

BGP-15 and lyophilized *P. coronarius* leaf extract was immediately dissolved in purified water. After adding the polymers it was stirred with the help of a magnetic stirrer until a solution was formed. In case of HPMC a thick gel was obtained at the end while with Carbopol 940 an opalescent solution was formed which was thickened and cleared by adding 4-5 drops of triethanolamine.

Composition	Quantity	Gel 1	Gel 2
Carbopol 940	0.5 g	+	-
HPMC	5.0 g	-	+
Triethanolamine	4-5 drops	+	-
P. coronarius	5.0 g	+	-
BGP-15	10.0 g	-	+
Purified water	ad 100.0 g	+	+

Table 1*.:* Composition of the formulated gels.

2.2.2. Texture analysis

Texture analysis was performed with the Brookfield CT3 Texture Analyzer. The samples were placed in the sample holder. During the investigation compression test was performed in normal mode with the following settings: target value (5 mm), target

load (4 g), target speed (0.5 mm/s). In the test the resistance of the gels were measured (13).

2.2.3 In vitro release of the active ingredients

In vitro release of the active ingredients was evaluated with Franz diffusion cell apparatus. The cell consists of an acceptor phase (the gels) and a receptor phase (pH=5.5 buffer solution). Between the two phases synthetic membrane cellulose-acetate membrane was used which was impregnated with isopropyl-myristate beforehand to mimic the lipophilic character of the skin. The released active ingredient in the receptor phase was constantly stirred at 300 rpm with magnetic stirrer. The whole system was heated to 32°C to model the skin's temperature. At predetermined time intervals 1 mL samples were taken. Samples from Gel 1 (containing *P. coronarius* flower) were analyzed with spectrophotometer at 254 nm, while samples from Gel 2 (containing BGP-15) were analyzed with HPLC (14).

The diffused amount of BGP-15 was measured with HPLC. The samples were filtered on 0.2 µm polyethersulfone membrane. The sample solutions were analyzed using a HPLC system (Merck-Hitachi, Tokyo, Japan ELITE with photodiode array detector (DAD)). The column was an Aquasil C18 (5 µm 100 × 2.1 mm) with a C18 guard column (5 µm, 4 × 3 mm) and kept at 40 °C, and the DAD was set to 254 nm. The mobile phase was an acetonitrile and water solution at a ratio of 1:9 (contain-ing 0.1% acetic acid), and a 1.0 mL flow rate was used. The analyses were performed with EZChrom Elite softwareTM (Hitachi, Tokyo, Japan), which was also used for collecting and processing the data. Standard solution (10 µL) and purified samples were injected.

2.2.4 pH measurement

The pH of the gels was measured using a Mettler Toledo pH meter. For this purpose, 5 g of the preparation was pre-measured, to which 20 ml of purified water was added, heated to 37°C and stirred with a magnetic stirrer. After cooling the dispersion to room temperature, it was filtered and the pH of the filtrate was measured using the apparatus. The electrode of the instrument was placed in the filtrate and the pH of the gel was read by pressing the "Read" button. The pH of the gels was measured again after 3 months to check for any changes. During the 3 months, the samples were kept in a climate chamber at 25°C, 60% relative humidity. The samples were stored in plastic jars. (15).

2.2.5 Statistical analysis

Data were analyzed with Excel (Microsoft 365), data present average values, n=3. Unpaired t-test was chosen to compare groups. Differences are regarded as significant, with $p < 0.05$. The results illustrated in the figures include the standard deviation.

3. Results

3.1 Texture analysis

The compression force required for the cylinder to penetrate the gels is shown in Figure 1. Based on these force measurements, the formulation containing BGP-15 and HPMC exhibit a firmer consistency. The Carbopol 940 based formulation is the softer. Lower resistance values are desirable, as they correspond to easier application and improved release of the active pharmaceutical ingredient.

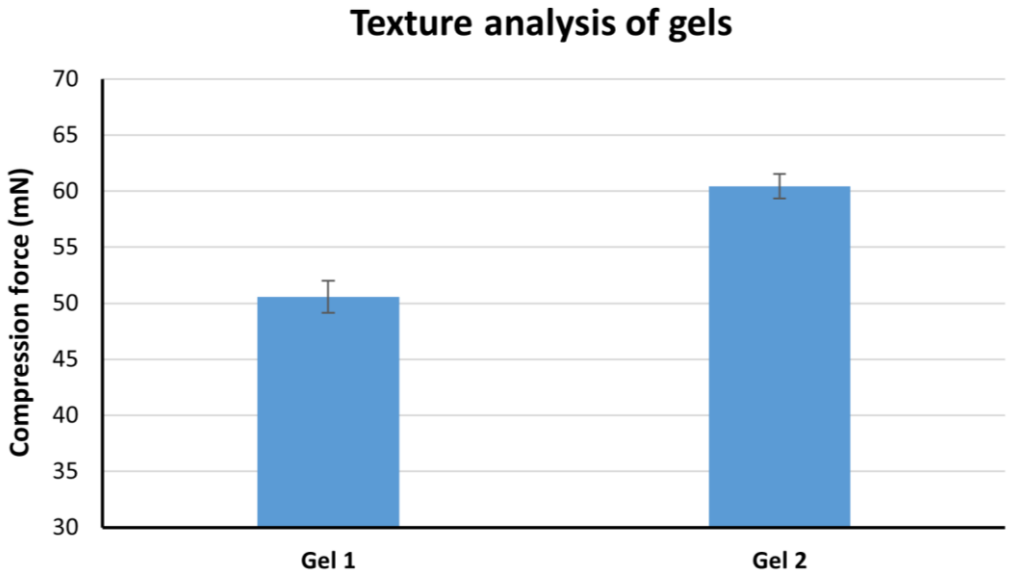

Figure 1.: Texture analysis of the gel formulations.

3.2 In vitro release

Figure 2 presents the diffused amount of active substances of the different compositions across cellulose acetate membrane impregnated with isopropyl myristate. From gel 1 27.64% of *P. coronarius* diffused to the receptor phase, while 26.81% of BGP-15 was released from gel 2. In both cases the majority of the active substance released within the first hour of the experiment. At the 60th minute 19.03%

of *P. coronarius* was released from gel 1 and 21.62% of BGP-15 was released from gel 2. After that a slowly increasing tendency can be observed.

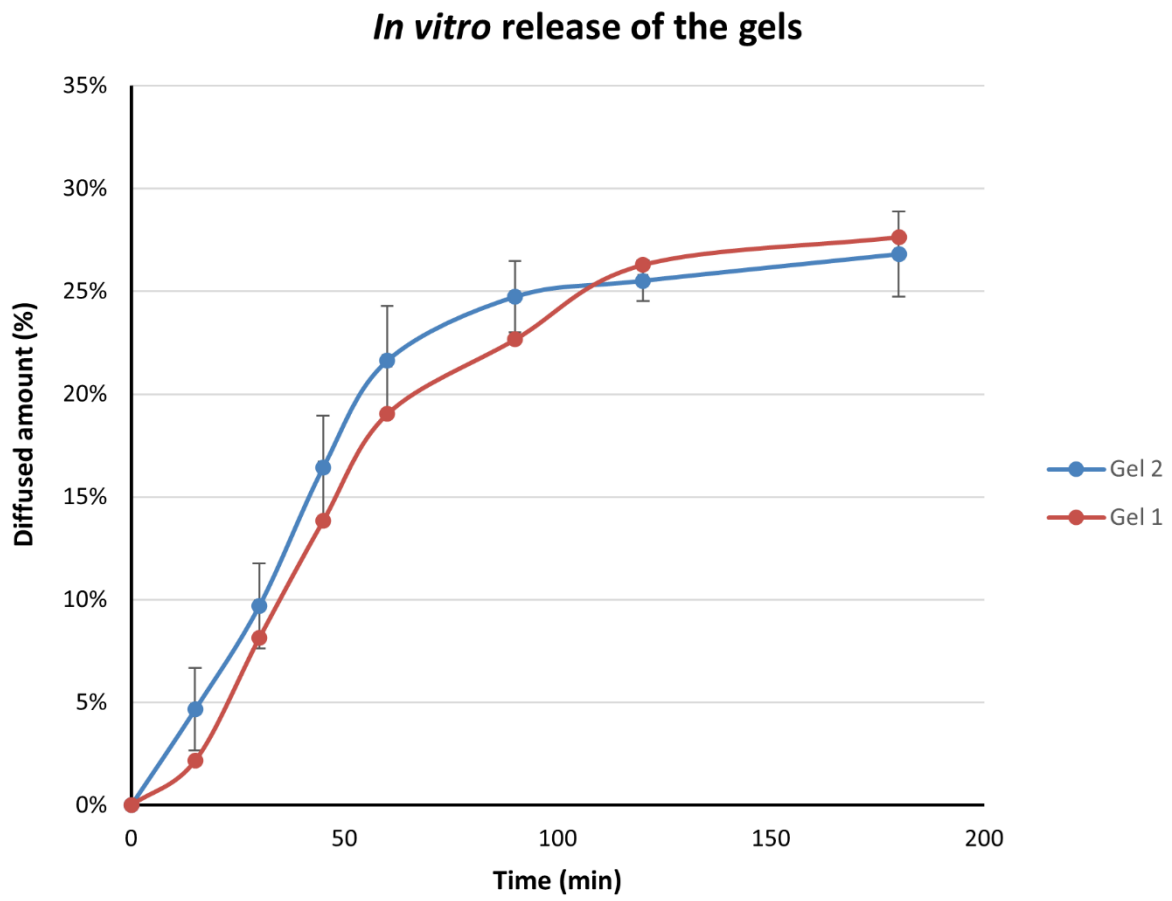

***Figure 2**.: In vitro* release of the gels.

3.3 pH measurement

At the time of formulation pH values were 4.8 for gel 1 and 4.2 for gel 2. After 3 months pH was measured again and the values were slightly increased. The pH was 5.3 for gel1 and 5.1 for gel 2. The values are listed in Table 2.

	pH at the time of formulation	pH after 3 months
Gel 1	4.8	5.3
Gel 2	4.2	5.1

***Table 2**.:* pH values of the formulated gels.

4. Discussion

The present study aimed to develop and compare two topical gel formulations incorporating either a natural (*P. coronarius* flower extract) or a synthetic (BGP-15) active substance, using two widely applied gelling agents: Carbopol 940 and HPMC. After formulation the aim was to test the gels from different aspects.

Texture analysis revealed no significant differences between the formulations. In case of gel 1 the results demonstrated a softer consistency and gel 2 exhibited higher firmness compared with the Carbopol-based formulation. This observation aligns with the known rheological behavior of HPMC, which generally forms more cohesive and viscous matrices compared with Carbopol. A firmer consistency may contribute to enhanced product stability, although softer gels offer advantages in ease of application and potentially improved spreadability on the skin (16,17).

The *in vitro* release studies further demonstrated that both Carbopol and HPMC gels allowed rapid initial release of the incorporated active substances. This early burst effect is advantageous for dermal formulations aimed at achieving rapid local therapeutic action. The release profile of *P. coronarius* from the Carbopol gel reached approximately 27.64% by 180 minutes, which is similar to the release of BGP-15 from HPMC gel (26.81%). Notably, more than two-thirds of this release occurred within the first 60 minutes for both substances, reflecting comparable permeability across the cellulose acetate membrane and confirming that both gel bases provide sufficient hydration and diffusion pathways for early drug transport. This finding supports the versatility of both polymer systems for delivering structurally different active substances (18).

The pH values of both gels are within an acceptable range for dermal application and demonstrated only minor increases after three months of storage. A gradual pH rise is typical in polymer-based gels and may result from polymer relaxation, partial neutralization, or interactions with water over time. Importantly, the measured final pH values (5.1–5.3) remain compatible with healthy skin, suggesting good stability and low risk of irritation during storage (19,20).

Overall, the results suggest that both Carbopol 940 and HPMC are appropriate gel bases for incorporating natural or synthetic active ingredients. While the Carbopol gel demonstrates superior softness and handling properties, the HPMC gel provides a

firmer, more structured matrix. Both systems support rapid release of the active substances, indicating their suitability for dermal formulations intended to deliver antioxidant or anti-inflammatory effects. The successful incorporation of both *P. coronarius* extract and BGP-15 expands the potential therapeutic applications of these gels, from natural skincare products to targeted pharmacological preparations.

Future investigations should be directed toward a more comprehensive preclinical evaluation of the developed formulation. In particular, *in vitro* cytotoxicity and biocompatibility studies using relevant cell lines, such as MTT assays, are necessary to confirm cellular safety. Furthermore, *in vitro* permeation studies across excised porcine ear skin should be conducted to better predict transdermal or topical drug delivery performance under physiologically relevant conditions. Provided that these experiments yield favorable results, subsequent in vivo studies may be warranted, potentially employing a suitable animal model such as rats, to assess pharmacokinetic behavior, efficacy, and systemic safety. In addition, long-term stability studies under controlled storage conditions are essential to evaluate the physicochemical integrity of the formulation over time, while comprehensive microbiological testing should be performed to ensure product safety and compliance with regulatory requirements.

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Data Availability Statement:

Data are available from the corresponding author with the permission of the head of the department. The data that support the findings of this study are available from the corresponding author (peto.agota@pharm.unideb.hu), upon reasonable request.

References

1. Garg T, Rath G, Goyal AK. Comprehensive review on additives of topical dosage forms for drug delivery. Drug Deliv [Internet]. 2015 Nov 17;22(8):969–87. Available from: http://www.tandfonline.com/doi/full/10.3109/10717544.2013.879355
2. Dini I, Laneri S. The New Challenge of Green Cosmetics: Natural Food Ingredients for Cosmetic Formulations. Molecules [Internet]. 2021 Jun 26;26(13):3921. Available from: https://www.mdpi.com/1420-3049/26/13/3921

3. Marto J, Baltazar D, Duarte A, Fernandes A, Gouveia L, Militão M, et al. Topical gels of etofenamate: in vitro and in vivo evaluation. Pharm Dev Technol [Internet]. 2015 Aug 18;20(6):710–5. Available from: http://www.tandfonline.com/doi/full/10.3109/10837450.2014.915571
4. Barnes TM, Mijaljica D, Townley JP, Spada F, Harrison IP. Vehicles for Drug Delivery and Cosmetic Moisturizers: Review and Comparison. Pharmaceutics [Internet]. 2021 Nov 26;13(12). Available from: http://www.ncbi.nlm.nih.gov/pubmed/34959294
5. AL-Smadi K, Ali M, Zhu J, Abdoh A, Phan K, Mohammed Y. Advances in Characterization of Transdermal and Topical Products using Texture Analyzer Systems. AAPS PharmSciTech [Internet]. 2025 Jun 3;26(5):157. Available from: https://link.springer.com/10.1208/s12249-025-03148-x
6. Gavinet B, Sigurani S, Garcia C, Roso A. Alternatives to Conventional Topical Dosage Forms for Targeted Skin Penetration of Diclofenac Sodium. Int J Mol Sci [Internet]. 2024 Jul 6;25(13):7432. Available from: https://www.mdpi.com/1422-0067/25/13/7432
7. Pető Á, Kósa D, Haimhoffer Á, Nemes D, Fehér P, Ujhelyi Z, et al. Topical Dosage Formulation of Lyophilized Philadelphus coronarius L. Leaf and Flower: Antimicrobial, Antioxidant and Anti-Inflammatory Assessment of the Plant. Molecules [Internet]. 2022 Apr 20;27(9):2652. Available from: https://www.mdpi.com/1420-3049/27/9/2652
8. Valko V, Fickova M, Pravdova E, Nagy M, Grancai D, Czigle S. CYTOTOXICITY OF WATER EXTRACTS FROM LEAVES AND BRANCHES OF PHILADELPHUS CORONARIUS L. Biomed Pap [Internet]. 2006 Jul 1;150(1):71–3. Available from: http://biomed.papers.upol.cz/doi/10.5507/bp.2006.007.html
9. Klecáková J, Chobot V, Jahodár L, Laakso I, Víchová P. Antiradical activity of petals of Philadelphus coronarius L. Cent Eur J Public Health [Internet]. 2004 Mar;12 Suppl:S39-40. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15141974
10. Pető Á, Kósa D, Fehér P, Ujhelyi Z, Sinka D, Vecsernyés M, et al. Pharmacological overview of the BGP-15 chemical agent as a new drug candidate for the treatment of symptoms of metabolic syndrome. Molecules. 2020;25(2).
11. Pető Á, Kósa D, Haimhoffer Á, Fehér P, Ujhelyi Z, Sinka D, et al. Nicotinic Amidoxime Derivate BGP-15, Topical Dosage Formulation and Anti-Inflammatory Effect. Pharmaceutics [Internet]. 2021 Nov 29;13(12):2037. Available from: https://www.mdpi.com/1999-4923/13/12/2037
12. Bácskay I, Hosszú Z, Budai I, Ujhelyi Z, Fehér P, Kósa D, et al. Formulation and Evaluation of Transdermal Patches Containing BGP-15. Pharmaceutics [Internet]. 2023 Dec 27;16(1):36. Available from: https://www.mdpi.com/1999-4923/16/1/36
13. Bodnár K, Papp B, Sinka D, Fehér P, Ujhelyi Z, Lekli I, et al. Development of Salvia officinalis–Based Self-Emulsifying Systems for Dermal Application: Antioxidant, Anti-Inflammatory, and Skin Penetration Enhancement. Pharmaceutics [Internet]. 2025 Jan 21;17(2):140. Available from: https://www.mdpi.com/1999-4923/17/2/140
14. Frei G, Haimhoffer Á, Csapó E, Bodnár K, Vasvári G, Nemes D, et al. In Vitro and In Vivo Efficacy of Topical Dosage Forms Containing Self-Nanoemulsifying Drug Delivery System Loaded with Curcumin. Pharmaceutics [Internet]. 2023 Jul

31;15(8):2054. Available from: https://www.mdpi.com/1999-4923/15/8/2054
15. Zhang F, Wang X, Guo N, Dai H, Wang Y, Sun Y, et al. Influence of Different pH Values on Gels Produced from Tea Polyphenols and Low Acyl Gellan Gum. Gels [Internet]. 2023 Apr 28;9(5):368. Available from: https://www.mdpi.com/2310-2861/9/5/368
16. Ozon EA, Anastasescu M, Musuc AM, Burloiu AM, Socoteanu RP, Atkinson I, et al. Formulation and Characterization of Carbopol-Based Porphyrin Gels for Targeted Dermato-Oncological Therapy: Physicochemical and Pharmacotechnical Insights. Int J Mol Sci [Internet]. 2025 Apr 11;26(8):3641. Available from: https://www.mdpi.com/1422-0067/26/8/3641
17. Biermann T, Mesecke L, Teves S, Ziesche I, Lachmayer R. Full-Factorial Rheological Investigation of Carbopol ETD2020 for Embedded Printing: Effects of pH and Carbomer Concentration. Materials (Basel) [Internet]. 2025 Jul 3;18(13):3164. Available from: https://www.mdpi.com/1996-1944/18/13/3164
18. Iglesias N, Galbis E, Romero-Azogil L, Benito E, Lucas R, García-Martín MG, et al. In-Depth Study into Polymeric Materials in Low-Density Gastroretentive Formulations. Pharmaceutics [Internet]. 2020 Jul 7;12(7). Available from: http://www.ncbi.nlm.nih.gov/pubmed/32645909
19. Lukić M, Pantelić I, Savić SD. Towards Optimal pH of the Skin and Topical Formulations: From the Current State of the Art to Tailored Products. Cosmetics [Internet]. 2021 Aug 4;8(3):69. Available from: https://www.mdpi.com/2079-9284/8/3/69
20. Lambers H, Piessens S, Bloem A, Pronk H, Finkel P. Natural skin surface pH is on average below 5, which is beneficial for its resident flora. Int J Cosmet Sci [Internet]. 2006 Oct 19;28(5):359–70. Available from: https://onlinelibrary.wiley.com/doi/10.1111/j.1467-2494.2006.00344.x