

## Article

# The Formulation of Dermato-Cosmetic Products Using *Sanguisorba minor* Scop. Extract with Powerful Antioxidant Capacities

Alexandra-Cristina Tocai (Moțoc)<sup>1</sup>, Adriana Ramona Memete<sup>2</sup>, Mariana Ganea<sup>3,\*</sup>, Laura Grațîela Vicaș<sup>3</sup>, Octavia Dorina Gligor<sup>4</sup> and Simona Ioana Vicas<sup>1,2,\*</sup>

<sup>1</sup> Doctoral School of Biomedical Science, University of Oradea, 410087 Oradea, Romania; tocai.alexandra@gmail.com

<sup>2</sup> Department of Food Engineering, Faculty of Environmental Protection, University of Oradea, 410048 Oradea, Romania; adrianamemete@yahoo.com

<sup>3</sup> Department of Pharmacy, Faculty of Medicine and Pharmacy, University of Oradea, 410028 Oradea, Romania; laura.vicas@gmail.com

<sup>4</sup> Faculty of Pharmacy, "Iuliu Hatieganu" University of Medicine and Pharmacy, 8 Victor Babes Street, 400012 Cluj-Napoca, Romania; gligor.octavia@umfcluj.ro

\* Correspondence: mganea@uoradea.ro (M.G.); svicas@uoradea.ro (S.I.V.)

**Abstract:** There has been a significant increase in the use of botanical resources for the formulation of topical products designed for medicinal and cosmetic applications. *Sanguisorba minor* Scop., a botanical species, exhibits a variety of properties and has significant potential for applications in the field of cosmetics. The aim of this study was to formulate topical preparations, incorporating an extract derived from the plant *S. minor* Scop. comprising a combination of roots, leaves, and flowers. In the initial phase, a total of seven combinations were prepared using extracts derived from the roots, leaves, and flowers of *S. minor* Scop. (*v/v/v*). These combinations were subsequently subjected to evaluation for their antioxidant capacity using four distinct methods: 2,2-diphenyl-1-picrylhydrazyl (DPPH), ferric reducing antioxidant power (FRAP), cupric reducing antioxidant capacity (CUPRAC), and Trolox equivalent antioxidant capacity (TEAC). An extract of plant organs in a ratio of 1:2:1 (*v/v/v*), which had a strong antioxidant capacity and demonstrated synergistic effects according to the DPPH, TEAC, and CUPRAC assays (with values of  $1.58 \pm 0.1$ ,  $1.18 \pm 0.09$ , and  $1.07 \pm 0.07$ , respectively), was selected for inclusion in three dermato-cosmetic products (hydrogel, emulgel, and cream). All the prepared preparations were evaluated in terms of topical formulation attributes and organoleptic characteristics. The testing of dermato-cosmetic products included assessments of their topical formulation properties and organoleptic characteristics. The hydrogel, emulgel, and cream exhibited varying degrees of stretchability. In addition, a study was carried out to assess the *in vitro* release of polyphenols from the cosmetic formulations using a Franz diffusion cell system. The results showed that the emulgel containing the extract of *S. minor* Scop. had the highest and most significant release of polyphenols, with a release rate of  $84.39 \pm 1.01\%$ . This was followed by the hydrogel and cream, which had release percentages of  $80.52 \pm 0.89$  and  $75.88 \pm 0.88$ , respectively, over an 8 h period. Thus, for the first time in the literature, a topical cosmetic product with high antioxidant potential containing *S. minor* Scop. extract was developed and optimized.

**Keywords:** *Sanguisorba minor* Scop.; antioxidant capacity; natural cosmetics; synergic effect; Franz diffusion cells



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## 1. Introduction

A cosmetic or toiletry that penetrates deeply enough into the skin barrier to be beneficial to the skin's structure and function is called cosmeceutical [1].

Cosmeceuticals are a combination of cosmetics and pharmaceuticals. Cosmeceuticals contain biologically active ingredients and are marketed as having medical or drug-like properties [2]. In the current context, cosmeceuticals are considered a subclass within cosmetic or drug categories. In Europe and Japan, cosmeceuticals are considered subclasses

of cosmetics; however, in the US, they are considered subclasses of drugs [3]. The Federal Food, Drug, and Cosmetic Act (FD&C Act) as well as the Fair Packaging and Labeling Act (FPLA) are the two most important laws related to cosmetics sold in the United States. Cosmetics are regulated by the FDA (Food and Drug Administration) under these laws. Other than color additives, cosmetic products and ingredients do not need FDA approval before they go on the market, but laws and regulations apply to cosmetics on the market in interstate commerce [4]. In the European Union, Regulation (EC) no. 1223/2009 offers no clear definition or regulation for cosmeceuticals. Cosmeceuticals are products between cosmetics and pharmaceuticals [5].

In recent years, natural cosmetic products have become more common due to their therapeutic benefits [6]. *Sanguisorba officinalis* L. is recognized as the most extensively distributed and researched species within the *Sanguisorba* genus. Nevertheless, *Sanguisorba minor* Scop. is now attracting interest due to its various beneficial effects on human health [7–9]. In general, *S. minor* Scop. is thought to possess curative properties due to its active components such as flavonoids, tannins, and phenolic acids [7,8], which may have therapeutic implications for wound healing and skin dermatitis.

*S. minor* Scop., which belongs to the family of Rosaceae, is a perennial plant that commonly grows in most parts of Europe, North Africa, Asia, and America [7,8,10–14]. Species of *S. minor* Scop. have been used in folk medicine for their diuretic, digestive, appetite-stimulating, and fever-relieving properties in infusions and tinctures [7,15–17]. According to Nordborg, *S. minor* Scop. grows at moist, cool altitudes and in subtropical to temperate climates [18]. As it prefers slightly dry calcareous soil with limestone rock on top or well-drained soil, *S. minor* Scop. can thrive in soils that are low in nutrients [18–23]. It has cold properties, tastes bitter and sour, and is non-toxic and fragrance-free [8,13].

*Sanguisorba minor* Scop. has been used as a food ingredient because young leaves are edible and available all year round. The herb has a nutty flavor with a cucumber undertone [7,8,13,14].

Generally, the biological activities of *S. minor* Scop. have not been investigated extensively. However, according to the literature, *S. minor* Scop. exhibits antioxidant [16,24–27], antiulcerogenic [17,28], antitumor [29], antimicrobial [10–12], neuroprotective [25,30], and anti-inflammatory activities [31,32]. There is a lack of particular knowledge regarding the use of *S. minor* Scop. for the treatment of skin diseases. However, it has been noticed that the roots of *S. officinalis* L. have shown efficacy in treating conditions such as urticaria, eczema, allergic dermatitis, and burns [8,33–36].

The presence of tannins, flavonoids, phenolic acids, and fatty acids in *S. minor* Scop. has been highlighted in phytochemical analyses. According to the findings of our previous study [7], the primary constituents identified in *S. minor* Scop. using HPLC–DAD–MS (ESI<sup>+</sup>) were punicalagin gallate and caffeic acid-glucoside in the roots; ellagic acid hexoside, catechin, B-type (epi) catechin dimer (isomer 1), quercetin-glucuronide, and kaempferol-glucuronide in the leaves; and 2,3-Hexahydroxydiphenoyl-glucose, sanguinin H-10 derivative, sanguinin H-1, quercetin-glucoside, and *p*-Coumaroylquinic acid in the flowers.

The utilization of creams derived from synthetic sources in the cosmetics industry has been associated with detrimental effects on the skin and the occurrence of allergic reactions. In light of these concerns, the development of pharmaceutical formulations derived from natural sources, commonly referred to as “green cosmeceuticals”, has emerged as a promising alternative. These eco-friendly products have demonstrated positive effects on the environment and human health while also exhibiting a reduced incidence of adverse reactions [37]. Antioxidants provide a dual purpose in various topical cosmetic formulations. Antioxidants protect products from potential oxidation processes. Furthermore, active antioxidant compounds present in cosmetic formulations have the ability to prevent damage to the skin from oxidative damage induced by UV radiation and the aging process [38]. Topically applying cosmetic products containing antioxidants can enhance the skin’s innate defense mechanisms. Antioxidants play a crucial role in preserving skin

health by protecting the skin from oxidative stress and effectively mitigating negative effects when applied topically [39,40].

The objective of our research was to find an extract with a potent antioxidant capacity by combining extracts from the roots, leaves, and flowers of *S. minor* Scop. in different ratios. This was done to find an extract that could be successfully integrated into various dermatocosmetic formulations. Thus, three different care products, namely, cream, hydrogel, and emulgel, were developed to include an extract obtained from *S. minor* Scop. All the acquired products were subjected to evaluations from both physico-chemical and organoleptic perspectives. In addition, the release of polyphenols from all three dermatocosmetic products was evaluated via *in vitro* investigations employing a Franz diffusion cell. To the best of our knowledge, there have been no reported cases in the specialized literature or by the cosmetic industry of skincare products containing *S. minor* Scop. extract up to now. Another aspect of novelty is a thorough examination of the combinations of extracts from the organs of the *S. minor* Scop. plant from the perspective of antioxidant capacity, given that these medicinal plants are typically used either whole or only as an organ for inclusion in cosmetic products.

## 2. Materials and Methods

### 2.1. Chemicals and Reagents

Mango butter, beeswax, olive emulsifier, vegetable glycerin, tocopherol, and fragard were purchased from Ellemental Oradea, Romania; carbomer and triethanolamine were purchased from Vitamar Import-Export S.R.L., Bucharest, Romania; and ethanol was purchased from Merck, Darmstadt, Germany. All of the ingredients came with a quality certificate. The distilled water was obtained in the private laboratories with a GFL/205458 type 2008 distiller.

The DPPH (2,2-Diphenyl-1-picrylhydrazyl), Trolox (6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid), and ABTS (2,2-azino-bis (3-ethylbenzothiazoline-6 sulfonic acid) were procured from Sigma Aldrich, Saint Louis, United States, while the 2,4,6-tris (2-pyridyl)-S-triazine (TPTZ) was procured from Fluka Chemicals, Buchs, Switzerland. The neocuproine was procured from Carl Roth Karlsruhe, Germany. All other reagents were of analytical grade.

A six-cell Franz diffusion system (Microette-Hanson system, model 57-6AS9, Copley Scientific Ltd., Nottingham, UK) was used.

### 2.2. Plant Material

*S. minor* Scop. was collected in May 2022 from Bucea village, Cluj country, situated between 46°96'30" N and 22°68'05" E. At 648 m altitude, Bucea village has a hilly and meadowy relief. *S. minor* Scop. plants were identified by the Department of Pharmaceutical Botany at the University of Oradea. Specimens of *S. minor* Scop. were kept in the Herbarium of the Faculty of Medicine and Pharmacy, Oradea, Romania, and registered in the NYBG Steere Herbarium under the code Uop 05 367-*S. minor* Scop. After the harvesting process, the roots, leaves, and flowers were cleansed using distilled water and subsequently dried in the absence of light for a duration of 21 days at room temperature. Before their application, the dried organs of *S. minor* Scop. were ground up using a coffee grinder (Heinner HCG-150SS, Bucharest, Romania). The powder obtained from the leaves and flowers was passed through a pharmaceutical sieve (no. I) with a mesh size of 5600 µm, while the powder from the roots was passed through a pharmaceutical sieve (no. II) with a mesh size of 4000 µm, according to the Romanian Pharmacopoeia, Edition X and European Pharmacopoeia 11.0 EDQM [41,42]. Subsequently, each sample was individually stored in an airtight, brown container.

### 2.3. Extraction Procedure

The bioactive compounds from the organs of *S. minor* Scop., such as the roots, leaves, and flowers, were extracted using a 70% ethanol solution. The extraction was performed using a ratio of 1 part of the plant material to 10 parts of the solvent (weight/volume). The

mixture was then allowed to macerate for a period of 7 days. Subsequently, the mixtures were centrifuged (using a NÜVE NF 200 Centrifuge, Ankara, Turkey) at 5000 rpm for 20 min. A rotary evaporator was used to remove ethanol from the extracts (Heidolph laborota 4010, Schwabach, Germany) [43]. The samples were labeled as SMR to indicate *S. minor* Scop. roots, SML to denote *S. minor* Scop. leaves, and SMF to represent *S. minor* Scop. flowers. Table 1 shows the ratios (v/v/v) used in the extracts as well as the sample codings in order to produce diverse combinations involving roots, leaves, and flowers.

**Table 1.** The combinations used for *S. minor* Scop. extracts and an explanation of their codifications.

Codification Samples	Codification Explanation
1:1:1	Equal parts of roots, leaves, and flowers of <i>S. minor</i> Scop. (v/v/v)
2:1:1	The ratio of roots, leaves, and flowers of <i>S. minor</i> Scop. was 2:1:1 (v/v/v)
2:2:1	The ratio of the roots, leaves, and flowers of <i>S. minor</i> Scop. was 2:2:1 (v/v/v)
2:1:2	The ratio of the roots, leaves, and flowers of <i>S. minor</i> Scop. was 2:1:2 (v/v/v)
1:2:1	The ratio of the roots, leaves, and flowers of <i>S. minor</i> Scop. was 1:2:1 (v/v/v)
1:2:2	The ratio of the roots, leaves, and flowers of <i>S. minor</i> Scop. was 1:2:2 (v/v/v)
1:1:2	The ratio of the roots, leaves, and flowers of <i>S. minor</i> Scop. was 1:1:2 (v/v/v)

#### 2.4. Development of the Cosmetic Formulations

The products were formulated and prepared according to Table 2 in the laboratory of a pharmacy. The cream was formed by mixing the oil phase, water phase, actives, and excipients, while the hydrogel and emulgel were formed when a gelling agent was added to the water phase and then continued with the actives or oil phase (in the case of emulgel) and excipients, as shown in Table 2.

**Table 2.** The quantities of components employed in the formulation of three cosmetic formulations.

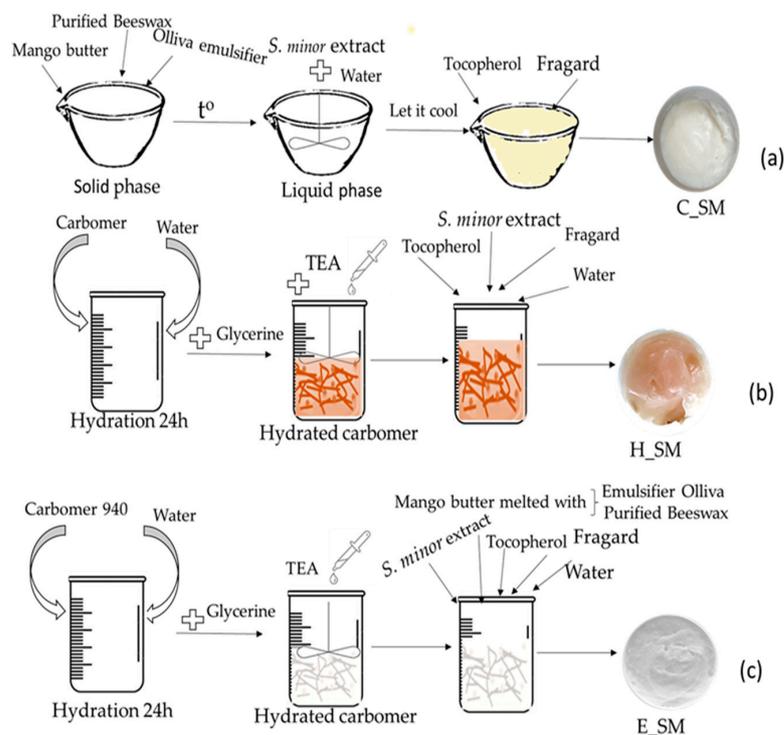
Components	Cream (g)	Hydrogel (g)	Emulgel (g)
Mango butter	7.50	-	7.50
Extract of <i>S. minor</i> Scop. *	1.00	1.00	1.00
Purified beeswax	2.00	-	2.00
Olliva emulsifier	3.00	-	3.00
Vegetable glycerin	3.40	3.40	3.40
Carbomer 940	-	1.00	1.00
TEA (triethanolamine)	-	1.00	1.00
Tocopherol	0.50	0.50	0.50
Fragard	0.60	0.60	0.60
Distilled water	82.00	92.50	80.00

\* Each cosmetic formulation contained 1 mL of liquid extract of *S. minor* Scop in a ratio of 1:2:1 (v/v/v).

All preparations were formulated with natural ingredients, according to our own protocol. All of the cosmetic formulations were formulated and prepared in the laboratory of a pharmacy and the experimental design of preparing the cream (C\_SM), hydrogel (H\_SM), and emulgel (E\_SM) is shown in Figure 1.

The C\_SM was prepared using the following protocol: the ingredients, including mango butter, beeswax, and Olliva emulsifier, were heated to a temperature of 80 °C in a heat-resistant glass that was placed in a water bath. The mixture was stirred moderately during the heating process. Separately, in another heat-resistant glass, the distilled water was heated together with the ethanol extract from *S. minor* Scop. up to a temperature of 80 °C. At the temperature of 80 °C, the distilled water together with the extract of *S. minor* Scop. was added to the main preparation vessel and kept under homogenization and vigorous stirring for 5–10 min, without cooling, until a homogeneous emulsion was

obtained. After obtaining the emulsion, glycerin was gradually added. The emulsion that was obtained was cooled to a temperature of 30 °C, with moderate stirring. After the composition had cooled, fragard and tocopherol were incorporated and thoroughly mixed until a uniform mixture was achieved.



**Figure 1.** The design of cosmeceutical products: (a) C\_SM-cream with *S. minor* Scop. extract; (b) H\_SM-hydrogel with *S. minor* Scop. extract; (c) E\_SM-emulgel with *S. minor* Scop. extract.

The cream was uniformly mixed and vigorously stirred for a duration of 5 min while it underwent the cooling process. The cream was later recovered in the original packaging in accordance with the established protocol (Figure 1).

The H\_SM was prepared via the following instructions: carbopol was dispersed within a solution containing glycerin and water. The mixing process was extended to achieve improved dispersion. Following a 24 h period of being left at room temperature, the mixture underwent analysis. When the carbopol hydration process was completed, TEA (triethanolamine) dispersed in a mixture of ethyl alcohol and water was added in small amounts and kept under continuous stirring until the gel became clear. To the extract of *S. minor* Scop., fragard and tocopherol were added one by one under continuous stirring and then the rest of the water was added. The H\_SM was later recovered in the original packaging in accordance with the established protocol (Figure 1).

The following steps were taken to prepare the E\_SM. The emulgel was formed through the dispersion of carbopol in a solution containing glycerin and water. The mixing process was prolonged for better dispersion. We allowed the mixture to remain at room temperature for a total of 24 h. Upon completing the carbopol hydration process, small amounts of TEA were introduced into a solution consisting of water and ethanol under continuous stirring until the gel achieved clarity. In parallel, the mango butter, beeswax, and Olliva emulsifier were melted and the composition was slowly mixed by adding the *S. minor* Scop. extract and, when the composition had cooled down, the tocopherol, fragard, and rest of the water were added. The E\_SM was later recovered in the original packaging in accordance with the established protocol (Figure 1).

Each individual ingredient possessed specific features, which are described in more detail in Table 3.

**Table 3.** The functions of each ingredient in the emulsions that were prepared.

Ingredients	Functions	Reference
Mango butter	Skin protector, emollient, moisturizer	[44]
<i>Sanguisorba minor</i>	Antioxidant	[45]
Beeswax	Natural emulsifier, humectant, antimicrobial	[46]
Olliva emulsifier	Biodegradable surfactant/emulsifier	[47]
Water	Solvent	[48]
Glycerin	Humectant, skin protector, solvent, viscosity controller	[49]
Carbopol 940	Emulsifier, stabilizer, suspender, thickener, gelling agent	[50]
Triethanolamine	Surface-active agent	[51]
Tocopherol	Antioxidant	[52]
Fragard	Preservative, antimicrobial	[53]

An extensive literature review revealed mango butter's antibacterial, anti-inflammatory, and antimicrobial properties, indicating its complementary use as a therapeutic or protective medicine [44]. Mango butter contains tocopherols, which reduce wrinkles and roughness of the skin, while its repairing and protecting properties allow it to be used in sensitive skin care products [44]. In addition to its antimicrobial, anti-inflammatory, and antioxidant properties, beeswax is generally nonirritating and does not cause acne [46]. In contrast, glycerin increases skin hydration by acting as a humectant and skin protector [49]. Since tocopherol (vitamin E) contains antioxidant properties, topical applications have become popular treatments for a variety of skin disorders. The presence of tocopherol in formulas will improve emollient properties and reduce inflammation, which can be useful for people with sensitive or acne-prone skin [54].

## 2.5. Antioxidant Capacity

### 2.5.1. DPPH (2,2-Diphenyl-1-picrylhydrazyl)

The antioxidant capacity of the ethanolic extract of *S. minor* Scop. obtained by the DPPH method was determined according to Brand-Williams et al. [55], with small modifications [56]. An amount of the sample (0.1 mL) was mixed with 2.9 mL of a DPPH 80  $\mu$ M solution and kept in the dark for exactly 30 min, after which, the absorbances were monitored at 517 nm using the UV spectrophotometer-mini-1240 UV-VIS (Shimadzu, Tokyo, Japan). The determination of the % inhibition of DPPH by the samples was carried out according to Equation (1):

$$\text{DPPH (\%)} = [(A_0 - A_1)/A_0] \times 100; \quad (1)$$

where  $A_0$  represents the absorbance read at 517 nm in the case of the blank (sample with only DPPH solution and solvent) and  $A_1$  represents the absorbance read at 517 nm in the case of the ethanolic extract from *S. minor* (Scop.).

The antioxidant capacity of *S. minor* (Scop.) extracts was expressed in mmol TE/mL. This result was determined using a calibration curve that was generated by testing various concentrations of Trolox, ranging from 60 to 1000 mM. The equation of the calibration curve was  $y = 970.07x + 0.6222$  and  $R^2 = 0.998$ .

### 2.5.2. FRAP (Ferric Reducing Antioxidant Power Assay)

The antioxidant capacity of the roots, leaves, and flowers of *S. minor* Scop. Was obtained by the FRAP method following Benzie and Strain [57], with a few modifications [9]. Thus, briefly, 2 mL of distilled water, 0.1 mL of extract/standard solution, and 0.5 mL of working FRAP solution were added to a test tube. The samples in the test tubes were vortexed and were allowed to react for 1 h in the dark at room temperature, after which, the absorbance was measured at 595 nm using the Shimadzu mini-UV-Vis spectrophotometer (Tokyo, Japan). A calibration curve was made against Trolox solutions of different concentrations (within the 0.06–1 mM range), the regression equations being  $y = 14019x + 0.0163$  and  $R^2 = 0.9969$ . Results were expressed as  $\mu$ mol Trolox equivalents (TE)/mL.

### 2.5.3. TEAC (Trolox Equivalent Antioxidant Capacity)

The antioxidant capacity of the roots, leaves, and flowers of *S. minor* Scop. obtained by the TEAC method was determined according to Arnao et al. [58], with minor modifications. In an Eppendorf tube, 10  $\mu$ L of Trolox standard or sample was homogenized with 1 mL of diluted ABTS solution at 30 °C and vortexed for 30 s. After vortexing, the contents were transferred to the spectrophotometric cuvette and the absorbance was read exactly 1 min after the addition of the ABTS reagent. The TEAC value was determined from the calibration curve against Trolox (percent decolorization vs. Trolox concentration) over a concentration range between 0–0.5 mM, having the regression equation  $y = 171.47x + 8.2807$  and  $R^2 = 0.9989$ . The results obtained were expressed in  $\mu$ mol Trolox equivalent (TE)/mL.

### 2.5.4. CUPRAC (Cupric Reducing Antioxidant Capacity)

The CUPRAC method, as described by Apak et al. [59], involves the use of a 1 mL copper (II) chloride solution ( $1 \times 10^{-2}$  M), 1 mL neocuproine (2,9-dimethyl-1, 10-phenanthroline) alcoholic solution ( $7.5 \times 10^{-3}$  M), 1 mL ammonium acetate aqueous buffer (pH 7), and 100  $\mu$ L *S. minor* Scop. extract, followed by water to make the final volume 4.1 mL. After the samples were left in the dark for 30 min, the absorbance at 450 nm was measured using a Shimadzu spectrophotometer mini UV-Vis (Tokyo, Japan), with the regression equation  $y = 3.8571x + 0.0034$ . Results were expressed in  $\mu$ mol Trolox equivalent (TE)/mL based on the regression equations  $y = 3.8571x + 0.0034$  and  $R^2 = 0.999$  obtained from the calibration curve with Trolox as a standard.

### 2.5.5. Determination of the Synergistic Effects (SEs) of *S. minor* Scop. Extract Mixtures

Using the following equation (Equation (2)), we calculated the synergistic effects (SEs) between individual extracts (roots, leaves, and flowers) and their combinations, as shown in Table 1:

$$SEs = \frac{\text{Experimental value}}{\text{Theoretical value}} \quad (2)$$

The experimental values were derived from the results of antioxidant assays performed with combined extracts, while the theoretical value was calculated by taking into account the ratios of the individual extracts. The following interpretation of the results was made: SEs > 1 are synergistic effects, SEs = 1 are additive effects, and SEs < 1 are antagonistic effects [60,61].

## 2.6. Physico-Chemical Parameter Determinations

### 2.6.1. Organoleptic Characteristics

Physico-chemical testing of the dermato-cosmetic formulas was performed to evaluate their physical properties, color, texture, phase separation, homogeneity, and fragrance [60]. The consistency and presence of coarse particles were checked by pressing a small amount of cream between the thumb and index finger. In addition, phase separation, immediate skin feel, and skin absorption were also evaluated [6].

### 2.6.2. Determination of pH

The pH was determined potentiometrically, according to the Romanian Pharmacopoeia [42], using a portable digital pH meter (InoLab pH 720, WTW—Wissenschaftlich Technische Werkstätten, Burladingen, Germany). In total, 5 g of sample was added to 20 mL of distilled water previously heated to  $37 \pm 2$  °C and vigorously stirred for 1 min. After cooling, the dispersion was filtered and the pH of the filtrate was determined. Each determination was performed in triplicate.

### 2.6.3. Density

The relative density was determined using a pycnometer according to the European Pharmacopoeia, Edition 7.

#### 2.6.4. Accelerated Stability Study

The creams were placed in glass containers and covered with aluminum foil for protection against light. Stability at thermostating for a minimum of 8 h at 4 °C and 40 °C was carried out according to the Romanian Pharmacopoeia, 10th Edition [42].

#### 2.6.5. Determination of Moisture and Volatile Substances

For the determination of moisture and volatile substances, g% gravimetric analysis was used. This procedure involves weighing a portion of the sample in an aluminum weighing pan and heating it in an oven at  $110 \pm 5$  °C for 1 h on a single occasion. The total volatile material is the difference in weight of the sample before and after heating [42].

#### 2.6.6. Determination of Type of Cream (Dilution Test)

When the creams were diluted with water, oil in water (O/W)-type creams showed good miscibility, while water in oil (W/O)-type creams showed poor miscibility [6].

#### 2.7. Spreadability Study

The spreadability study was determined by means of an Ojeda–Arbussa extensometer [62]. The extensometer consisted of two overlapping square glass plates. Under the lower plate, there was graph paper with two perpendicular lines that intersected in the center of the plate, where a circle with a diameter of approximately 1 cm was drawn [63]. Briefly, 1 g of the sample was placed on the lower plate of the extensometer, next to the central circle. The upper plate was overlapped at intervals of 1 min and weights from 50 to 500 g were added. The diameters of the formed circles were read each time. The weight and surface reading data are shown in Table S1, Supplementary Materials. The areas of the circles ( $\pi r^2$ ) were then calculated.

#### 2.8. In Vitro Polyphenol Release from Topical Dermato-Cosmetic Formulas

Evaluation of the in vitro release of polyphenols from topical preparations containing *S. minor* Scop. extract was performed using a six-cell Franz diffusion system with synthetic membranes (Microette-Hanson system, model 57-6AS9, Copley Scientific Ltd., Nottingham, UK) with a surface of diffusion of 1.767 cm<sup>2</sup> and a volume of 6.5 mL for the receiver chamber. The receptor chamber in each diffusion cell was filled with a phosphate buffer (pH 7.4) mixed with 30% freshly prepared ethanol. Synthetic membranes (Tuffryn<sup>®</sup>, PALL Life Sciences HT-450, lot T72556, Ann Arbor, MI, USA) made of polysulfone with a diameter of 25 mm and a pore size of 0.45 µm were hydrated by immersion in the receptor medium for 30 min before use and then mounted between the donor and acceptor compartments of the Franz diffusion cell.

Each sample was brought into the diffusion cell capsule at a weight of approximately 0.500 g. The system was maintained at  $32 \pm 1$  °C and the receptor medium was continuously stirred (600 rpm) using a magnetic stirrer to avoid diffusion layer effects. A 0.5 mL sample of the receptor solution was collected at different intervals of time (15 min, 30 min, 1 h, 2 h, 3 h, 4 h, 5 h, 8 h, 12 h, and 24 h) to measure the total amount of polyphenols using the Folin–Ciocalteu method. In order to ensure an even volume (6.5 mL) throughout the experiment, a new receptor medium was introduced at the specified intervals instead of using the extracted sample [64,65]. To determine the polyphenol content, the protocol involved combining 0.1 mL samples taken at various time intervals with 1.7 mL of distilled water and 0.2 mL of freshly diluted Folin Ciocâlteu reagent (1:10, v/v). The solution was agitated vigorously and, subsequently, 1 mL of a sodium carbonate solution with a concentration of 7.5% was introduced. The specimens were stored at room temperature in the absence of light for a duration of 2 h. Subsequently, the optical density was determined at a wavelength of 765 nm using a Shimadzu mini UV-Vis spectrophotometer (Tokyo, Japan). The total phenolic content was estimated from the calibration curve obtained from different concentrations of gallic acid (0.1–0.5 mg/mL) and expressed as gallic acid equivalents (GAE)/mL ( $y = 27.637x + 0.0069$  and  $R^2 = 0.9994$ ). The percentage of polyphenol

extract released was determined at each time interval, considering the initial quantity of polyphenols present in products according to Gavra et al. [66].

### 2.9. Sensory Evaluation of Dermato-Cosmetic Products

The sensory analysis was conducted by a group of 23 women and 17 men of various age groups (6 individuals aged 18–30, 16 aged 31–44, 12 aged 45–50, and 6 aged 51–60). Out of these, 29 participants were from urban areas and 11 were from rural areas. The sensory evaluation was performed at a post-secondary school in Oradea, Romania, that specializes in health education. The participants were offered six dermato-cosmetic samples, each containing approximately 10 mL of the product. These samples were stored in transparent glass containers labeled with random numbers. The volunteers proceeded to apply the formulations to their hands. Plain water and paper towels were provided for rinsing the skin between samples. The volunteers were asked to complete a questionnaire assessing the intensity of sensory properties using a scale from 0 to 10 (where 0 represents “none” and 10 represents “extremely strong”) in two sessions over the course of a month. The list contained 7 descriptors or attributes commonly used to characterize cosmeceutical formulations: 3 appearance attributes (color, odor, texture) and 4 skin parameters (feel on the skin, rapidity of skin penetration, persistence of odor on skin, overall evaluation of indexes). Finally, participants were asked to rate their overall liking of the product on a 10-point scale to see which of the samples they preferred.

### 2.10. Statistical Analysis

Every assay was carried out in triplicate, and the analytical data are shown as the mean value  $\pm$  standard deviation (SD). Tukey’s multiple comparison tests (one-way ANOVA) were used to analyze the data at a  $p < 0.05$  significance level.

## 3. Results

### 3.1. Characterization of the Combinations of Plant Tissues Belonging to the *S. minor* Scop. Plant from the Point of View of Antioxidant Capacity

Table 4 presents results related to the antioxidant capacity of the extracts derived from the roots (SMR), leaves (SML), and flowers (SMF) of *S. minor* Scop., as well as the combinations of them. Table 4 clearly demonstrates that the root extract exhibited the greatest antioxidant capacity as determined by the DPPH, TEAC, and CUPRAC methods. Conversely, the antioxidant capacity of the *S. minor*’s Scop. leaves and flowers varied depending on the method used. Leaves exhibited a greater antioxidant capacity than flowers when evaluated using the DPPH and FRAP methods. According to the results of the TEAC and CUPRAC methods, the flowers exhibited a greater antioxidant capacity than the leaves. Following the combinations of the roots, leaves, and flowers of *S. minor* Scop., the combined extracts showed varying effects on antioxidant capacity. Four in vitro methods were employed to assess the antioxidant capacity of extracts derived from the combination of root, leaf, and flower extracts of *S. minor* Scop. The cumulative antioxidant effect (SE) of these mixtures was also assessed, demonstrating the efficacy of the combinations. In the DPPH test, there were no significant differences observed between the samples, except for a significant difference between the 2:1:2 and 1:2:2 samples. The 2:1:2 sample provided the highest value ( $66.62 \pm 3.37$  mmol TE/mL) while the 1:2:2 sample obtained the lowest value ( $43.67 \pm 4.71$  mmol TE/mL) after completing the DPPH test (Table 4). Conversely, the 2:1:1 sample exhibited additive effects in relation to antioxidant capacity, while the other samples demonstrated synergistic effects. A synergistic effect was observed when combining extracts in four samples (2:1:2, 1:2:1, 1:2:2, and 1:1:2) during the TEAC test and three samples (2:1:1, 2:2:1, and 1:2:1) during the CUPRAC test. Sample 1:2:1 exhibited a synergistic effect in all tested methods, except for the FRAP method. This can be attributed to the distinct composition of the bioactive compounds found in the plant tissues of *S. minor* Scop. [12] as well as the different mechanisms employed by the tested methods [67].

**Table 4.** The antioxidant capacity and synergistic effects (SEs) of extract mixtures from the organs of *S. minor* Scop.

Tests \ Samples	SMR	SML	SMF	1:1:1	2:1:1	2:2:1	2:1:2	1:2:1	1:2:2	1:1:2
DPPH (mmol TE/mL)	90.87 ± 13.07 <sup>A</sup>	18.66 ± 2.76 <sup>B</sup>	9.16 ± 0.89 <sup>C</sup>	55.59 ± 1.75 <sup>a</sup>	56.68 ± 12.26 <sup>a</sup>	51.97 ± 5.77 <sup>a</sup>	66.62 ± 3.37 <sup>ab</sup>	54.36 ± 3.46 <sup>a</sup>	43.67 ± 4.71 <sup>a,c</sup>	55.05 ± 9.77 <sup>a</sup>
SEs	-	-	-	1.42 ± 0.43 <sup>a</sup> (synergistic)	1.08 ± 0.23 <sup>a</sup> (additional)	1.14 ± 0.13 <sup>a</sup> (synergistic)	1.52 ± 0.08 <sup>a</sup> (synergistic)	1.58 ± 0.10 <sup>a</sup> (synergistic)	1.49 ± 0.16 <sup>a</sup> (synergistic)	1.72 ± 0.31 <sup>a</sup> (synergistic)
FRAP (μmol TE/mL)	8.31 ± 0.30 <sup>A</sup>	8.88 ± 0.01 <sup>B</sup>	8.65 ± 0.08 <sup>A,B</sup>	51.0 ± 4.05 <sup>a</sup>	54.23 ± 5.62 <sup>a</sup>	45.15 ± 6.81 <sup>ab</sup>	56.44 ± 0.62 <sup>a</sup>	45.81 ± 0.99 <sup>a</sup>	36.72 ± 3.74 <sup>b</sup>	49.49 ± 7.64 <sup>a</sup>
SEs	-	-	-	0.61 ± 0.05 <sup>a</sup> (antagonistic)	0.65 ± 0.07 <sup>a</sup> (antagonistic)	0.54 ± 0.08 <sup>ab</sup> (antagonistic)	0.68 ± 0.01 <sup>a</sup> (antagonistic)	0.55 ± 0.01 <sup>a</sup> (antagonistic)	0.44 ± 0.05 <sup>b</sup> (antagonistic)	0.60 ± 0.09 <sup>a</sup> (antagonistic)
TEAC (μmol TE/mL)	3.26 ± 0.17 <sup>A</sup>	1.28 ± 0.09 <sup>B</sup>	1.58 ± 0.27 <sup>B</sup>	1.23 ± 0.05 <sup>b</sup>	2.26 ± 0.16 <sup>a</sup>	1.35 ± 1.12 <sup>b</sup>	3.09 ± 0.89 <sup>a</sup>	2.18 ± 0.16 <sup>a</sup>	1.94 ± 0.16 <sup>a</sup>	2.97 ± 0.05 <sup>a</sup>
SEs	-	-	-	0.60 ± 0.03 <sup>b</sup> (antagonistic)	0.97 ± 0.07 <sup>a</sup> (additional)	0.63 ± 0.53 <sup>b</sup> (antagonistic)	1.41 ± 0.41 <sup>a</sup> (synergistic)	1.18 ± 0.09 <sup>a</sup> (synergistic)	1.08 ± 0.09 <sup>a</sup> (synergistic)	1.54 ± 0.03 <sup>a</sup> (synergistic)
CUPRAC (μmol TE/mL)	182.10 ± 3.14 <sup>A</sup>	71.54 ± 1.29 <sup>C</sup>	126.29 ± 4.44 <sup>B</sup>	136.56 ± 10.34 <sup>a</sup>	153.99 ± 29.94 <sup>a</sup>	139.49 ± 2.40 <sup>a</sup>	141.06 ± 0.18 <sup>a</sup>	121.06 ± 0.18 <sup>ab</sup>	103.68 ± 13.12 <sup>b</sup>	127.07 ± 4.43 <sup>a</sup>
SEs	-	-	-	1.05 ± 0.08 <sup>a</sup> (additional)	1.10 ± 0.21 <sup>a</sup> (synergistic)	1.11 ± 0.02 <sup>a</sup> (synergistic)	1.02 ± 0.00 <sup>a</sup> (additional)	1.07 ± 0.07 <sup>a</sup> (synergistic)	0.89 ± 0.11 <sup>a</sup> (antagonistic)	1.00 ± 0.03 <sup>a</sup> (additional)

Data are expressed as mean ± SD (n = 3). The coding of the samples from *S. minor* Scop. organs (root, leaves, and flowers) is provided in Table 1. SMR—root extract, SML—leaf extract, and SMF—flower extract of *S. minor* Scop. SEs—synergistic effects, where SEs > 1 are synergistic effects, SEs = 1 are additional effects, and SEs < 1 are antagonistic effects. Different lowercase letters represent statistical significance between combined samples within the same antioxidant test ( $p < 0.05$ , Tukey's multiple comparison test). Different uppercase letters represent statistical significance between organ samples (roots, SMR; leaves, SML; flowers, SMF) within the same antioxidant test ( $p < 0.05$ , Tukey's multiple comparison test).

### 3.2. Physico-Chimic Characteristics

The organoleptic characteristics of creams are shown in Table 5. For each cosmetic product, C\_SM, H\_SM, E\_SM, and control samples made without *S. minor* Scop. extract were labeled as CTRLC\_M-control cream, CTRLH\_M-control hydrogel, and CTRLM-control emulgel.

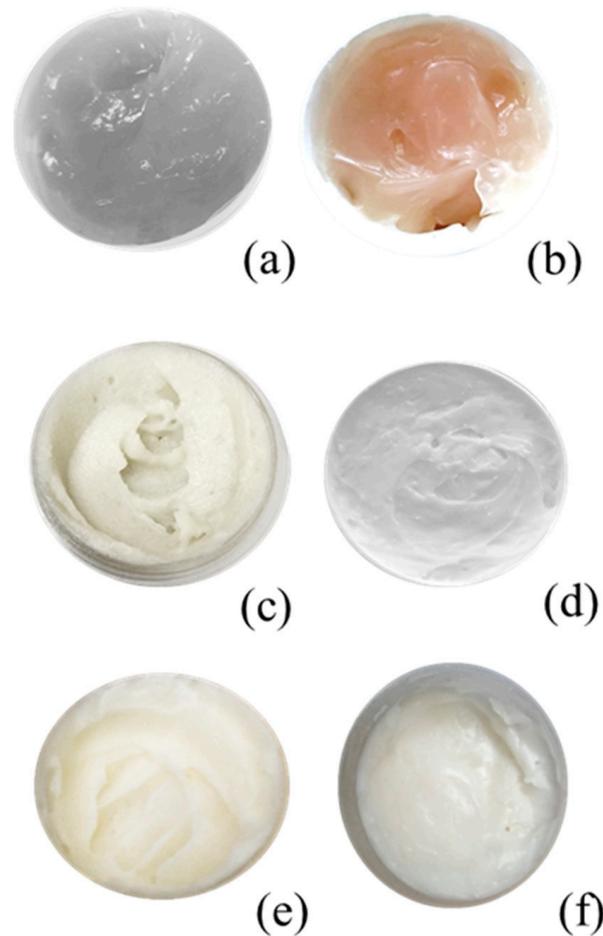
**Table 5.** Physico-chemical characteristics of dermato-cosmetic formulations.

Physico-Chemical Characteristics	CTRLH_M	H_SM	CTRLM	E_SM	CTRLC_M	C_SM
Overall appearance	Solid, homogeneous	Solid, homogeneous	Solid, homogeneous	Solid, homogeneous	Solid, homogeneous	Solid, homogeneous
Fragrance	Odorless	Characteristic	Odorless	Characteristic	Odorless	Characteristic
Color	Colorless	Light orange	White	White	White	Cream-colored
Physical appearance	Translucent gel, viscous consistency	Translucent gel, viscous consistency	Emulsion with a milky, homogeneous appearance	Emulsion with a milky, homogeneous appearance	Opaque, homogeneous	Opaque, homogeneous
Texture	Viscous	Viscous	Smooth, creamy	Smooth, creamy	Smooth, creamy	Smooth, creamy
Consistency	Good	Good	Good	Good	Good	Good
Phase separation	No	No	No	No	No	No
Immediate sensation on the skin	Quickly penetrated the skin without a greasy film	Quickly penetrated the skin without a greasy film	Quickly penetrated the skin without a greasy film	Quickly penetrated the skin without a greasy film	Some greasiness was observed and no grittiness	Quickly penetrated the skin without a greasy film
Absorption	Less than 1 min	1–2 min	1–2 min			
pH (22.5 °C)	pH = 7.49 ± 0.07 <sup>a</sup>	pH = 7.50 ± 0.03 <sup>a</sup>	pH = 7.00 ± 0.03 <sup>b</sup>	pH = 7.12 ± 0.04 <sup>b</sup>	pH = 7.55 ± 0.02 <sup>a</sup>	pH = 6.17 ± 0.03 <sup>c</sup>
Density (g/cm <sup>3</sup> )	1.10 ± 0.04 <sup>a</sup>	1.13 ± 0.03 <sup>a</sup>	1.11 ± 0.03 <sup>a</sup>	1.16 ± 0.02 <sup>a</sup>	0.95 ± 0.03 <sup>b</sup>	1.02 ± 0.03 <sup>b</sup>
Moisture and volatile substances (g%)	90.15 ± 1.07 <sup>b</sup>	95.04 ± 0.04 <sup>a</sup>	78.12 ± 0.05 <sup>c</sup>	78.37 ± 0.05 <sup>c</sup>	24.80 ± 0.03 <sup>e</sup>	43.32 ± 0.04 <sup>d</sup>
Determination of solubility	Methyl alcohol: partially soluble Warm water: soluble Petroleum ether: soluble	Methyl alcohol: partially soluble Warm water: soluble Petroleum ether: soluble	Methyl alcohol: partially soluble Warm water: soluble Petroleum ether: soluble	Methyl alcohol: partially soluble Warm water: soluble Petroleum ether: soluble	Methyl alcohol: soluble Warm water: soluble Petroleum ether: insoluble	Methyl alcohol: soluble Warm water: soluble Petroleum ether: insoluble
Determination of stability during thermostating	Stable, without phase separation	Stable, without phase separation	Stable, without phase separation			
Determination of the type of emulsion	W/O	W/O	O/W	O/W	O/W	O/W

CTRLH\_M—hydrogel control without *S. minor* Scop. extract; H\_SM—hydrogel with *S. minor* Scop. extract; CTRLM—emulgel control without *S. minor* Scop. extract; E\_SM—emulgel with *S. minor* Scop. extract; CTRLC\_M—cream control without *S. minor* Scop. extract; C\_SM—cream with *S. minor* Scop. extract; O/W—oil-in-water base; W/O—water-in-oil base. Data are expressed as mean ± SD (n = 3). Different lowercase letters represent statistical significance between dermato-cosmetic formulations within the same line ( $p < 0.05$ , Tukey's multiple comparison test).

The dermato-cosmetic products containing *S. minor* Scop. extract exhibited noticeable differences compared to the control samples. The hydrogel exhibited a distinct color, while the control appeared lacking in color. Regarding the emulgel, the color remained consistent, while, for the cream, the control was white and the cream itself had a slightly lighter yellow color. The dermato-cosmetic products containing *S. minor* Scop. extract exhibited a unique smell derived from this plant, whereas the control products lacked any fragrance. The overall appearance exhibited homogeneity, with no detectable phase separation, and the average pH of all cosmetic formulations was considered adequate.

Considering the organoleptic properties, color was the distinguishing feature among the six samples, along with variations in texture. The difference was evident, as shown in Figure 2. The physico-chemical characteristics of the different cosmetic forms varied. H\_SM, for example, exhibited a gel-like consistency that demonstrated rapid absorption into the skin. This gel had a moisture content exceeding 90% and was formulated as a water-in-oil (W/O) emulsion. On the other hand, E\_SM was an emulsion with a milky appearance that was absorbed by the skin in less than a minute. It had a moisture level above 70% and was formulated as an oil-in-water (O/W) emulsion. Lastly, C\_SM was a homogeneous cream that took approximately 2 min to penetrate the skin. It had a humidity level exceeding 40% and was also formulated as an oil-in-water (O/W) emulsion.



**Figure 2.** Elaborated dermatocosmetic preparations: (a) CTRLH\_M (hydrogel control without *S. minor* Scop. extract); (b) H\_SM (hydrogel with *S. minor* Scop. extract); (c) CTRLM (emulgel control without *S. minor* Scop. extract); (d) E\_SM (emulgel with *S. minor* Scop. extract); (e) CTRLC\_M (cream control without *S. minor* Scop. extract); (f) C\_SM (cream with *S. minor* Scop. extract).

### 3.3. The Spreadability of the Cosmetic Formulations

The results of the calculation of the radius of the surfaces of the circles of the cosmetic formulations are shown in Table 6.

Based on the obtained results, the spreadability increased with the increase of added weights. Also, the larger the surfaces, the better the spreading capacity of the topical preparations. The spreading capacity, influenced by the presence of the hydroalcoholic extract obtained from the *S. minor* Scop. plant, was highest in descending order in H\_SM, E\_SM, and C\_SM.

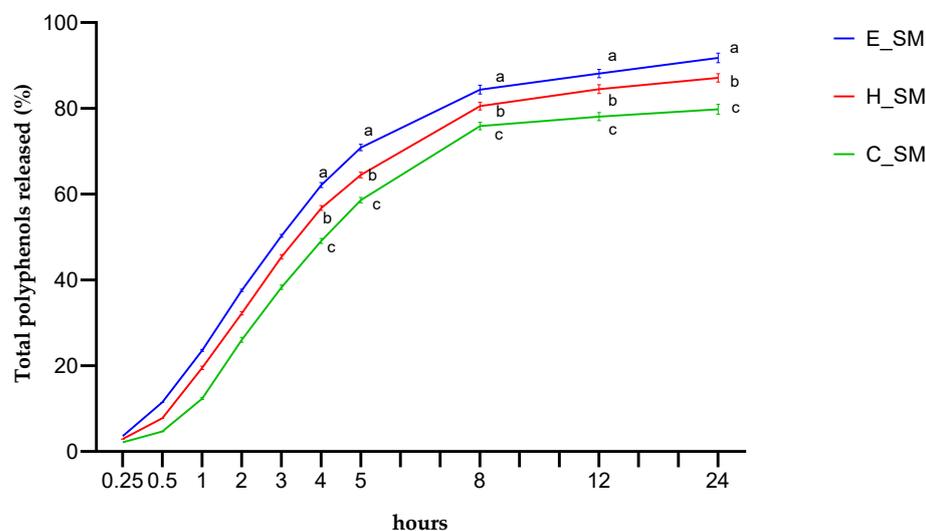
**Table 6.** The circle surfaces from the investigated dermato-cosmetic samples.

Weight (g)	Stretching Capacity Results (cm <sup>2</sup> )		
	C_SM	E_SM	H_SM
0	7.11 ± 0.47 <sup>b</sup>	3.16 ± 0.12 <sup>c</sup>	12.62 ± 1.05 <sup>a</sup>
50	9.12 ± 0.94 <sup>b</sup>	3.81 ± 0.37 <sup>c</sup>	15.23 ± 1.45 <sup>a</sup>
100	10.17 ± 0.92 <sup>b</sup>	5.31 ± 0.32 <sup>c</sup>	19.65 ± 1.03 <sup>a</sup>
150	11.89 ± 1.11 <sup>b</sup>	7.08 ± 0.62 <sup>c</sup>	19.62 ± 0.93 <sup>a</sup>
200	13.50 ± 0.82 <sup>b</sup>	12.58 ± 1.03 <sup>b</sup>	21.25 ± 1.73 <sup>a</sup>
250	15.23 ± 1.84 <sup>b</sup>	13.90 ± 1.35 <sup>b</sup>	22.90 ± 1.92 <sup>a</sup>
300	16.63 ± 1.05 <sup>b</sup>	19.67 ± 1.44 <sup>b</sup>	24.62 ± 2.04 <sup>a</sup>
350	18.11 ± 1.12 <sup>c</sup>	21.23 ± 1.95 <sup>b</sup>	26.40 ± 1.82 <sup>a</sup>
400	19.62 ± 1.54 <sup>b</sup>	24.59 ± 2.04 <sup>a</sup>	28.28 ± 1.92 <sup>a</sup>
450	21.25 ± 2.04 <sup>b</sup>	28.28 ± 2.73 <sup>a</sup>	28.26 ± 2.13 <sup>a</sup>
500	22.91 ± 1.82 <sup>b</sup>	30.19 ± 2.02 <sup>a</sup>	28.27 ± 2.67 <sup>a</sup>

Data are expressed as mean ± SD (n = 3). Different lowercase letters represent statistical significance between dermato-cosmetic formulations within the same line ( $p < 0.05$ , Tukey's multiple comparison test). C\_SM—cream with *S. minor* Scop. extract; E\_SM—emulgel with *S. minor* Scop. extract; H\_SM—hydrogel with *S. minor* Scop. extract.

### 3.4. Release Studies

The gradual release of polyphenols was observed in all tested dermato-cosmetic formulas, with a direct correlation with the duration of time (ranging from 1 to 8 h). Subsequently, the quantity of polyphenols reached a constant level. Figure 3 shows the gradual release of polyphenols from dermato-cosmetic formulations within an interval of 24 h. The penetration of topically administered natural substances, along with the bioavailability and action of the pharmaceutical form, is influenced by three key factors: the skin, the active substances, and the vehicle.



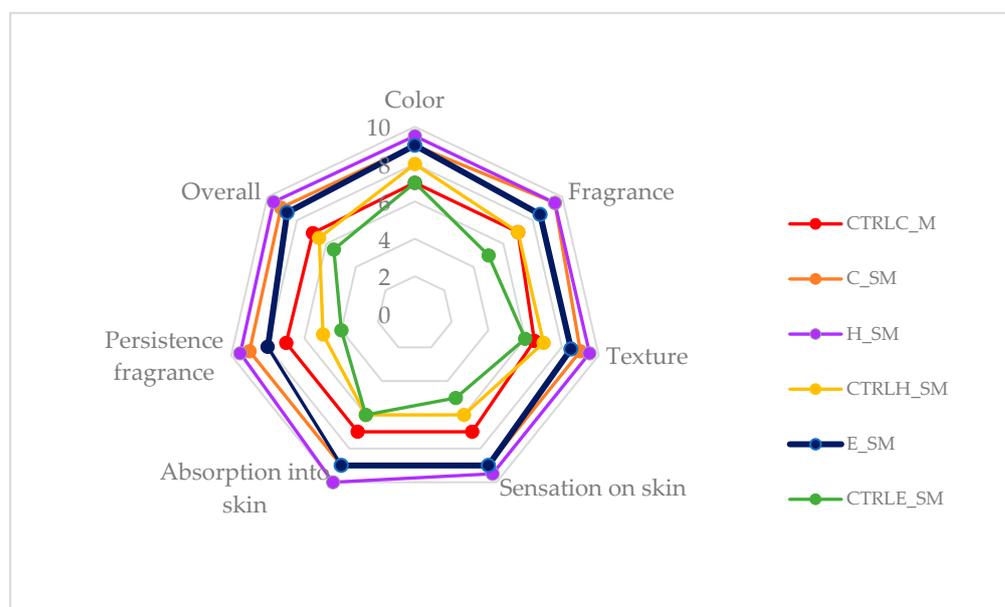
**Figure 3.** Percentage of total polyphenols released over time (h) from dermato-cosmetic products containing *S. minor* Scop. extract. Cream—C\_SM (green), hydrogel—H\_SM (red), and emulgel—E\_SM (blue). The error bars represent the standard deviation of the mean values derived from three repeated tests. Different lowercase letters represent statistical significance between dermato-cosmetic formulations ( $p < 0.05$ , Tukey's multiple comparison test).

From Figure 3, it can be observed that after 4 h, the release percentages of phenolic compounds from the cosmetic formulations based on *S. minor* Scop. were over 49%. After 8 h of testing, it was noted that the yield of phenolic compounds from the cosmetic formulations exceeded 75%. In summary, the emulgel formulation that contained the *S. minor* Scop. extract exhibited the highest yield, reaching  $91.77 \pm 1.11\%$ . There was a statistically significant difference observed between the three cosmetic formulations at

all tested time points (Figure 3). The emulgel exhibited the highest capacity for releasing polyphenols from the incorporated extract, followed by the hydrogel and cream. After 12 h, the release percentage of the cosmetic formulations exceeded 78%. This suggests that all of these formulations can be effectively used as natural products with antioxidant properties.

### 3.5. Sensory Characterization of *S. minor* Scop. Dermato-Cosmetic Products

A sensory test was performed to evaluate the degree of acceptability of the dermato-cosmetic formulations (C\_SM, H\_SM, and E\_SM) by the volunteers, and the results can be observed in Figure 4. In addition to its antioxidant activity, the ethanolic extract was incorporated into different cosmetic formulations to contribute aromatic properties. Differences were noted with respect to both color and texture. Sensory analysis was performed to highlight consumer preferences regarding products that contain *S. minor* Scop. extract. Three control samples (CTRLC\_M, CTRLH\_M, CTRLM\_M) containing no *S. minor* Scop. extract were used as references. The attributes tested in the case of samples CTRLC\_M, C\_SM, CTRLH\_M, H\_SM, CTRLM\_M, E\_SM, CTRLM\_M, and E\_SM were color, smell, texture, sensation upon entering the skin, rapidity of entering the skin, persistence of the smell, and overall analysis.



**Figure 4.** The effects of sensory evaluations of cosmeceutical formulations: CTRLC\_M (cream control without *S. minor* Scop. extract); C\_SM (cream with *S. minor* Scop. extract); H\_SM (hydrogel with *S. minor* Scop. extract); CTRLH\_M (hydrogel control without *S. minor* Scop. extract); E\_SM (emulgel with *S. minor* Scop. extract); CTRLM\_M (emulgel control without *S. minor* Scop. extract).

The group that performed the sensory analysis was made up of 23 women and 17 men of different ages (6 people between 18 and 30 years old, 16 people between 31 and 44 years old, 12 people between 45 and 50 years old, and 6 people between 51 and 60 years old), in which 29 people came from an urban environment and 11 people came from a rural environment.

Sensory characterization confirms which properties most influence consumer acceptance. All the volunteers thought that the tested products had a good spread on the skin, but many preferred H\_SM for its texture, speed of entering the skin, color, and pleasant fragrance. After H\_SM, the preference was for C\_SM, with high values for texture, sensation upon entering the skin, and persistence of the smell. The participants were also asked about the optimal time of day to administer the cream/hydrogel/emulgel containing *S. minor* Scop. extract. The majority stated that they use these cosmetic products in the morning. When asked about the usefulness of these products and their future intentions, they expressed a positive response.

#### 4. Discussion

The current study focuses on the characterization and investigation of *Sanguisorba minor* Scop., a plant that receives limited attention in the existing literature. However, many beneficial pharmaceutical effects such as antioxidant, anti-inflammatory, and antimicrobial activities have been noticed during traditional applications [12,16,32]. This study is original because it involves extracting components from various tissues of the *S. minor* Scop. plant, specifically, the root, leaves, and flowers, and creating different combinations of these extracts. The extracts were subsequently assessed for their antioxidant capacity in order to identify the extract with the most powerful antioxidant potency. Antioxidants have the capacity to neutralize the harmful effects of oxidative damage caused by free radicals, thereby preventing or reducing the harm caused by reactive oxygen and reactive nitrogen species.

In our previous study [12], we highlighted that *S. minor* Scop. is a valuable source of bioactive compounds, particularly tannins. Among the plant's organs, the roots and leaves contain the highest concentrations of these compounds. The leaves and flowers of the plant contain flavanols and flavonols, with quercetin-glucuronide being the predominant compound in the leaves. These compounds are well known for their powerful antioxidant properties.

The methods used to determine the antioxidant capacity in vitro can be classified into three groups based on their mechanism of action. The first group involves an assay that depends on single electron transfer (SET). The second group involves an assay that centers on hydrogen atom transfer (HAT). The third group involves an assay that measures the ability of samples to remove reactive oxygen species or reactive nitrogen species, such as superoxide anion radicals, hydroxyl radicals, singlet oxygen, peroxyxynitrite, and hydrogen peroxide. The SET-reaction-based methods include the TEAC, FRAP, CUPRAC, DPPH, and TEAC techniques [68]. The most commonly used methods for evaluating the antioxidant capacity of medicinal plants are SET-mechanism-based approaches [69].

The products, which varied in the proportions of bee pollen and Aronia, showed complex properties and demonstrated strong antioxidant effects. These effects were particularly notable due to the synergistic or additional impact of the combined antioxidants. Tirla et al. [61] observed a significant synergistic effect when using a 1:2 (*v/v*) ratio of chokeberry (*Aronia melanocarpa*) extract to pollen.

In the case of antiradical activity, mixtures of natural flavonoids are commonly used to scavenge almost all types of free radicals and reactive oxygen species (ROS). Flavonoids inhibit the generation of ROS and prevent further skin aging by inhibiting multiple factors that cause ROS generation. For example, the flavonoids derived from green tea leaves/seeds and wine grape leaves and oligomers of these compounds are particularly effective at protecting the skin from free radicals [70–72]. Flavonoids in *Bauhinia variegata* L. prove to have antioxidant properties against oxidative damage by neutralizing radicals, binding iron, and decreasing power [73]. The major bioactive molecules from the fruits of *Aesculus indica* (Wall. Ex Cambess.) are quercetin and mandelic acid, which have notable antioxidant properties to reduce oxidative stress caused by reactive oxygen species [74]. *Pinus cembra* L. bark extract shows a better ability to scavenge free radicals than needle extract, and its phytochemical compounds contain more total phenolics and flavonoids than needle extract [75]. Sarkar and Mandal utilized scavenging assays for ROS to examine the antioxidant properties of hydroalcoholic extracts from *Cajanus cajan* and other Indian medicinal plants. They found a positive correlation between flavonoid and phenolic content in the studied plants and higher antioxidant activity [76]. Consequently, *S. minor* Scop. presents a significant amount of phenols and flavonoids and possesses antioxidant activity [9,12].

Plants that contain high levels of antioxidants may be able to provide treatment for UV-induced oxidative damage to the skin [66]. The use of antioxidants from natural sources may offer new possibilities for the treatment and prevention of UV-mediated diseases [66,77,78]. From our previous studies, the antioxidant activity of *S. minor* Scop. roots, leaves, and

flowers was evaluated, as well as the total polyphenol and flavonoid contents [9,12]. In addition to protecting against UV radiation, polyphenols reduce inflammation and are strong antioxidants [3,79]. There are flavonoids and tannins that have antimicrobial, antioxidant, and anti-inflammatory properties [80,81]. Punicalagin gallate and quercetin-glucuronide are two well-known, potent antioxidant compounds; they provide protection from oxidative stress [12,13,82] and are present in *S. minor* Scop. roots, leaves, and flowers. There has been an increasing interest in antioxidant compounds because they represent a promising alternative to UV-protecting cosmetic products [83,84]. In this context, phenolic compounds play a crucial role since they are readily available and widely distributed among *S. minor* Scop plants.

Yun et al. [85] formulated a cream with ziyuglycoside I isolated from *Sanguisorba officinalis* L. and examined the protective effects of the skin cream against UVB-induced hairless mice. This cream had precautionary roles in UVB-induced skin damage such as MMP-2 expression (matrix metalloproteinase), MMP-9 expression (matrix metalloproteinase), IL-1 $\beta$  expression, and photoaging in mice. Mlozi et al. [66] formulated herbal creams from methanolic leaf extracts of *Tephrosia vogelii* for their antifungal and antibacterial properties [86]. In another study carried out on topical formulations containing *Rosa canina* extract, it was found that the formulations had antioxidant properties due to the presence of quercetin and its derivative quercetin-3-O-glucuronide, which inhibit ROS overproduction and offer chemoprotection for mitochondrial function through antioxidative action. These creams were highly useful due to their bioactive contents, which included flavonoids, terpenes, tannins, and terpenoids [66,85,86].

By combining an extract from *Ocimum basilicum* and *Trifolium pratense*, Antonescu et al. [87] created a herbal hydrogel whose efficacy in healing wounds was evaluated through an in vivo test on an animal model as well as an assay based on a scratch test. In vitro tests showed that hydrogel formulations with *Ocimum basilicum* and *Trifolium pratense* extracts at a concentration of 50  $\mu\text{g}/\text{mL}$  completely recovered the dermal fibroblast monolayer. Following 13 days of treatment with the hydrogel, wound contraction time was improved and healing was complete. Also, this hydrogel was tested on a patient with *Psoriasis vulgaris*; his skin lesions were remitted and his psychological condition was also improved by the reduction in itching.

In another study, Lin et al. [88] developed a herbal hydrogel based on green tea, *Zingiber officinale* Rosc, *Phyllanthus emblica*, and salicylic acid. The gel was tested in vivo for its anti-inflammatory properties and effectiveness in controlling sebum secretion. It was found that polymer-based hydrogels with good mechanical properties, rheological characteristics, and surface morphologies were retained around injured skin, and their microstructures allowed cells to colonize the gel, thus supporting wound healing. Dejeu et al. [64] used caffeic acid for the rheological behavior of carbopol hydrogels and observed that the higher the amount of carbopol used in the formulation of the hydrogels, the greater the release of caffeic acid from the liposomes in the hydrogels over a longer period. Thus, Zagórska-Dziok et al. [89] developed various types of extracts from *Cornus mas* L. into hydrogel matrices, thereby obtaining efficient antioxidant properties and positive effects on the viability of skin cells in vitro. For cosmetic purposes, Pinto et al. [90] used different percentages of hydro-alcoholic *Castanea sativa* Bur extracts in a hydrogel base, with 50% of the extracts being chosen because of their high total phenols and flavonoid contents and antioxidant capacity, as well as their technological properties, which made them suitable for skin application. With the growing interest in hydrogels based on herbal extracts, the developed formulations may gain significant traction in the cosmetics industry. In one study, the efficacy of the topical application of an *Ocimum basilicum* emulgel exhibited the highest percentage of wound contraction, similar to the commercially available silver sulfadiazine cream [91]. An emulgel formulation containing 20% green tea extract and 5% rose oil showed a significantly higher hydration effect on human skin by enhancing the skin barrier function [92]. Emulgel shows better stability than other transdermal preparations; for example, creams show breaking or phase inversion and ointments show rancidity [93].

The application of Franz diffusion cells for evaluating skin permeability is now recognized as a prominent research instrument, offering supplementary insights into the interconnections between the skin and the products being tested. Typically, Franz diffusion cells have been used with excised human or animal skin [94]; however, a more convenient alternative is to utilize synthetic membranes. Synthetic membranes, which come in various forms, are employed in drug diffusion studies or analyses of active compounds in products due to their ability to mimic the properties of skin. Typical membranes include polysulfone, silicone, and cellulose [95]. This study employed a polysulfone-based membrane to detect the *in vitro* release of polyphenols from three dermato-cosmetic products containing *S. minor* Scop. extract. As in our study, the emulgel formulation that contained the extract of *S. minor* Scop. exhibited the highest yield from the release study. Emulgels have been less extensively studied in comparison to creams or hydrogels. However, our study found that the release percentage from emulgels, when using the cell Franz diffusion system, was the most efficient. One study investigated [65] the effects of combining *Taraxaci folium* and *Matricariae flos* plant extracts in different ratios. The aim was to create a mucoadhesive polymeric film that would have beneficial properties for treating acute gingivitis. The release of bioactive compounds from mucoadhesive films has been shown utilizing polysulfone membranes in the Franz cell apparatus. The results indicated a gradual release of the phytocomplex from the mucoadhesive film. Another study [64] utilized a Franz diffusion cell system to assess the release of caffeic acid from hydrogels based on carbopol. The porous polysulfone membrane, specifically designed for Franz cell testing, facilitated the diffusion of caffeic acid, which was released from carbopol-based hydrogels. The experiment found that hydrogels with a 0.5% concentration of carbopol released caffeic acid at percentages ranging from 87.69% to 89.27% within the first 8 h. Hydrogels with twice the amount of carbopol released caffeic acid at percentages between 84.98% and 86.29% within the first 12 h.

Research findings by Pinto et al. [90] also suggest that hydrogels with *Castanea sativa* hydroalcoholic extracts have the highest antioxidant activity compared to formulations without the extract. A study by Zosimidou et al. [96] also found that antioxidant measurements based on sea buckthorn oil enhanced the antioxidant activity of emulsions up to seven times compared to emulsions without buckthorn oil.

## 5. Conclusions

Testing the antioxidant capacity of combinations of the organs of the *S. minor* Scop. plant demonstrated that the ethanolic extract derived from a combination of roots, leaves, and flowers shows a significant antioxidant capacity and exhibits a synergistic effect. Thus, three cosmetic formulations (cream, hydrogel, and emulgel) were developed based on a 1:2:1 (*v:v:v*) ethanolic extract obtained from the organs of *S. minor* Scop. The hydrogel demonstrated the highest level of stretchability compared to the other two formulations that were tested. From the point of view of the release of phenolic compounds from the cosmetic formulations, the best result was obtained in the case of the emulgel. Through the sensory evaluation, the hydrogel and cream with *S. minor* Scop. extract were appreciated as cosmetic forms from the perspectives of color, smell, texture, sensation of entering the skin, speed of entering the skin, and persistence of the smell on the hand. In light of these results, we investigated the potential use of an extract with strong antioxidant properties from *S. minor* Scop. plant tissues in three distinct cosmetic formulations. The results obtained strongly support the recommendation to utilize *S. minor* Scop. as a source of biomolecules with antioxidant effects for the development of topical cosmetic products in both oil-in-water and water-in-oil formulations.

These findings provide opportunities for additional research on assessing anti-aging characteristics for the development of alternative cosmetic formulations, including hand creams, face creams, facial serums, and facial masks. Additional research is necessary to assess the safety of gels and creams, which should include laboratory experiments

investigating the viability and toxicity of cells in vitro. In vivo testing, including patch tests and sensitization studies, is also essential.

**Supplementary Materials:** The following supporting information can be downloaded at <https://www.mdpi.com/article/10.3390/cosmetics11010008/s1>: Table S1. The surfaces of the initial circles.

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