Polymer(Korea), Vol. 42, No. 6, pp. 1005-1013 (2018)
https://doi.org/10.7317/pk.2018.42.6.1005

ISSN 0379-153X(Print)
ISSN 2234-8077(Online)

솔방울 탄화물의 외용제 제조: 물리적 안정성 평가 및 관능 평가

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(2018년 5월 28일 접수, 2018년 5월 31일 수정, 2018년 6월 1일 채택)

Topical Formulation of Carbonized Pine Cones: Physical Stability Assessment and Sensory Evaluation

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(Received May 28, 2018; Revised May 31, 2018; Accepted June 1, 2018)

초록: 미분화된 솔방울 탄화물(CPC)을 함유한 외용제로서 고분자 하이드로젤 기반 크림과 오일 기반 유기젤을 개발하였다. 현미경 관찰을 통해 유상 전반에 걸쳐서 CPC가 균질하게 분산되었다. 원심분리 조건(1000-20000×g, 10분, 20도) 하에서, 유기젤에 비하여 수화젤 기반 제제의 물리적 안정성이 더 컸다. 수화젤 기반 고보습 크림2(HUMC2)와 라우르산/바셀린 기반 젤2(LV2)는 각각 수성 및 유기젤의 대표 제제로 선택되었으며, 두 제제 모두 전단박화의 유동학적 거동특성을 나타내었다. 별도로, '가상 집기력 시험법'을 설정하여 제제의 실질적 적용 시 흐름특성을 평가하였다. 사람을 대상으로 한 관능 평가에서 HUMC2가 퍼짐성, 보습성, 수세성 측면에서 LV2보다 높은 점수를 나타내었으나, 광택성 점수는 LV2가 HUMC2보다 높았다. 결론적으로 대부분의 평가에서 HUMC2가 LV2보다 우수했다, 그러나 HUMC2가 제한적인 CPC 탑재능력(10% w/w 미만)을 보인 반면 LV2는 높은 CPC 탑재능력(약 40% w/w)을 나타내었다.

Abstract: Polymeric hydrogel-based creams and oil-based organogels were formulated to develop a topical preparation containing carbonized and triturated powder of pine cone (CPC). Microscopic observation showed homogenous dispersion of CPC throughout the oil phase. Under centrifugal stress (1000-20000×g, 10 min, 20 °C), the physical stability of the hydrogel-based formulation was greater than those of organogels. Hydrogel-based ultra-moisturizing cream2 (HUMC2) and lauric acid/Vaseline-based gel2 (LV2) were selected as representative aqueous and organogel formulations, respectively, and both showed shear-thinning behavior in rheograms. A simulated pinch strength test was established to evaluate flow properties of the formulations for practical application. In human sensory evaluation, HUMC2 showed a higher score than LV2 regarding spreadability, moistness, and removal capacity, whereas the shininess score of LV2 was higher than that of HUMC2. In conclusion, HUMC2 was superior to LV2 in most evaluations, but had limited CPC-loading capacity (< 10% w/w), compared to the high loading capacity of LV2 (approximately 40% w/w).

Keywords: carbonized pine cones, o/w cream, organogel, physical stability, pinch strength test, sensory evaluation.

Introduction

Pine cones are the seed-producing cones of the pine tree, *Pinus densiflora Siebold et Zuccarini*. Pine cones have been used in folk medicine owing to their antimicrobial effects, which are caused by active oxygen production via their constituent lignin-carbohydrate complexes.[1] They also exert antiviral effects, inhibiting virus multiplication.[2,3] Carbonized pine cones (CPC) have been prepared by complete combustion of pine cones at extremely high temperatures of 100-300 °C, followed by pulverization using a 50-200 mesh sieve. A CPC-containing semisolid formulation has been patented in Korea to treat burns,[4] in which several excipients such as sesame oil, purified lanolin, white petrolatum, and selective organic acids form a cream or ointment base. However, with a high CPC content, such conventional formulations revealed imperfec-

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tions in either the physical stability of the homogenous dispersion or consumer acceptance for dermal application. We therefore needed to develop an advanced topical preparation to overcome the above limitations as well as enhance skin hydration.

Various types of topical formulations, including creams, hydrogels, and organogels, are currently in use.[5] Creams are the most common preparation, wherein oil and water are balanced in the presence of surfactant to make a homogenous dispersion, which can be of either an oil-in-water (o/w) or a water-in-oil (w/o) type. Recently, we developed a hydrogel-based ultra-moisturizing cream (HUMC) that efficiently hydrates the skin and increases the dermal delivery of both hydrophilic and lipophilic molecules.[6] As HUMC contains Carbopol 934P, an acrylic acid polymer crosslinked with polyalkenyl polyethers or divinyl glycol, it offers a stabilized, networked gel structure, resulting in advantages such as relatively high viscosity, compatibility with various active ingredients, bioadhesive properties, and thermal stability.[7,8] However, creams and hydrogels have limitations on their capacities to hold high levels of water-insoluble solid particles. Oil-based formulations, including organogels, might be a preferable alternative, as insoluble particles can easily be dispersed throughout the oil component. Upon dermal application, organogels, oils, or oleaginous fatty acids contained in organogels form a thin occlusive film on the skin surface, preventing transepidermal water loss, thereby potentially enhancing skin hydration.

Achieving pharmaceutical elegance in topical formulations generally requires not only the physical stability of the homogenous dispersion, but also patient acceptance of dermal application. To predict physical stability, products are subjected to accelerated conditions such as centrifugal force,[9] temperature stress,[10] and light exposure.[11] Meanwhile, to compare the organoleptic properties of products, such as odor, moistness, shininess, and spreadability, sensory evaluations via a panel test are generally recommended.[12] The descriptive analysis method, using a trained panel of skin-feel evaluators, can provide instructive information for research.[13]

The present study was performed to develop a novel CPC-containing topical preparation with excellent dispersion stability and *in vivo* performance upon dermal application. Based on the dispersion compatibility of CPC, different types of aqueous creams and oil-based organogels were formulated and subjected to stability assessment at 25 °C under accelerated gravitational force. Flow properties of selected formulations were further characterized by a pinch strength squeezing test and rheological observation. Finally, panel sensory evaluations were employed to compare the organoleptic properties of the products.

Experimental

Materials. CPC and sesame oil were kindly provided by Glami Co., Ltd. (Cheorwon, Korea). Carbopol 934P polymer was purchased from Lubrizol Advanced Materials, Inc. (Cleveland, OH, USA). Carnosine (β-alanyl-L-histidine) was purchased from Tokyo Chemical Industry Co. (Toshima, Japan). OliveM 1000 (sorbitan ester and cetearyl ester of olive oil fatty acids), cetyl alcohol, stearic acid, and lauric acid were supplied by Duksan Chemical Co., Ltd. (Seoul, Korea). Vaseline (white petrolatum) was obtained as a gift from Gattefosse (Saint-Priest, France). Urea was supplied by Duksan Chemical Co., Ltd. (Seoul, Korea). Glycerine was kindly gifted by Daejung Chemical Co. Ltd (Seoul, Korea). Triple distilled water was used for all experiments.

Field-emission Scanning Electron Microscopy (FE-SEM). The morphological features of CPC were observed using FE-SEM (Sigma, Car Zeiss, Oberkochen, Germany). CPC particles dispersed in ethanol were dropped onto a cover glass and air dried. The dried, sample-loaded cover glass was placed onto a copper grid using double-sided tape and coated with platinum for 2 min under a vacuum. Samples were viewed at an acceleration voltage of 5 kV.

Particle Size Analysis. Particle size measurement was performed using a laser light scattering particle size analyzer (Horiba LA-910, Kyoto, Japan) using the following settings: a relative refractive index of 1.06; an ultrasonic chamber power of 40 W and 39 kHz; a stirring flow rate of 340 mL/min (level 3) using 95-100 mL water medium; and a detection size range of 0.02-1000 μm. The CPC concentration in the particle size analyzer chamber was 0.5% w/w, and measurements were performed at least in triplicate to produce the error ranges of volume-averaged mean sizes.

Dispersion Compatibility Test of CPC. To determine the dispersion compatibility of CPC with the excipients used in the formulation, CPC was added to various test media, such as water, sesame oil, a physical mixture of water and oil, and Tween 20 (0.5%) in an o/w emulsion. The samples were vigorously mixed for 1 h using a stirrer (Vortex Genious 3, Staufen, Germany), and dispersion behavior was visually observed. Separately, to examine the partitioning behavior of CPC in an o/w emulsion, microscopic observation was per-

Table 1. Composition of Aqueous Cream and Oil-based Organogel Formulations

	Aqueous creams				Oil-based organogels			
	C1	C2	HUMC1	HUMC2	L1	L2	LV1	LV2
API								
CPC	10	8	8	8	40.8	40	38.2	39.1
Polymeric base								
Carbopol 934P	-	-	0.5	0.5	-	-	-	-
Carnosine	-	-	0.5	0.5	-	-	-	-
Oil phase								
Cetyl alcohol	5	5	5	1	-	-	-	-
Sesame oil	12.5	10	10	10	51.2	50	47.8	48.9
OliveM 1000	0.5	0.5	0.5	0.5	-	-	-	-
Stearic acid	-	-	2	2	-	-	-	-
Lauric acid	-	-	-	-	8	10	8	6
Vaseline	-	-	-	-	-	-	6	6
Aqueous phase								
Urea	-	-	3	3	-	-	-	-
Glycerin	-	-	5	5	-	-	-	-
D.W	q.s. ad 100.0				-	-	-	-

All measurements were in grams (g).
CPC, carbonized pine cone; C, cetyl alcohol cream; HUMC, hydrogel-based ultra-moisturizing cream; L, lauric acid gel; LV, lauric-Vaseline gel.

formed using a fluorescence microscope (Moticam Pro 285A, Beijing, China), using Nile red as a fluorescent probe.

Preparation of Cream Formulations. Two types of cream formulation were prepared, as shown in Table 1. To prepare C1 and C2 creams, a conventional emulsification method was employed, as previously reported.[14] CPC was dispersed in a pre-heated oil phase containing OliveM 1000 as an emulsifier, mixed with pre-heated water, and then homogenized using a homogenizer (Ultra-Turrax T25; 11000 rpm, 10 min). Temperature was maintained at 60 ºC throughout. Separately, HUMC1 and HUMC2 creams were prepared using the same procedure, except for the process of polymer addition: Carbopol 934P (0.5%) was pre-dissolved in the aqueous phase containing urea and glycerin as a humectant, and neutralization with carnosine (0.5%) was performed at the last step of the procedure. All preparations were incubated at ambient conditions for 24 h, to allow aging.

Preparation of Organogel Formulations. Different organogels were prepared and their compositions are listed in Table 1. CPC was dispersed in a pre-heated oil phase, mixed with other excipients, and then homogenized as described above (11000 rpm, 10 min). Temperature was maintained at 80 ºC throughout. Lauric acid was used as a viscosity-building agent for L1 and L2 formulations, whereas Vaseline was also added in the preparation of LV1 and LV2 formulations, to adjust the consistency. All preparations were incubated at 25 ºC for 24 h, to allow aging.

Physical Stability Test under Centrifugal Stress. Centrifugal stress is a useful tool for assessing and predicting the physical stability of semisolid formulations.[15] A physical stability test under accelerated gravitational forces was performed to observe the phase separation behavior of the formulations. The samples were stored on a shelf at 25 ºC for 90 days. Samples (2 g) were placed in disposable centrifugal tubes (Corning, NY, USA) and centrifuged at various gravitational forces in the range of 1000-20000×g, for 10 min at 20 ºC, using a fixed-angle centrifuge (Hanil Smart R17, Seoul, Korea). After centrifugation, the volume of the separated oily top layer was measured, and the relative ratio of the separated volume *versus* the total volume of the sample was calculated and expressed as the separation ratio in percent (SR, %). All experiments were performed in triplicate and averaged.

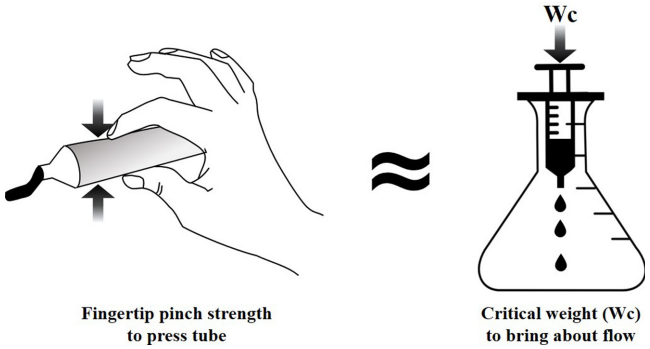


Figure 1. Illustration of the simulated pinch strength test.

Simulated Pinch Strength Test. To evaluate the suitability of the flow properties of the prepared formulations for practical application, a simulated pinch strength test was employed as depicted in Figure 1. The fingertip pinch strength test involves using hand strength to grip the objective tightly, using the thumb tip and the index finger tip.[16] In this experiment, we designed an *in vitro* device to measure the critical weight (W_C, kg), defined as the force required to induce sample flow. A definite volume (1 mL) of each test sample was aspirated into 3 mL disposable syringes and stored at either 4 °C (refrigerator) or 25 °C (ambient). After stabilization for 24 h, each syringe was fixed vertically to the neck of an Erlenmeyer flask, in which a beaker was fixed to the plunger. The beaker was filled with water at a speed of 300 mL/min, until the plunger was depressed and the sample preparation began to flow from the syringe. The total volume of water required was measured and recorded as W_C. All experiments were performed in triplicate and averaged.

Rheological Evaluation. Viscosity was assessed using the Advanced Rheometric Expansion System (Rheometric Scientific, Malvern, U.K), using parallel plates (40 mm in diameter) with a gap of 5.0 mm. Experiments were conducted under a steady shear flow at 25 °C. Shear rates ranged from 0.01 to 300 s^{-1}. HUMC2 and LV2 vehicles were tested. All experiments were performed in triplicate and averaged.

Sensory Evaluation of Various Formulations. The human study was approved by the ethics committee (Protocol number: ID-1041078-201802-HR-030-01, Chung-Ang University, Korea), and all subjects provided written informed consent to participate in the study. Also, all procedures complied with the Declaration of Helsinki, as revised in 2013. Twelve healthy volunteers, aged 26-55, living in and around Seoul, Korea, were selected for the panel and familiarized with the terminology, evaluation procedures, and rating scales. The panel members were educated to understand the definitions and scales for the evaluation parameters, including reference points during training sessions. Volunteers then evaluated samples to assess their sensory attributes, including spreadability, odor, moistness, shininess, and capacity for removal, as listed in Table 2. The panels graded the test samples on a scale from 1 to 5 for each parameter, and the values were averaged.

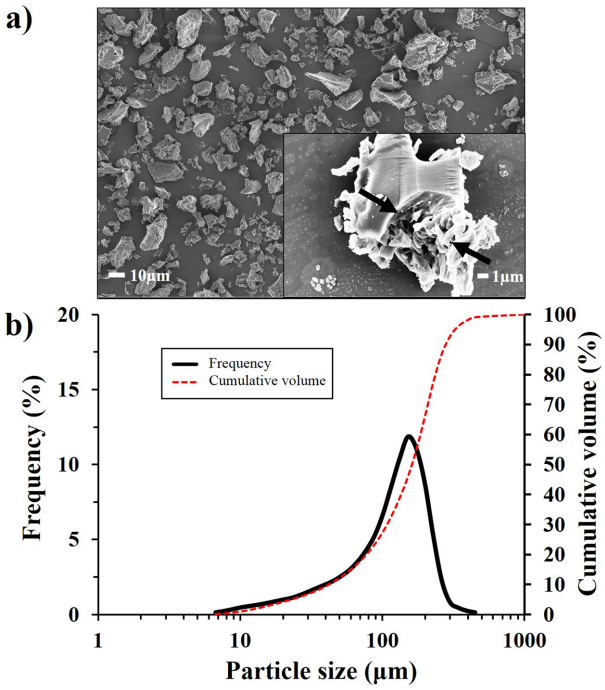
Statistical Analysis. All reported data are represented as the mean ± standard deviation (SD). Statistical significance was determined using Student's t-test and set at $p<0.05$, unless otherwise indicated.

Results and Discussion

Powder Characteristics of CPC. As shown in Figure 2(a), CPC particles had an irregular crystal shape, with numerous micropores on the surface. Figure 2(b) shows the particle size analysis of the CPC dispersion in distilled water. The size distribution was unimodal, but positively skewed: the cumulative sizes of 10% (d10) and 90% (d90) were 45 and 281 μm, respectively, while the geometric mean diameter (d50) was 118 μm. Due to the microporous surface, the properties of

Table 2. Parameter Descriptions and Scores for the Sensory Evaluation of HUMC2 and LV2

Parameter	Definition	Descriptive terms (score)
Spreadability	Degree to which the product spreads easily on the skin	poor (1), acceptable (2), fair (3), good (4), optimal (5)
Odor	Degree to which the product gives an unpleasant smell	disgusting (1), unpleasant (2), neutral (3), pleasant (4), very pleasant (5)
Moistness	Degree to which the product gives a moisturizing feeling on the skin	poor (1), acceptable (2), fair (3), good (4), optimal (5)
Shininess	Degree to which the product looks shiny or matte on the skin	uneven (1), matte (2), shiny (3), very shiny (4), extremely shiny (5)
Removal capacity	Degree to which the product washes off the skin using water	unwashable (1), hardly washable (2), washable (3), easily washable (4), freely washable (5)



Data are represented as the mean ± SD (n = 3).
Arrows in insert indicate the porous structure of CPC

Figure 2. (a) SEM images of CPC (magnification 1000×; insert represents 15000×); (b) particle size distribution of CPC.

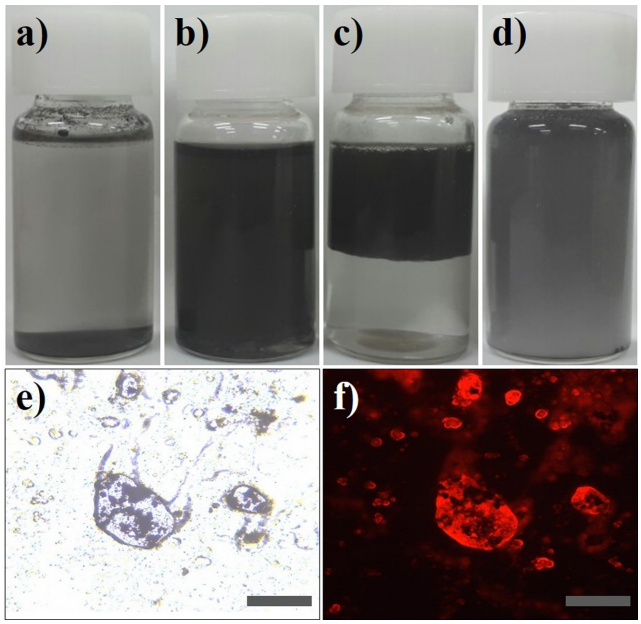


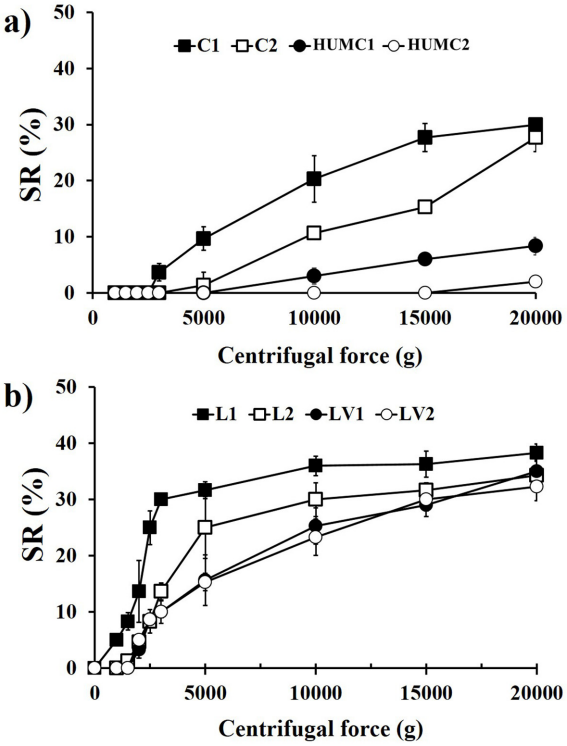
Figure 3. Visual observations for the dispersion compatibility of CPC (upper panel) and optical microscopy (lower panel, magnification 400×): dispersed in (a) distilled water; (b) sesame oil; (c) oil and water mixture; (d) o/w emulsion; Nile red-containing o/w droplet under (e) white-field; (f) fluorescence-field light sources. Scale bar indicates 50 μm.

CPC could be expected to be similar to those of charcoal, a combustion-derived carbon particle,[17] which has been used to remove organic micropollutants in water,[18] similarly, the use of a skin patch containing activated charcoal can absorb toxins, bacteria, fungi, and other pathogens in the treatment of injuries, bites, and other disorders.[19] Thus, CPC-containing topical formulations could aid wound healing by absorbing microbes and exudates in the wounded area.

Dispersion Compatibility of CPC. It is important to investigate the compatibility of CPC with other ingredients to produce a homogeneous final product. Figure 3 shows the dispersion compatibility of CPC in both water and oil components. CPC partially aggregated in distilled water and settled at the bottom of the vessel, but dispersed homogenously throughout oil (Figures 3(a) and 3(b)), suggesting the necessity for an oil component in the formulation. As expected, in a physical mixture of oil and water, CPC mainly partitioned into the oil layer (Figure 3(c)). In contrast, as shown in Figure 3(d), CPC homogenously dispersed in an o/w emulsion, wherein a CPC-entrapped internal phase was dispersed throughout the external phase, resulting in diminished black color due to the compensation of the milky appearance of the typical emulsion. For further analysis, we applied Nile red, a water-insoluble fluorescent probe, to the emulsion containing CPC, and observed this microscopically under either white-field or fluorescent-field light sources (Figures 3(e) and 3(f)). Black spots of CPC overlapped with the red spots of the probe, indicating the partitioning of CPC to the internal oil phase. Therefore, we concluded that the introduction of an oil component would be essential for the successful development of CPC-containing topical formulations.

Physical Stability Evaluation. Topical formulations were prepared as either aqueous creams or oil-based organogels, and subjected to physical stability assessment under gravitational stress. Formulations which withstood the harsh stress conditions were expected to be physically stable. Figure 4 represents the physical stability of the various formulations as a plot of SR (%) *versus* gravitational force: as gravitational force increased, SR values also increased. In general, aqueous creams showed greater stability under all tested degrees of gravitational stress than did oil-based organogels. Among the cream-based formulations, HUMC2 showed the greatest stability, with an SR value of less than 2% at the highest gravitational force (20000×g). HUMC formulations were also more

stable than C formulations. This could be attributed to the polymeric base, which affords a relatively stable network structure. The carboxyl group of Carbopol in water solution became extended due to electrostatic self-repulsion, and the dissociation of the carboxyl group enhanced viscosity by forming hydrogen bonds between the carboxyl group and water.[20] At specific gravitational force (10000×g), SR (%) values were observed to be 20.3 (C1), 10.5 (C2), and 2.1 (HUMC1), whereas HUMC2 showed no separation at all. The relative instability of HUMC1 compared with HUMC2 might be attributed to the imbalanced composition (cetyl alcohol content varied, but the quantity of OliveM 1000 used as an emulsifier remained constant). CPC content greatly affected the stability of the C formulations, suggesting destabilization behavior of CPC, possibly due to an increase in total surface area of the microporous particle. Meanwhile, organogel is a bicontinuous semisolid formulation with an external apolar solvent phase immobilized within the spaces available in its three-dimensional networked structure, wherein van der Waals forces are involved for weak attraction.[21] As a result, the SR values of all organogels greatly increased when gravitational force was increased beyond 2000×g, even though LV formulations were relatively stable compared with L formulations. Increased lauric acid content stabilized the organogels, and the addition of Vaseline further stabilized the formulation.

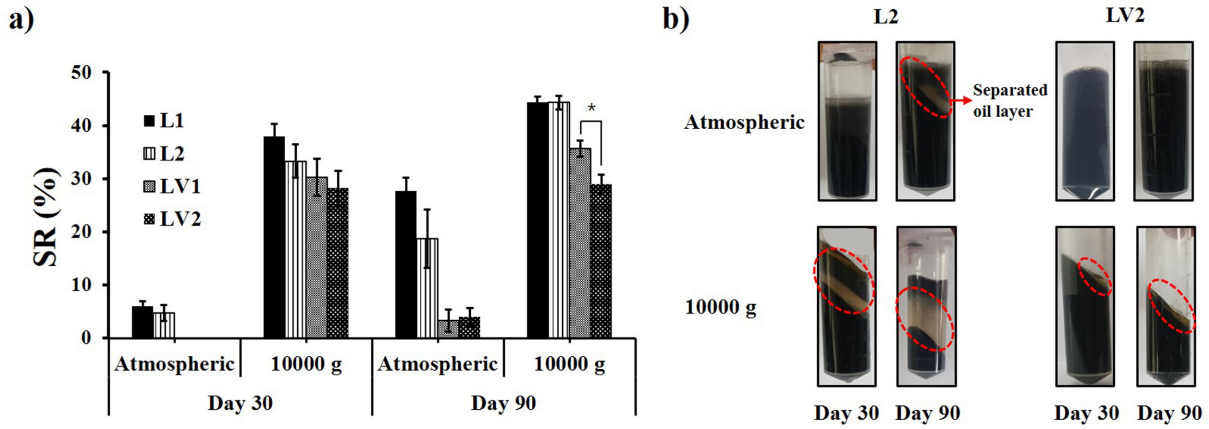


Data are represented as the mean ± SD (n = 3).

Figure 4. Physical stability plot of the separation ratio (SR, %) against centrifugal force: (a) aqueous cream formulations; (b) oil-based organogel formulations.

All formulations were stored for 3 months at 25 ºC to observe storage stability. All cream formulations were practically stable, resulting in no appreciable separation during the observation period. However, oil-based organogels were unstable, revealing time dependency as shown in Figure 5. After storage for 30 days, LV organogels showed no separation at all, whereas L organogels showed minor separation (5-6% for SR values under atmospheric pressure). However, under accelerated gravitational forces (10000×g), SR values greatly increased, in the order of 38 (L1) > 33.3 (L2) > 30.3 (LV1) > 28.3 (LV2), although significant differences were not found with $p<0.05$. Upon storage for 90 days, all organogels showed separation under atmospheric conditions, although the SR values of LV formulations were significantly less than those of L formulations. Meanwhile, under accelerated conditions (10000×g), the SR values of all organogels increased further: 44.3 for L1 and L2; 35.7 for LV1; and 29 for LV2. In particular, a significant difference in storage stability between LV1 and LV2 was found: these formulations showed a similar stability pattern throughout the experiment, except for after 90 days of storage under accelerated conditions.

Flow Properties in The Simulated Pinch Strength Test. Pinch strength is a grip strength test using the thumb tip and index finger tip, reported to be measured by using the standard, adjustable-handle Jamar dynamometer and the pinch gauge 16, wherein the average pinch strengths for men and women were approximately 7.5 and 4.97 kg, respectively. If too much pinch strength is required to squeeze the formulation out of the tube, this causes inconvenience to the patient in clinical use. In this experiment, employing the simulated pinch strength test as depicted in Figure 1, W_C (critical weight to flow) was measured for samples stored at different temperatures (Table 3). Upon storage at 25 ºC, all formulations showed W_C values between 0.8-1.1 kg, indicating good flow properties. In contrast, upon storage at 4 ºC, the W_C values of organogel samples increased significantly, while those of the cream formulations remained constant. In particular, the L2 formulation showed a notable difference in W_C values: 0.95 at 25 ºC; and 4.6 at 4 ºC. The value obtained at 4 ºC is close to the average female pinch strength, indicating difficulty in squeezing the sample out of the tube. These differences may be attributable to the following:



Data are represented as the mean ± SD (n = 3).
*significantly different with $p < 0.05$

Figure 5. Stability comparison of different organogels as a function of storage time and separation gravity: (a) plot of the separation ratio (SR, %); (b) visual observation for the oil separation.

Table 3. Critical Weight (W_C, kg) of the Various Formulations Stored at Different Temperatures

Temperature	C2	HUMC2	L2	LV2
25 °C	0.93 ± 0.26	1.1 ± 0.38	0.95 ± 0.19	0.79 ± 0.45
4 °C	0.97 ± 0.25	1.2 ± 0.08	4.6 ± 0.32	1.05 ± 0.04

Data are represented as the mean ± SD (n = 3), measured in the simulated pinch strength test.

first, cream formulations contained less CPC (8-10% w/w) than organogel formulations (approximately 40% w/w on average). A lower solid content should have been favorable for stabilizing dispersion. Second, the presence of the emulsifier (0.5% w/w of OliveM 1000) may have aided the formation of a stable o/w cream. Furthermore, a polymeric base should have aided dispersion, as the consistency of the Carbopol-induced hydrogel was not temperature-sensitive.[22] Third, the lauric acid component of the organogels, with a freezing point of 43.9 °C, is easily solidified at refrigerated temperature, resulting in stiffness of the loaded sample. Furthermore, the incorporation of Vaseline (a thermally stable oleaginous vehicle) enhanced the consistency of the organogels, resulting in the superiority of LV2.

Rheological Properties of Selected Formulations. Based on the observations for physical stability and flow properties, HUMC2 and LV2 formulations were selected for further evaluation. The rheological properties of HUMC2 and LV2 are shown in Figure 6. Both formulations are non-Newtonian fluids and belong to a shear-thinning system, as their viscosity is initially high, but decreases with increasing shear rate. These formulations were categorized as plastic fluids, based on the appearance of a yield stress: 27.24 Pa for LV2 and 134.17 Pa for HUMC2. The yield stress of HUMC2 was higher than that of LV2 due to the hydrogen bond-forming capacity of the carboxyl group in the polymer, as discussed above. In contrast, organogel has no capacity to form hydrogen bonds, but relies on van der Waals forces to weakly trap the solvent molecules in the external phase.[23] We previously reported that the networked gel structures of the hydrogel vehicles give them sufficient strength to resist low shear stress, but the material flows when shear stress surpasses yield stress 6. However, after a threshold, the slopes (viscosity) became similar, as the structured network collapsed and turned into a flowing liquid. This phenomenon is known as rheomalaxis, that is, the permanent loss of viscosity of a high-molecular-weight polymer solution subjected to high shear rates.[24] High shear rates are capable of breaking covalent bonds in polymers, resulting in low molecular weight polymers with decreased solution viscosity.

Organoleptic Properties in Sensory Evaluation. Upon application to the human skin, oil-containing formulations give a wide range of sensations including waxy, greasy, oily, shiny, and sticky feelings.[25] In recent years, several techniques have been developed to objectively measure skin properties in dermato-cosmetic research.[26] Quantitative descriptive analysis (QDA) of cosmetic products and ingredients is known to provide detailed, reliable, and consistent information on various sensory characteristics.[27] This analysis includes a complete list-

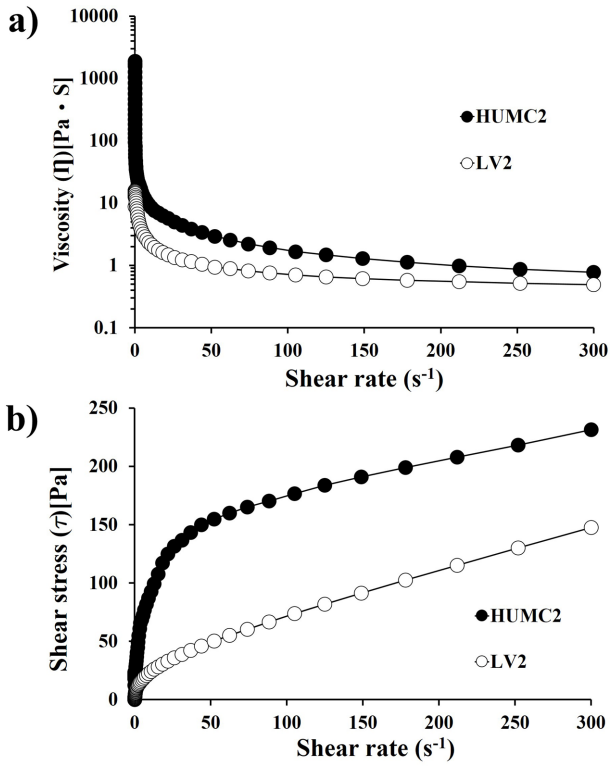


Figure 6. (a) Viscosity; (b) flow curves of HUMC2 and LV2.

ing of sensory attributes based on perceptions, order of occurrence of these attributes, the relative intensity measure for each attribute over several trials, and statistical analyses of the responses.[28] However, the main drawbacks of QDA are that it is comprehensive, time-consuming, and consequently, expensive.[29] An alternative simplified sensory study protocol has been proposed to provide valuable information while developing products.[30] Thus, in this study, sensory evaluation was performed in terms of spreadability, odor, moistness, shininess, and the capacity for removal.

Table 4 shows the results of sensory evaluation scores as the average of twelve panels. Despite the limited number of panels, some important consequences were found. In the spreadability evaluation, HUMC2 and LV2 showed values of 2.78 (acceptable to fair) and 1.78 (poor to acceptable), respectively. Neutralized Carbopol gels showed a relationship between their viscosity and bioadhesive strength,[31] which may have resulted in good spreadability. Although the consistency of LV2 was increased by employing lauric acid as an organogelator, as discussed above, organogel has a weakly-associated network structure in virtue of van der Waals attraction, compared with a relatively strong hydrogen bond in the polymeric formulation. For odor evaluations, values were not significantly different: 2.33 for HUMC2 and 2.44 for LV2, indicating an unpleasant to neutral sensation. The faint grain-like odor of sesame oil may have been an influencing factor, as all components in HUMC2 and LV2 were odorless, except for the sesame oil. In the moistness evaluations, HUMC2 was superior to LV2. We previously reported the efficient skin hydration properties of HUMC,[6] in which several ingredients were additionally included: glycerin, preventing crystallization of the stratum corneum model lipid mixture;[32] stearic acid, increasing skin permeability by invoking disruption of the densely packed lipids that fill the extracellular spaces of the stratum corneum;[33] and urea, as a well-known moisturizer in pharmaceutical fields. In the shininess evaluation, however; LV2 (3.11: shiny to very shiny) outperformed HUMC2 (2.67: matte to shiny). This difference is probably due to the high oil content of LV2, which renders a glossy effect, and Vaseline content, as a widely-used waxy lubricant. In the case of HUMC2, the polymeric base diminished the pearl-like effect of the cetyl alcohol. Meanwhile, regarding the capacity for removal by washing with water, HUMC2 (3.67: washable to easily washable) clearly outperformed LV2 (1.44: unwashable to hardly washable). As HUMC2 is a gel-based o/w type cream, it is easily diluted and removed by water.[34] On the contrary, LV2 is composed of oleaginous materials only, without any aqueous component. Overall, HUMC2 displayed more favorable qualities in the sensory evaluation, even though LV2 had a favorable appearance.

Table 4. Sensory Evaluation Results for HUMC2 and LV2

Parameters	HUMC2	LV2
Spreadability	2.78 ± 0.97	1.78 ± 1.09
Odor	2.33 ± 0.7	2.44 ± 0.72
Moistness	3.78 ± 1.32	2.33 ± 1.54
Shininess	2.67 ± 0.97	3.11 ± 1.00
Removal capacity	3.67 ± 1.00	1.44 ± 0.53

Data are represented as the mean ± SD (n = 12 for panels).

Conclusions

CPC-containing topical formulations have been successfully developed as either aqueous creams or oil-based organogels. HUMC2 and LV2 were selected among the various formulations. Both formulations belonged to a shear-thinning system, determined by rheological observation. HUMC2 was superior to LV2 in terms of physical stability, flow properties,

and sensory evaluation. LV2 had the advantage of high CPC loading capacity of approximately 40% w/w, whereas HUMC2 had limited CPC loading capacity of less than 10% w/w.

Acknowledgments: This research was supported by the National Research Foundation of Korea (NRF) Grant funded by the Korea government (MSIP) (No. 2016R1A2B4011449). This research was also supported by the Chung-Ang University Research Scholarship Grants in 2016.

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