IFSCC 2025 full paper (IFSCC2025-1027)

"A New Formulation of Retinol Stabilization – Bio 3D Printing Solid-phase Retinolsome"

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1. Introduction

This study proposes a solidified 3D formulation that encapsulates retinol through liposomes and then 3D printing in a layered structure with a 3D three-dimensional structure so that real consumers can use retinol which is very effective when putting it into their cream.

3D printing is a manufacturing technology that creates a three-dimensional object by stacking materials one by one using computer-aided design (CAD) [4]. In this study, we used the material extrusion (ME) method, a lamination manufacturing process that selectively extrudes materials through nozzles or holes mounted on the equipment head, to process and apply them in the form of filaments, and to laminate them into the desired shape while extruding through nozzles [2, 6]. The size and detail of the layer are determined by the size of the nozzle and the speed and force at which it melts and repels [1]. The nozzle is heated to raise the temperature, and the molten filament solidifies at room temperature to take its shape in order to melt and repel the material through the nozzle [5]. In addition, 3D printing allows the design of complex cosmetic formulations that do not contain stabilizers or auxiliary ingredients used in existing cosmetics, thereby controlling the release of active ingredients.

The liposome is a capsule-type skin transdermal absorption system that can stably absorb the active ingredients of cosmetics into the skin. It also has a structure similar to that of the skin due to its microscopic spherical structure made up of phospholipids, so it is used in cosmetics to penetrate deeply into the skin and increase its absorption.

Retinol, one of the fat-soluble vitamins, is an endogenous compound that naturally exists in the human body and has excellent skin care effects such as improving wrinkles. However, retinol has the disadvantage of easily reacting to external environments such as light, temperature, moisture, and oxygen.

Therefore, this study aims to improve the basic stability of retinol through liposomalization to improve the problems of retinol, and to form a double protective film by manufacturing Retinolsome with Sandwich and Sample B using base Gel through 3D printing modeling.

2. Materials and Methods

2.1. Retinol Liposome(Retinolsome) Manufacturing

Retinol is dissolved in an emulsion containing lipids and cholesterol. Then, using an M/F device, the process is repeated three times at 1000 bar pressure to form liposomes of the measured size.

2. 2. Bio 3D Printing Gel Formulation Process

When preparing A (Base Gel), prepare sample i in a glass beaker of Table 1 and completely dissolve it at 80°C and leave it to stand for about 30 minutes to cool to 40°C or less. Put the prepared A into a 10mL syringe dispenser.

When preparing B (Retinolsome Gel), prepare sample Ⅰ in a glass beaker and completely dissolve it at 80°C and leave it to stand for about 30 minutes to cool to 40°C or less. Cool the cooled ii (conversion of retinol to liposome). Put the prepared B into a 10mL syringe dispenser.

Table 1. Bio 3D Printing Gel Formulation

	INCI	A(Base Gel)	B(Retinolsome Gel)
i	Poloxamer 407	29.00	23.20
	PEG-32	38.00	30.40
	PEG-32 Stearate	3.00	2.40
	Polyglyceryl-10 Oleate	3.00	2.40
	Algin	3.00	2.40
	Caprylic/Capric Ttiglyceride	10.00	8.00
	Water	19.00	15.20
ii	Retinolsome	-	20.00

2. 3. CAD Design and 3D Printing Fabrication

To output the Bio 3D Printing Gel to the 3D printer with the desired design, we entered the desired design techniques using CAD (Computer-Aided Design) software, constructed the 3D structure, and converted it to STL file format.

For compatibility with 3D bio-printing (ROKIT INVIO Corp., Seoul, Korea), New Creator K software (version 1.57.76, Seoul, Korea) was used.

The conditions in Table 2 are set in the software, and after completing the slicing process using the slicer software, the corresponding G-code file is generated. After installing a syringe in a Bio 3D Printing machine with the corresponding program set, it is printed using the Material Extrusion Method (ME). In the study, B(Retinolsome Gel) was printed by adding it like a Sample A between A(Base Gel) or wrapping the A(Base Gel) with an outer wall to increase stability.

After one day, the moisture in the printing Gel evaporated, resulting in a solid 3D Solid-phase Retinolsome.

Table 2. Optimized Printing Parameters Determined by Pre-Screening

Slicer Parameters	Value Settings and Types
Print Speed (mm/s)	2
Travel Speed (mm/s)	8
Infill Pattern	Lines / Concentric
Infill Density (%)	10 / 15
Bed Temperature (°C)	25
Dispenser Temperature (°C)	25
Extrusion Multiplier (%)	600

2. 4. Application of 3D Solid-phase Retinolsome in Cream Formulation

The 3D Solid-phase Retinolsome and cream are applied at a 1:1 ratio, and the cream is a basic emulsifier-based cream formulation without any active ingredients added.

2. 5. Quantification of Retinol by High-Performance Liquid Chromatography (HPLC)

The analysis was conducted to compare the temperature and content changes of the cream containing general retinol and the retinol applied to 3D Solid-phase Retinolsome in the Cream.

3D Solid-phase Retinolsome and Cream were applied at a 1:1 ratio and analyzed using high-performance liquid chromatography (HPLC).

The Mobile phase used 90% MeOH, and the Solvent analyzed IPA: EtOH by preparing a 1:1 ratio solution. Measurement was performed according to the following conditions: wavelength was 325 nm, Flow was 1.0ml/min, Column Temperature was 25, Injection volume was 10ml, and Run time was 20 min.

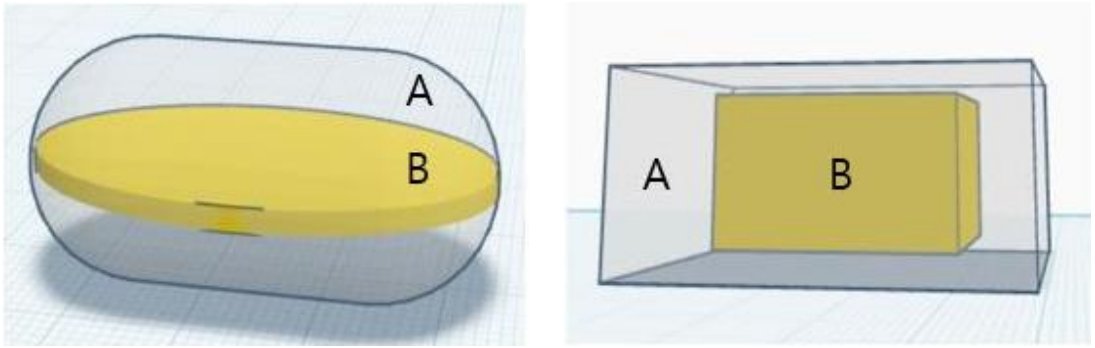
2. 6. Comparison of melting rates in creams with different compositions

Algin 1% A and Polyglyceryl-10 Oleate 1% A are manufactured in a glass beaker according to the ratio shown in Table 3, then completely melted at 80°C, and cooled to below 40°C at room temperature for about 30 minutes. After that, the manufactured sample is loaded into a 10 mL syringe. The manufacturing method is similar to A (Base Gel) in Table 1. The manufactured Gels were 3D printed with the same program design and then applied to general cream at a ratio of 1:4 to check the melting speed.

Table 3. Bio 3D Printing Gel Formula

INCI	A(Base Gel)	Algin 1% A	Poloyglyceryl-10 Oleate 1% A
Poloxamer 407	29.00	29.00	29.00
PEG-32	38.00	38.00	38.00
PEG-32 Stearate	3.00	3.00	3.00
Polyglyceryl-10 Oleate	3.00	3.00	1.00
Algin	3.00	1.00	3.00
Caprylic/Capric Ttiglyceride	10.00	10.00	10.00
Water	19.00	21.00	21.00

3. Results



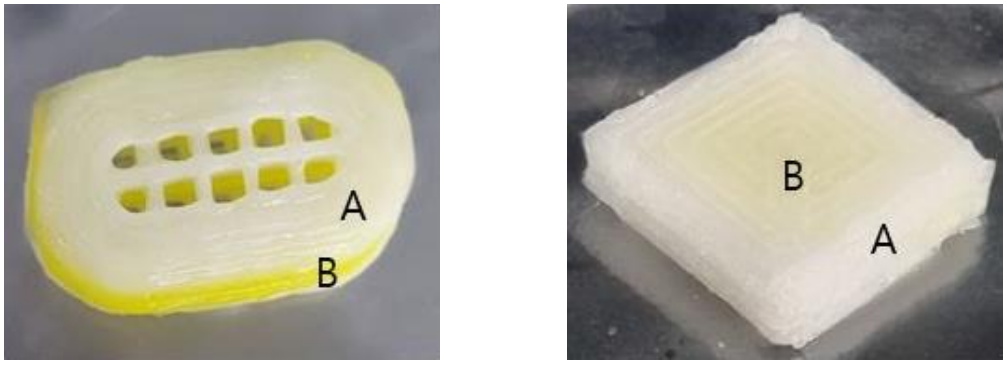
(a) (b)

Figures 1. 3D CAD Design. (a) CAD-rendered 3D structure of Sample A; (b) CAD-rendered 3D structure of Sample B.

Figure 1 is a design based on CAD (Computer-Aided Design), which varies from structure to structure depending on whether it is sealed or not with the external environment.

The Sample A is a semi-closed structure that places B(Retinolsome Gel) inside the A(Base Gel), a design method that minimizes contact with the external environment to maintain the stability of retinol.

Sample B is a closed structure and the A(Base Gel) is completely surrounded by the B(Retinolsome Gel), which is a design method that completely separates retinol from the external environment.



(a) (b)

Figures 2. 3D Printing solid Structures Based on CAD Designs for Encapsulating Retinol. (a) printed object of Sample A; (b) printed object of Sample B.

Figure 2 is the result of printing a programmed model based on CAD drawings designed with a 3D structure using a 3D printer.

It is a capsule-shaped structure designed to stably block retinol from the external environment.

In the Sample B, as in the design drawing, the A(Base Gel) was printed to completely surround the B(Retinol Gel), and the retinol was implemented as a closed structure completely separate from the external environment.

The Sample A is also implemented as designed, and the retinol is designed not to come into direct contact with the external environment, confirming that it is a semi-closed structure with minimal contact.

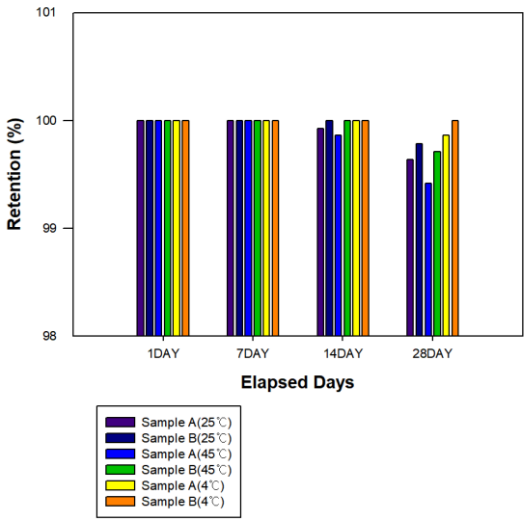


Figure 3. HPLC Quantification Depending on 3D Structural Configuration

Following the design of Bio 3D Printing Solid-phase Retinolsome (Sample A, Sample B), the retinol contents were compared by HPLC for 28 days. After storage at three temperature conditions (25℃, 45℃, 4℃), both samples remained constant, of which the Sample B remained almost unchanged for 28 days. This can be attributed to the fact that the Sample B completely blocked exposure to the external environment, thus maintaining the stability of the retinol well.

The Sample B was designed to be insensitive to changes in the external environment such as temperature and humidity, so it was effective in preventing retinol instability. The structure of the Sample A that minimized exposure to the external environment showed changes compared to the structure of the Sample B, but there was no significant difference. This result shows that the Sample B is designed to protect retinol more effectively.

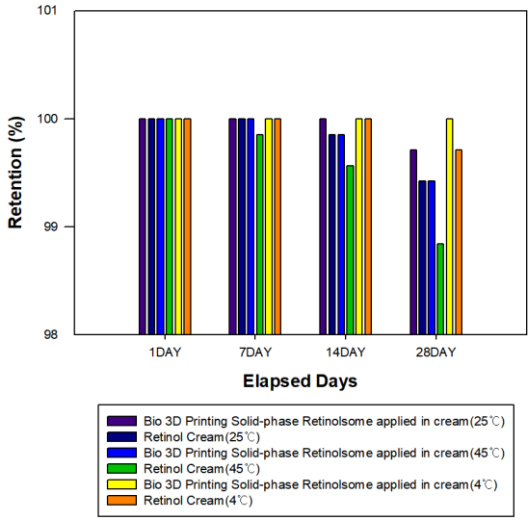


Figure 4. Quantitative Analysis of Retinol Content by HPLC (Bio 3D Printing Solid-phase Retinolsome applied in Cream VS Retinol Cream)

Figure 4 is a graph showing the changes in retinol content and samples stored under the three temperature conditions for 28 days of retinol cream and cream containing Bio 3D Printing Solid-phase Retinolsome through HPLC analysis. It was found that the temperature change did not significantly affect the stability of retinol as the contents of the cream containing Bio 3D Printing Solid-phase Retinolsome remained almost unchanged when stored at 25℃, 45℃, and 4℃.

On the other hand, retinol cream showed a slight decrease in content after storage during the same period. In particular, the decrease at 45℃ was most remarkable. These results show that the stability of retinol decreases with temperature. In Figure 4, it was found that the retinol content of the cream containing Bio 3D Printing Solid-phase Retinolsome remained constant over time. In contrast, the retinol content of the retinol cream gradually decreased over time.

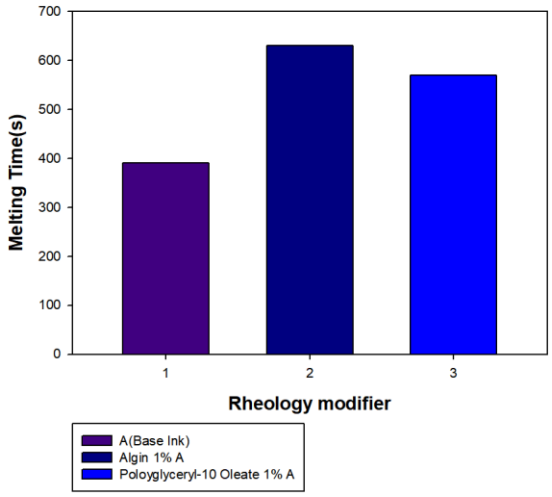


Figure 5. Comparison of melting rates in creams with different compositions

To compare the speed at which the Bio 3D printing Solid-phase melts in the cream, the viscoelasticity regulator ingredients were evaluated. As a result, the lower the content of Algin and Polyglyceryl-10 Oleate, the slower the dissolution speed in the cream tended to be. Based on

this, when compared with the A (Base Gel) recipe in Table 1, it took a longer time to dissolve when the content of Polyglyceryl-10 Oleate was lower, and it took an even longer time when the content of Algin was lower. Through this, it was confirmed as the result in Figure 5 that Algin and Polyglyceryl-10 Oleate have a great effect on the dissolution speed of the cream.

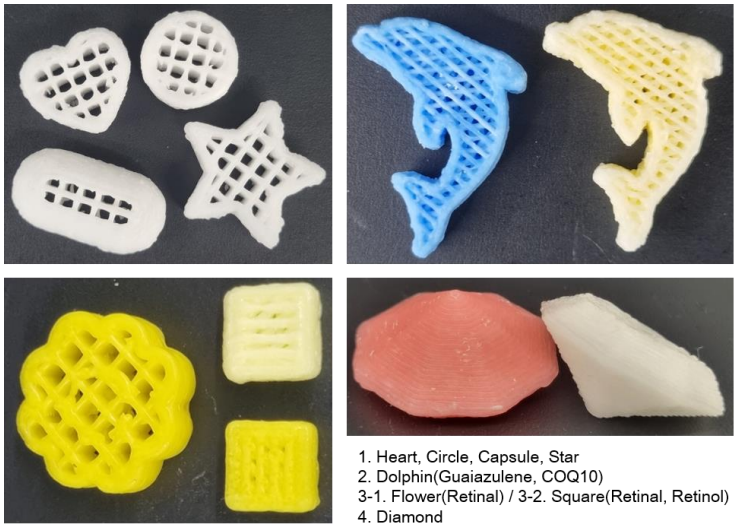


Figure 6. 3D printing Solid-phase with a variety of active ingredients, designs, and colors

Figure 6 is the result of the 3D differentiation of various designs and colors using various effective ingredients such as COQ10, Guaiazulene, and Retinal, Retinol. This allows consumers to configure products by considering the composition of ingredients, shape, and color.

4. Discussion

In this study, retinol, an unstable raw material, was stabilized by liposomalization and placed in solidified Base Gel to stabilize it from the external environment further.

Unlike existing retinol products, it has been confirmed that safety and efficacy have been improved even when exposed to the external environment (light, temperature) without special storage.

As such, solid cosmetics using 3D printing have shown the potential to secure the external environment more reliably than methods involving stabilizers or auxiliary ingredients used in conventional cosmetics, a new formulation that can secure the stability of the unstable raw material market in the cosmetics industry. Although this product is a solid cosmetic, it can be easily used in a variety of creams and essences due to its fast melting properties, and consumers can freely choose cream that suits their taste. This maximizes ease of use while expanding the scope of product application to further increase consumer satisfaction. In addition, products using 3D printing can be produced in the design and capacity that consumers want, enabling complex products and personalized cosmetics.

Through this study, the proposed formulation has confirmed its potential for use in the personalized cosmetics market, which has the potential to present a new direction for related markets in the future.

5. Conclusion

In this study, we prepared a formulation in which raw materials of liposomal retinol, an active ingredient vulnerable to external environments, were solidified through 3D printing.

In this study, high-performance liquid chromatography (HPLC) analysis confirmed that retinol was successfully captured even after 3D printing, and efficacy analysis confirmed that retinol content can help maximize retinol's skincare effect by maintaining stable retinol activity without separate storage. In addition, by adjusting the 3D printing parameters, it is possible to 3D print various designs (e.g. hearts, dolphins), which can not only personalize the appearance of cosmetics but also adjust the dosage of active ingredients to manufacture complex products and personalized cosmetics.

6. References.

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