Stabilization of Vitamin A Using the various cubosomes

SS_236

Seung Yeon Son[1], Dong Ock Kim[1], Yu Jin Kang[1], Young Ah Park[2], Hong Geun Ji[1],
[1]H&A PharmaChem, R&D center, Bucheon, 14558, Korea
[2]Interdisciplinary Program in BioCosmetics, Sungkyunkwan University, Suwon, 16419, Republic of Korea

Introduction:

Cubosomes are a kind of nanoparticles made of specific amphiphilic lipids such as monooleinm which is a biological component. Due to its molecular structural properties, it has a cubic-shaped bi-continuous aqueous channel in an aqueous solution, and is utilized to improve the delivery ability of nutrients and drugs, and to control the release of molecules, so that it can be delivered with high efficiency.[2] Cubosomes are very small in size and are friendly to the cell membrane of skin cells, so they can easily penetrate into the cell gap, Cosmetics that apply active ingredients such as wrinkle improvement, whitening, antibacterial, and anti-inflammatory has been developed, and technology to safely deliver these ingredients to the skin is continuing research. Using the particle structure characteristics of cubosomes, an active ingredient was loaded and used to deliver substances into the skin.[3].

Materials & Methods:

1) Preparation of cubosomes of various contents using three polymers

Cubosomes are composed of three types of amphiphilic lipids, stabilizers, and water. Glyceryl monooleate(GMO),[4] the most commonly used lipid, was used. Pluracare F127, Poloxamer 188 and PEC-10K were used as a stabilizer surfactant.[4-5] GMO, surfactant, and water are set at different ratios to prepare cubosomes. Cubosomes are manufactured by adjusting the ratio of the raw material used.[1]

Phase	Ingredient	% by weight					
A	**Monomuls 90-018**	5.00	10.00	**15.00**	20.00	25.00	30.00
	Polymers	7.50	15.00	**22.50**	30.00	37.50	45.00
B	**Water**	85.50	73.00	**60.50**	48.00	35.50	23.00
	1,2-Hexanediol	2.00	2.00	**2.00**	2.00	2.00	2.00

2) Preparation of cubosomes containing Retinal

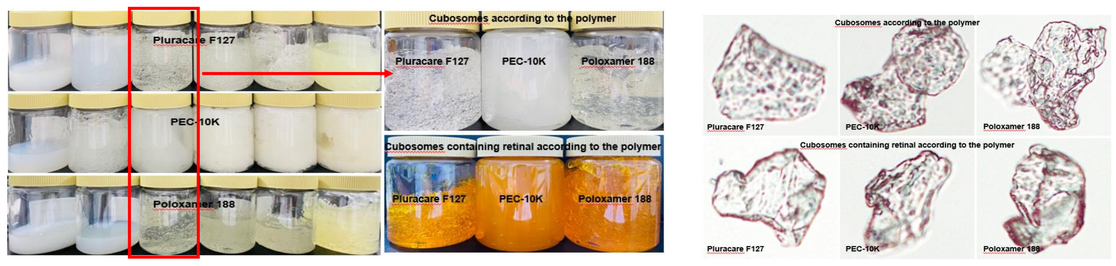
One of the most stable samples prepared in 6 different amounts is selected to manufacture cubosomes containing retinal for each polymer.

Phase	Ingredient	% by weight
A	Monomuls 90-018	15.00
	Polymers	22.50
	Retinal	**1.00**
B	Water	60.50
	1,2-Hexanediol	2.00

Results & Discussion:

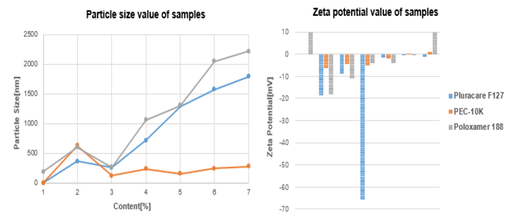
1) Appearance and Microscope

The emulsified statd is different depending on each polymer and content.
At the content of No. 3, cubosomes formation is well seen.



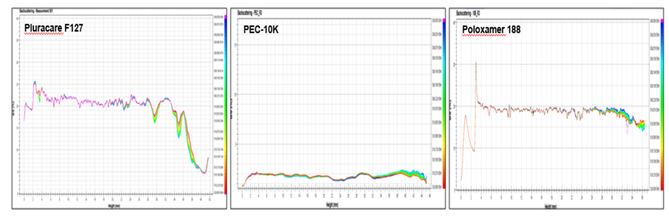
2) Particle size and Zeta potential

As the polymer content increased,
the particle size also increased.
The zeta potential of cubosomes using
Pluracare F127 was stably measured.
Retinal containing cubosomes were also
measured with similar size and zeta potential.



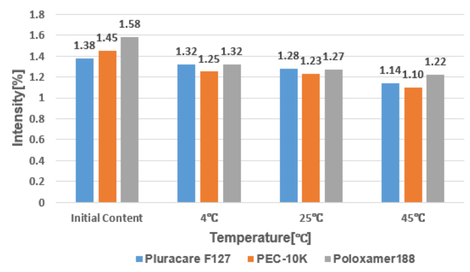
3) Turbiscan

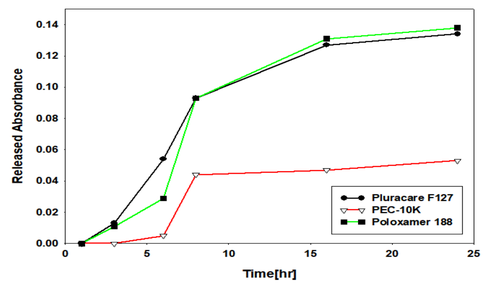
Overall, aggregation occurs
in the upper layer,
but there is no significant change
and it can be seen as a stable state.



4) HPLC & *In Vitro(Franz Diffusion Cell)*

The content of cubosomes containing retinal was analyzed at the beginning of 1% or more, and the titer hardly decreased after three month and was stably maintained.
In the case of the in vitro, it is seen that cubosomes containing retinal
are released from at least 3 hours, and it is confirmed that the amount of release also increases as the time increases.





Conclusions:

In this study, cubosomes were applied to cosmetics.
When the conditions for forming cubosomes that deliver cosmetic active ingredients well are found, it can be applied to cosmetics as a new delivery vehicle.
Overall, the higher the ratio of amphiphilic lipids to the stabilizer, the better the cubosomes are formed, and the higher the amount of water,
the better the cubosomes are formed. Retinal-containing cubosomes were prepared by selecting the content to form stable cubosomes, and thus stability was analyzed.
It gradually increases in size as the proportion of lipids increases.
Zeta potentials are measured similarly without significant differences.
We were able to confirm the stability of cubosomes through turbiscan and rheology.
In this study, cubosome is expected to be able to replace not only retinal but also retinol, which can be stably applied in cosmetics.

Aknowledgments:

This work was supported by the Technology Innovation Program (or Industrial Strategic Technology Development Program (10077704, Development of skin-sensitized organic-inorganic hybrid with improved skin penetration for functional cosmetics) funded By the Ministry of Trade, Industry &Energy (MOTIE, Korea).

References:

1. P.VISHNU, N.SADHANA, K.NAVEENBABU, M.SUNITHA REDDY, K.MAHESWARI(2020), Preparation and Evaluation of Valsartan Cubosomes, ISSN 0975-2366
2. Anbarasan. Ba , Fatima Grace. Xa, Shanmuganathan S(2015), AN OVERVIEW OF CUBOSOMES - SMART DRUG DELIVERY SYSTEM, Chennai - 116
3. Gopal GARG,* Shailendra SARAF, and Swarnlata SARAF(2007), Cubosomes: An Overview, Biol. Pharm. Bull. 30(2) 350—353
4. Adam J. Tilley a,b , Calum J. Drummond b , Ben J. Boyd(2012), Disposition and association of the steric stabilizer Pluronic F127 in lyotropic liquid crystalline nanostructured particle dispersions, Journal of Colloid and Interface Sience 392(2013) 299-296
5. Seyedeh Parinaz Akhlaghi , Iris Renata Ribeiro, Ben J. Boyd, Watson Loh(2016), Impact of preparation method and variables on the internal structure, morphology, and presence of liposomes in phytantriol-Pluronic® F127 cubosomes, Collids and Surfaces B : Biointerfaces 145(2016) 845-853