Polymersome : Stabilization of Amphiphilic Block Copolymer Nanoparticles

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Abstract

Drug delivery technology that delivers effective ingredients to the skin is being developed in combination with nanotechnology. In this study, polymersomes are used as a material to increase stability and skin permeability. Depending on the properties of the block copolymer, polymersomes of various types can be produced and provide improved structural stability compared to liposomes. The amphiphilic agent used to prepare polymersomes is a PEG-PCL based copolymer. First, a polymer and hydrogenated lecithin are mixed in an appropriate ratio. Polymersomes are prepared using a microfluidizer, a high-pressure micro-emulsification process. The Particle size and zeta potential of the synthesized block polymer are measured. After a period of time, various oils and retinol applied to the proportion of polymersomes with little change in particle size [1]. Also, the stable structure is confirmed through the analysis of the properties using an electron microscope. When polymer and oil are applied during the manufacturing process, it can be seen that emulsification takes place. It can be confirmed that dispersion stability and viscosity and more stable when compared to liposomes. In this study, we found the optimal ratio to form a stable structure of polymersomes. The Synthesized polymersomes can increase skin permeability, so it is expected to secure technological competitiveness in the cosmetic industry.

Keywords: Polymersome, Bolck Copolymer, Polymer-hybrid, Liposome, Retinol

Introduction.

The skin is composed of several layers of cells, protecting it from external microorganisms and harmful substances. In order to permeate the cosmetic to the skin, a component similar to the cell membrane is brought into contact with the skin [2]. The double layer of cell membrane is then assimilated, opening the barrier of the skin membrane. When the skin membrane is opened, cosmetics that can penetrate the skin can enter the skin. In general, skin active ingredients used in cosmetics are easily denatured by light, temperature and air, so their application to products requiring long-term preservation such as cosmetics is limited [3]. Drug delivery technology that delivers effective ingredients to the skin is being developed in combination with nanotechnology [4]. Liposomes, a typical nano-sized drug delivery system in cosmetics, are composed of phospholipids, which are the main components of biological membranes and have a structure composed of two components, hydrophilic and lipophilic, such as hydrogenated lecithin, ceramide and cholesterol. Due to this structure, polar and non-polar substances can be captured and transported into cells [5]. However, there are problems such as material instability due to oxidative degradation of phospholipids, low emulsion stability and low capture efficiency of active ingredients. Also, since the skin penetration of the active material is not achieved, the effect applied to the skin is limited [6]. In this study, hydrogenated lecithin, a representative component of liposomes, is combined with a polymer to increase skin absorption. This is a new drug delivery system called polymersome, which increases stability and skin permeability. Polymersomes are self-assembled polymer-based bilayer vesicles made of block copolymers [7]. It is composed of a copolymer including a hydrophilic block, which is a hydrophilic polymer, and hydrophobic block, which is a conductive polymer, and has biocompatibility and biodegradability properties similar to lipids [8]. Depending on the characteristics of the block copolymer, various types of polymersomes can be produced, and the particle shape can penetrate the stratum corneum well, thereby maximizing the effect on the skin. In this study, we focused on the application of biocompatible polymers to the cosmetic industry by using the self-assembling, tunable physicochemical properties of film-forming copolymers.

Materials and Methods.

1) Preparation of polymersome according to the ratio of hydrogenated lecithin

The amphiphilic agent used to prepare polymersomes is a PEG-PCL based copolymer. First, a polymer and hydrogenated lecithin are mixed in an appropriate ratio. (Table 1) Polymersomes are prepared using a microfluidizer, a high-pressure micro-emulsification process. The particle size and surface charge (zeta potential) of the synthesized block polymer are measured.

Table-1. Prescription of polymersomes formulation

Phase	Ingredient	% by weight					
A	Hydrogenated Lecithin	0.5	1.0	1.5	2.0	2.5	3.0
	PEG-PCL	2.0	2.0	2.0	2.0	2.0	2.0
B	Water	95.5	95.0	94.5	94.0	93.5	93.0
	1,2-Hexanediol	2.00	2.00	2.00	2.00	2.00	2.00

2) Preparation of polymersome according to the ratio of various oils ratio

Oil is applied to a proportion of the six polymersomes that does not change significantly in particle size over time. There are three types of oil used for polymersome produciton: vegetable oil(Caprylic/Capric Triglyceride), ester oil(Cetyl Ethylhexanoate) and hydrocabon-based oil(Squalane). (Table 2)

Table-2. Prescription of polymersomes containing oils formulation

Phase	Ingredient	% by weight				
A	Hydrogenated Lecithin	2.0	2.0	2.0	2.0	2.0
	PEG-PCL	2.0	2.0	2.0	2.0	2.0
	Water	93.0	91.0	89.0	87.0	84.0
	1,2-Hexanediol	2.0	2.0	2.0	2.0	2.0
B	Oils	1.0	3.0	5.0	7.0	10.0

After measuring the particle size of the polymersome to which the three oils are applied, the ratio of the oil that does not change the most over time is selected to finally prepare a

polymer-hybrid that captures retinol. Using vegetable oil with the most compatibility with retinol, retinol was included in liposomes and polymer-hybrids, respectively, and comparative analysis was performed. All polymer hybrids are manufactured by high pressure emulsification process.

Results.

It can be seen that polymersomes are produced differently each content depending on the ratio of amphiphilic polymer to hydrogenated lecithin. As the content increases, the transparency of the polymersomes decrease and the particle size increase overall. (Figure 1) The zeta potential is on a stable state at -30mV. As a result of re-measurement of the particle size after 6 months, the polymersome to which 2% of hydrogenated lecithin was applied had a particle size of 191.3nm on the day of manufacture and 192.0nm after 6 months, stably maintained without any significant difference. When each of the three oils is applied in a stable ratio, the emulsification of the polymersome occurs well, and through this, it can be confirmed that the compatibility with the oil is good. In addition, as the amount of oil increases, the particle size also increases. (Figure 1)

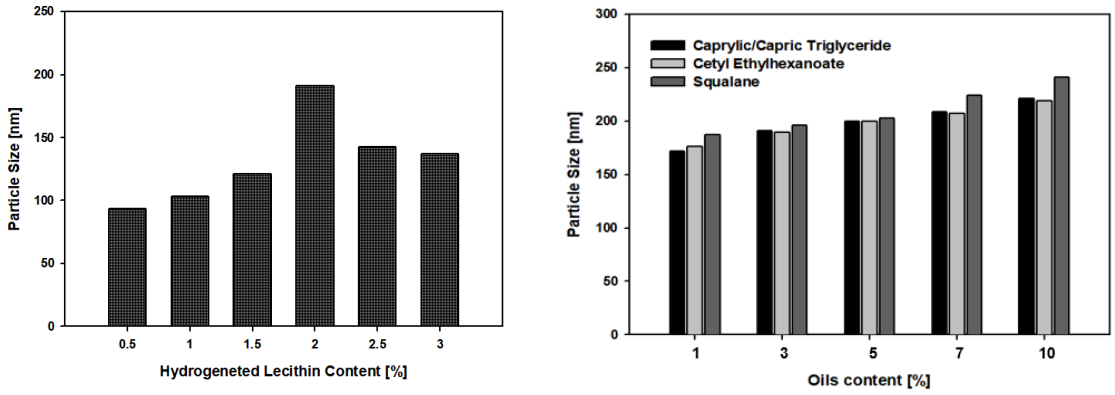


Figure 1. Particle size of polymersome

Finally, a polymer-hybrid obtained by applying retinol to vegetable oil with a stable polymersome formation rate was prepared and compared with liposomes. Both are liquid with viscosity, and the polymer-hybrid has better transparency than liposomes. The particle

size is smaller at 157.0nm for liposomes and 114.0nm for polymer-hybrid. The structure was observed using a low temperature electron microscope. (Figure 2)

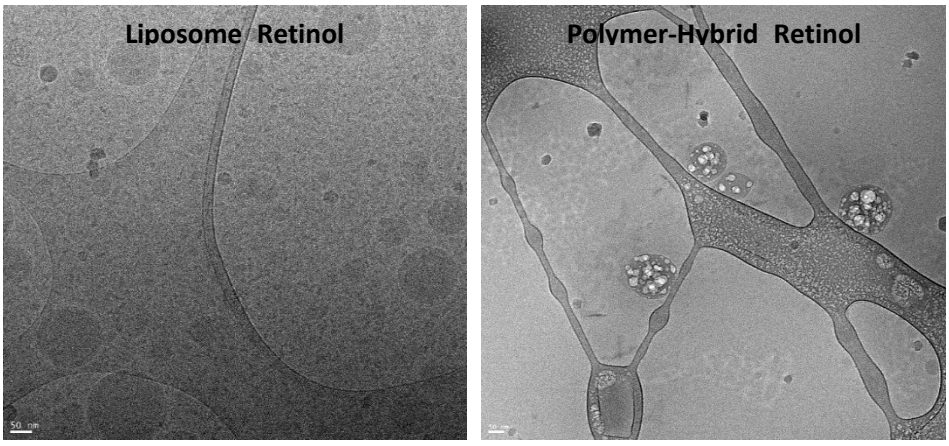
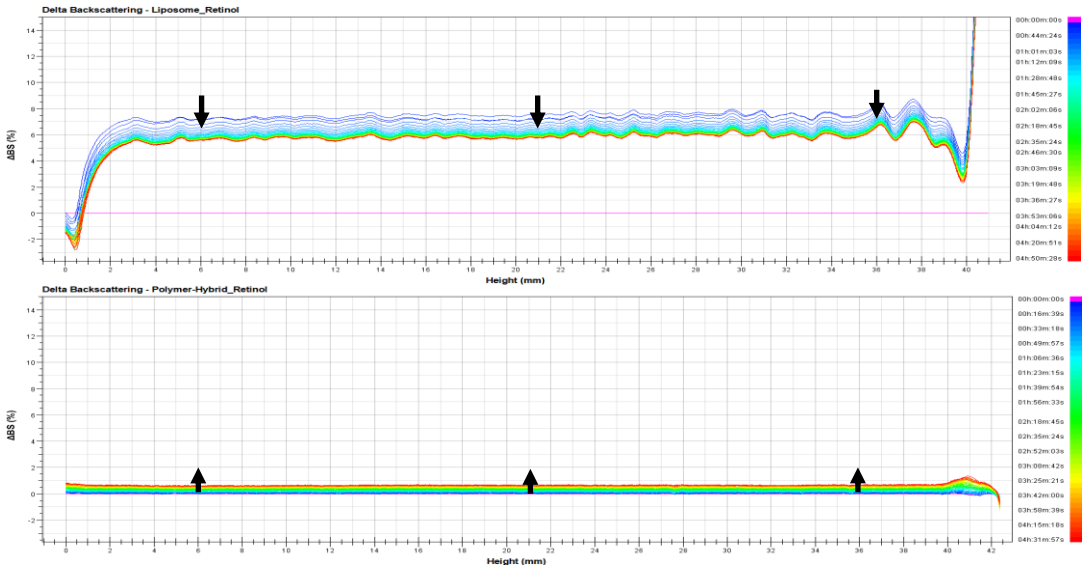


Figure 2. Electron Microscopic Images, Liposome-Retinol and Polymer-hybrid-Retinol

The dispersion stability and rheological analysis of the two formulations containing retinol were compared. The dispersion stability is measured by repeatedly scanning the height of the sample over time. In both samples, the initial t_0 profile BS(%) of the analysis appears flat, so they are in a homogeneous state. In the case of liposomes, the BS(%) value decreases and in the polymer-hybrid, the BS(%) value increases. Flocculation and coalescence occur with respect to the height of the entire sample, and it can be seen as an effect of the change in particle size. TSI (Global) means the stability index over time at the total height of the sample. Generally, the higher the TSI index, the more unstable the sample is. Comparing the two samples, it can be determined that the polymer-hybrid is relatively stable because the TSI value is smaller than that of the liposome. (Figure 3)



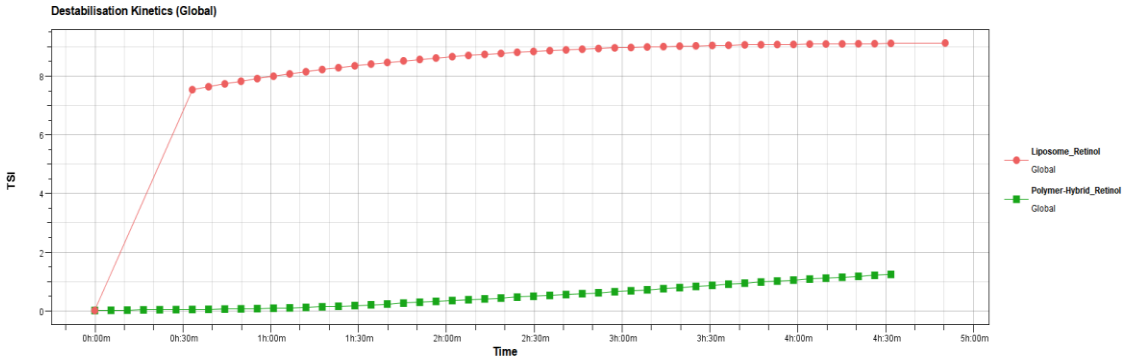
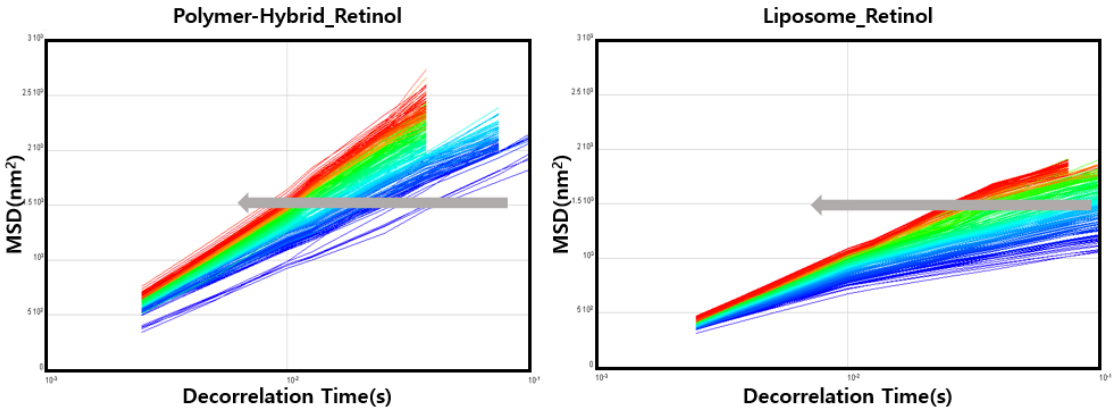


Figure 3. Turbisca data, Liposome-Retinol and Polymer-hybrid-Retinol

Two types of viscoelastic properties were analyzed according to the rheology method to determine what kind of deformation the polymersome is as a cosmetic ingredient. The MSD(Mean Square Displacement) curves of the two formulations containing retinol are constantly shifted to the left, indicating that both samples have excellent uniformity. When the MSD curve is overlaid from 20 hours, which is a section where the analysis point of the sample is parallel, it can be seen that both samples decrease and the viscous aspect decreases over time, and the polymer-hybrid has higher viscous properties than the liposome. (Figure 4)



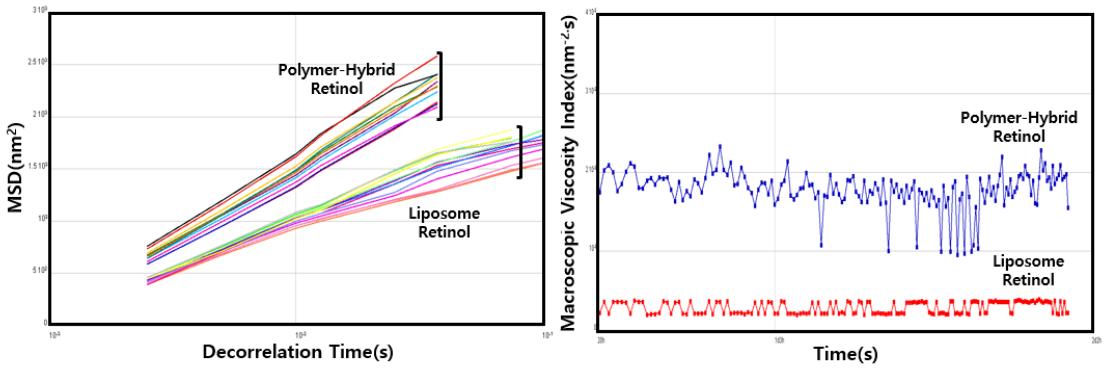


Figure 4. Rheology data, Liposome-Retinol and Polymer-hybrid-Retinol

The FT-IR spectra were shown that the PEG-PCL and polymer-hybrid are similar with typical features. Unlike liposomes, it shows similar peak formation at 2300-2400cm^{-1}. (Figure 5)

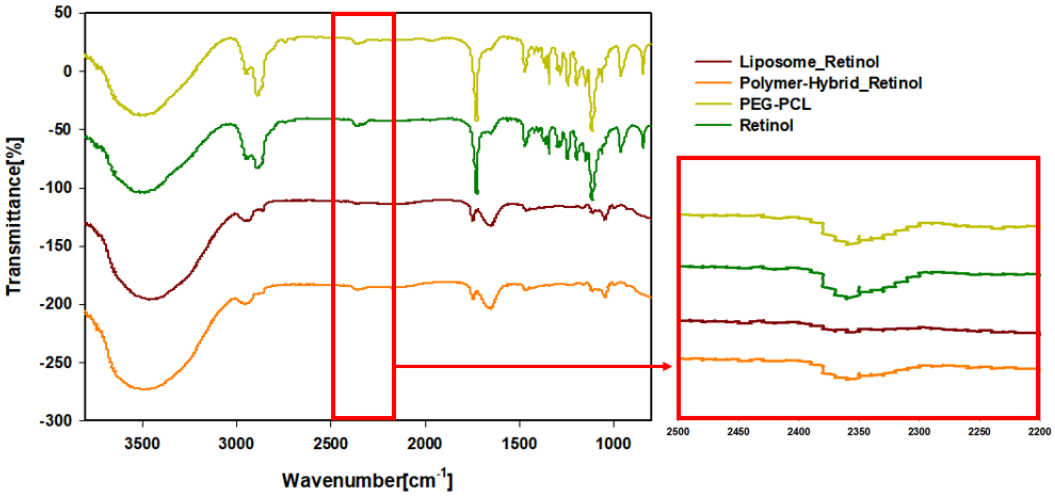


Figure 5. FT-IR data, PEG-PCL, Retinol, Liposome-Retinol and Polymer-hybrid-Retinol

Discussion.

In this study, a polymer-hybrid, a carrier that delivers the active ingredients of cosmetics to a desired site, was prepared using an amphiphilic polyethylene glycol and hydrophobic polycaprolactone, which are biodegradable polymers with an amphiphilic emulsifier function and a percutaneous absorption promoting function. Based on the results of thermodynamic stability, this dermatological fluid can be widely developed in the cosmetic industry, such as developing new cosmetic formulations that can apply active ingredients such as wrinkle

improvement, whitening, antibacterial, anti-inflammatory and enhancing skin efficacy. In addition, the amphiphilic substances used in this study have molecular reciprocity and self-association power, so they can be used not only in cosmetics but also in various industries.

Conclusion.

In this study, we found the optimal ratio to form a stable structure of polymersomes. It can be confirmed that the polymersome has excellent emulsifying power with oil due to its compatibility with various oils, and based on this, retinol, an active material that is unstable in the external environment, was collected. When compared to liposome, structural differences of the polymer-hybrid containing retinol were confirmed under an electron microscope. The particle size of the polymer-hybrid was also relatively small. Through dispersion stability and rheology analysis, the polymer-hybrid was able to obtain much more stable data than liposome. Therefore, it is expected that polymer-hybrid can increase skin permeability than liposome when applied to cosmetic formulations. In summary, a polymer-hybrid was developed as a system that can stably capture retinol from the external environment, and it is expected that other active ingredients as well as retinol can be grafted.

Acknowledgments.

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Conflict of Interest Statement.

NONE..

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