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Preparation and Characteristics of NLC Coenzym Q10 with A Combination of Hyaluronic Acid

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ABSTRACT

Coenzyme Q10, often also known as ubiquinone, coenzyme Q10 or Q10, is soluble in lipids and is naturally present in plants, animals and in mitochondria. Coenzyme Q10 functions as an antioxidant that can protect the body from damage caused by free radicals. Hyaluronic acid is known as a hydrophilic polymer derived from polysaccharides which has the ability to increase percutaneous penetration by changing the composition of tightly arranged stratum corneum cells to increase the permeability of the skin. Nanostructured Lipid Carrier is a modification of the SLN system, consisting of a mixture of solid and liquid lipids (oil), stabilized by aqueous surfactant solution, is one method to increase drug penetration through the stratum corneum because it has several advantages. The purpose of this study was to see the effect of adding hyaluronic acid to the characteristics of the Nanostructure Lipid Carrier (NLC) as anti aging. Examination of characteristics including organoleptic, pH, particle size and polydispersity index was carried out. The results of organoleptic NLC coenzyme Q10-HA examination obtained dark orange color, liquid consistency, lipid efficacy odor and soft texture. The pH measurement results of the preparation ranged from 5.05-5.23. The results of the particle size examination ranged from 267-128 nm and the particle size distribution ranged between 0.308-0.200

Keywords: Coenzym Q10, Hyaluronic Acid, NLC

INTRODUCTION

Background

Coenzym Q10 is a natural compound found in the inner membrane of the mitochondria, with the role of forming ATP as an electron carrier in the respiratory cycle in the mitochondria⁽¹⁾. Networks that require large energy and high metabolic rates such as the liver, kidneys, heart and muscles have large intrinsic concentrations of Q10 compared to other tissues. The ubiquinol reduction form is a potent antioxidant compound and is able to recycle and regenerate other antioxidants such as Isopropyl palmitate and Vitamin C⁽¹⁾.

There are two main routes of drug penetrating the stratum corneum, including the transepidermal pathway and the transappendage pathway⁽²⁾. One of the factors that can affect penetration ability through intercellular and transcellular pathways is the price of the partition coefficient (log P). The optimal log P value for the penetration of substances penetrating the stratum corneum is 2-3⁽³⁾. Coenzym Q10 is a fat soluble compound with a log P of 19.4 so that coenzym Q10 has a penetration that is not good at penetrating the skin.

To increase percutaneous penetration requires a penetration enhancer (skin enhancer) that is safe and can be degraded by the body. One of the penetration enhancers that has these criteria is hyaluronic acid. Hyaluronic acid (HA) is known as a polysaccharide-derived hydrophilic polymer that has the ability to increase percutaneous penetration by changing the arrangement of the tightly arranged stratum corneum cells to increase the permeability of the skin⁽⁴⁾.

3 The Nanostructured Lipid Carrier (NLC) is the second generation of the Solid Lipid Nanoparticle (SLN) system. Nanostructured Lipid Carrier is a modification of the SLN system, consisting of a mixture of solid and liquid (oil) lipids, stabilized by aqueous surfactant solution, is one method to increase drug penetration through the stratum corneum because it has several advantages⁽⁵⁾. One of the advantages is that the presence of dense lipids in the system can control drug release so that it can act as a drug reservoir. NLC formulas contain lipids and surfactants, which can increase penetration^{(6),(7)}. Good NLC characteristics can be shown from pH value, viscosity, particle size, particle morphology, drug entrapment efficiency, drug release, in percutaneous penetration in vitro and physicochemical stability. Characteristic testing is done to determine the characteristics of a good NLC so that it can proceed to penetration testing.

METHODS

Chemicals

The materials that used in this study such as coenzyme Q10 (Kangcare Bioindustry, China), hyaluronic acid, cetyl palmitate, olive oil, span 80, Tween 80, ethanol pa, sodium acetate pa, and glacial acetic acid pa (Materials that used in this study if not stated, otherwise it has Pharmaceutical grade purity).

Place and time of research

8 This research was conducted in October 2018 until December 2018. It was held at the Department of Pharmaceutical, Faculty of Pharmacy, Airlangga University, Indonesia.

Preparation of NLC coenzyme Q10 with hyaluronic acid (HA)

The NLC coenzyme Q10-HA system was made using the High Shear Homogenization method. In the first stage, the oil phase in the form of cetyl palmitate, olive oil and the active ingredient coenzyme Q10 were melted at 60°C. At the same time, Tween 80, span 80, HA, ethanol and acetate buffer pH 5.0 ± 0.2 were heated to a temperature of 60°C in separate containers. Then Tween 80 and Span 80 were added to the mixture of oil phase and coenzyme Q10, stirred with High Shear Homogenizer at a speed of 5000 rpm for 5 minutes. After that, the water phase was added gradually, such as the ethanol mixture and buffer acetate, into the oil phase with the same temperature, time and speed. After the last droplet, the ultraturrax speed was increased to a speed of 16,000 rpm for 5 minutes. The cooling step which was carried out by transferring the NLC and the High Shear Homogenizer onto the hot plate, then stirred using a magnetic stirrer at a speed of 500 rpm to reach room temperature.

Fourier transform infrared (FTIR)

Analysis of coenzyme Q10 FTIR NLC spectrum with HA combination. Before analysis, 2 mg samples were mixed with 300 mg KBr powder for pellets. Pellet KBr was observed at 4000-450 / cm using Jasco FT-IR 5300, Easton MD, USA.

Organoleptic

Organoleptic examination was done visually including shape, color, and smell.

pH test

5 pH measurements were carried out using a calibrated pH meter. Electrode was inserted into 50 mL of the formula and then the number was indicated by the pH meter.

Droplet size and Polydispersity index (PI)

The size and distribution of particle size were carried out using the Delsa™ Nano Sub Micron Particle Size Analyzer. Formula was weighed about 1.0 gram plus aquadest until volume of 10 mL. The sample was inserted into the cuvette then the cuvette was inserted into the sample holder. The device was turned on and the particle size menu was selected. The data, which was observed, was the average droplet diameter and polydispersity index (PI). Polydispersity index (PI) was described variations in the sample. PI values less than 0.2 indicate that the sample was monodispersion.

1
Statistical analysis

Statistical analysis was performed by one-way analysis of variance (ANOVA) for repeated measurements. The post hoc (Bonferroni) test was used to perform multiple comparison analysis (SPSS program, USA, version 15) and differences were considered significant at a level of $p < 0.05$.

RESULTS

Organoleptis

Table 1. The results of organoleptic examination of the NLC coenzyme Q10-HA system

Formula	Organoleptic examination			
	Color	Smell	Consistency	Texture
F1	Orange	The distinctive smell of lipids	Liquid	Soft
F2	Orange	The distinctive smell of lipids	Liquid	Soft
F3	Orange	The distinctive smell of lipids	Liquid	Soft

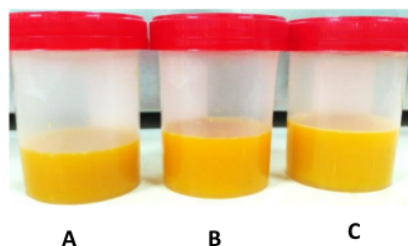


Figure 1. NLC Coenzyme Q10-HA formula with various concentrations of A) Formula 1 coenzyme Q10 with 1% HA; B) Formula 2 coenzyme Q10 with 1.5% HA; C) Formula 3 coenzyme Q10 with 2% HA.

pH Test

Table 2. The results of the pH testing of the NLC coenzyme Q10-HA system

Formula	Ingredients							Mean ± SD pH
	Coenzyme Q10	HA	Cethyl palmitate	Olive oil	Span 80	Tween 80	Ethanol	
F1	1	1	4.8	1.8	1.8	18.44	3.42	5.21±0.017
F2	1	1.5	4.8	1.8	1.8	18.44	3.42	5.13±0.017
F3	1	2	4.8	1.8	1.8	18.44	3.42	5.07±0.2

Particle Size dan poldispersity index

Table 3. The results of particle size measurement and coenzyme Q10 NLC particle size distribution with HA combination

Formula	Mean ± SD	
	Particle Size	PI
F1	128.1±1.22	0.308±0.01
F2	155.3±1.95	0.28±0.04
F3	267.3±147.44	0.200±0.08

Fourier Transform Infrared (FT-IR)

FTIR coenzyme Q10 spectra, HA and FTIR spectra NLC coenzyme Q10 system with HA combination was shown in the figure .

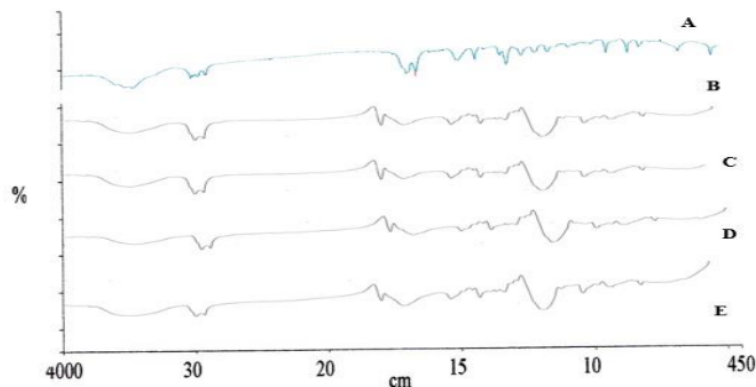


Figure 2. (A) Coenzyme Q10 infrared spectrum (B) spectrum infrared blank (C) infrared spectrum formula 1 (D) infrared spectrum formula 2 and (E) infrared spectrum formula 3.

DISCUSSION

NLC characteristics of coenzyme Q10 with HA combination are determined. Based on the examination of organoleptic NLC with HA combination, a system with a liquid consistency was produced, dark orange and has a soft texture (table 1 and figure 1). The greater the concentration of HA in the NLC system, the system consistency increases. The pH produced in each formula ranged from 5.05-5.23 (table 2 and figure 2) where the pH is in the pH range of the skin which is 4.0-6.5, so that it can minimize the occurrence of irritation, because the pH too acidic can cause pain in the skin and pH that is too alkaline can cause irritation because the pH is too alkaline can cause fungal and bacterial infections⁽⁸⁾.

Examination of particle size and particle size distribution was carried out using the Delsa Nano Particle Size Analyzer tool. The results of examination of particle size revealed that there were no significant differences in each formula. While for the measurement results of particle size distribution it can be seen that F1 with a small particle size of 128.1 has a large particle size distribution. The smaller the particle size the particle size distribution is increasingly heterogeneous, whereas if the particle size is greater, the particle size distribution value will be more homogeneous⁽⁹⁾.

Based on FTIR results it is known that the IR spectrum in all NLC formulas coenzyme Q10-HA is identical to NLC (blank). This shows that there is no chemical bond between the NLC (blank) system and coenzyme Q10 which can result in loss of Q10 coenzyme activity in the NLC system.

CONCLUSION

The coenzyme Q10 formulation with HA combination affects the characteristics. Increased HA levels lowered pH, but the pH of the preparation was still in the range of skin pH, elevated HA levels increased particle size, but the particle size of the dosage was still in the range of particle size of NLC which was 100-1000 nm.

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