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Corresponding author: A. Alper Öztürk
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Preparation and Characterization of Vitamin A Palmitate Loaded PLGA Based Nanodermacosmetics

Lala Baghirova[1], A. Alper Öztürk[2]

[1]Anadolu University, Graduate School of Health Sciences, Department of Cosmetology, Eskişehir, Turkey.

[2]Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Eskişehir, Turkey.

Corresponding author: aaozturk@anadolu.edu.tr

Abstract:

The way nanotechnology is used in the dermacosmetic / cosmetics industry under today's conditions is to transfer very small sized products such as nanoparticles produced in nanometric dimensions to the cosmetic content. Vitamin A palmitate is a very important component of many important and various biological functions such as reproduction, embryological development, cellular differentiation, growth, immunity and vision. Vitamin A palmitate also has antioxidant and sunscreen effects. This study describes the development and evaluation of poly (lactic-*co*-glycolic acid) (PLGA) nanoparticles for dermal delivery of Vitamin A palmitate. Structures of PLGA nanoparticles were elucidated by particle size, polydispersity index (PDI) and zeta potential. The particle size of the blank formulation was 181.77 nm whereas particle size of Vitamin A palmitate containing nanoparticles was 196.33 nm. The average PDI of all nanoparticle formulations were below 0.12 and all prepared nanoparticles had a negative zeta potential value. Particle size, PDI and zeta potential values of formulations prepared confirmed the successful preparation of Vitamin A palmitate into PLGA nanoparticles. Nanoparticle formulations seem to be promising for dermal delivery of Vitamin A palmitate for dermacosmetic use.

Keywords: PLGA, Vitamin A Plamitate, Nanoparticle, Dermacosmetic, Nanocosmetic.

1. Introduction

Nano structuration modifies chemical, physical, and biological properties of materials leading to a range of new applications in health, including novel delivery systems for pharmaceutics and cosmetics, advanced materials for implants and biosensors, tissue engineering, and new tools for diagnosis (Guterres et al. 2019). The use of nanotechnology-based carriers to encapsulate drug or cosmetic active agents offers advantages such as increased absorption

bioavailability, improved intracellular penetration, and controlled drug / cosmetic delivery (Öztürk et al. 2020a). It has been hundreds of years ago in the development of nanomaterials for cosmetic purposes. Gold and silver nanoparticles have been used by women as nail colors. Also, liquid formulations containing gold nanoparticles were used as anti-aging in the Middle Ages. However, in recent years, nanoscale materials have been used more widely in the development of cosmetics (Shokri, 2017). Polymeric nanoparticles have been shown to be versatile for cosmetic applications. They find special place in the cosmetic arena because these nanoparticles can improve the stability of labile ingredients, offer efficient protection for the skin from harmful UV radiation, target the active ingredient to the desired layer of the skin or to the hair follicles, enhance photostability, antioxidant and antimicrobial effects, and control the release or the volatilization for prolonged time (Guterres et al. 2019). Poly (lactic-co-glycolic acid) (PLGA) is a United States Food and Drug Administration (FDA) approved, biocompatible and biodegradable copolymer that is widely used as a matrix for nanoparticles (Öztürk et al. 2020b). Topical application of antioxidants that act as photoprotective, which can preserve or restore a healthy skin barrier, is very common. Antioxidants are often used in anti-aging products. Vitamin A palmitate acts on keratinization, which is thought to be abnormal, as well as epithelization in dry and rough skin. It also absorbs the sun's harmful UV radiation (Gaspar et al., 2013). Therefore, the purpose of this study is to prepare and characterize Vitamin A loaded nanoparticles with better wound healing and better antiaging properties.

2. Materials and Methods

2.1. Materials

Vitamin A Palmitate was received from Dermoskin® (Matilek Foreign Trade Limited Company), Istanbul, Turkey as a kind gift. Resomer® RG 502 H [Poly (D, L-lactide-*co*-glycolide), acid-terminated, lactide: glycolide 50:50, Mw: 7.000–17.000] and Span® 60 were purchased from Sigma-Aldrich (St. Louis, MO, USA). Pluronic® F-68 (Poloxamer-188) was purchased from Alfa Aesar (Kandel, Germany). All other chemicals used were of analytical grade

2.1. Methods

PLGA-based nanoparticles were prepared by following the nanoprecipitation technique with some modifications (Öztürk et al., 2018). Briefly, a weighed amount of PLGA (60 mg) was dissolved in 3 mL acetone together with Span® 60 (20 mg). Next, 3 mL of this solution was added dropwise at a rate of 5 $mL.h^{-1}$ into 10 mL of Pluronic® F-68 aqueous solution (0.5%,

w/v) under magnetic stirring. Acetone was then allowed to evaporate at room temperature under magnetic stirring for 4 h. The resulting aqueous dispersion was centrifuged to collect the nanoparticles (11.000rpm, 45min, 4ºC) (Rotina 420R, Hettich Zentrifugen, Tuttlingen, Germany). After the nanoparticles were collected, 5 mL of distilled water was added in order to wash particles. The nanoparticles dispersed in water were again subjected to the above mentioned centrifugation process. This process was repeated twice to wash the nanoparticles.

For Vitamin A Palmitate-loaded PLGA-based nanoparticle preparation, briefly, the procedure started by adding 3 mg Vitamin A Palmitate to the organic phase. Then, 3 mL of such solution with drug were added dropwise at rate $5mL.h^{-1}$ into 10 mL of Pluronic® F-68 aqueous solution (0.5%, w/v) under magnetic stirring. Acetone was then allowed to evaporate at room temperature under magnetic stirring for 4h. The resulting aqueous dispersion was centrifuged to collect the nanoparticles (11.000 rpm, 45 min, 4ºC) (Rotina 420 R, Hettich Zentrifugen, Tuttlingen, Germany). This process was repeated twice to wash the nanoparticles. Formulation ingredients are given in Table 1.

Table 1. Formulation ingredients

Code	PLGA	Vitamin A Palmitate	Span 60	Acetone	Pluronic F-68
NP-1 Blank	60 mg	-	20 mg	3 mL	10 mL
NP-1	60 mg	6 mg	20 mg	3 mL	10 mL

***PLGA**: Resomer® RG 502 H, **Pluronic F-68:** 0.5%, w/v solution.

The particle size and polydispersity index of nanoparticle formulations were measured using a dynamic light scattering technique (DLS) on the Zetasizer Nano (Zetasizer Nano ZS, Malvern Instruments, Malvern, UK). Particle size and polydispersity index of nanoparticle prepared were measured by dispersing the formulation in distilled water. Zeta potential values were determined using the same instrument in a disposable folded capillary zeta cell, at 25ºC room temperature and diluted with distilled water. All samples were measured in triplicate and the average values and standard deviation of the measurements were calculated.

3. Results

Particle size, polydispersity index and zeta potential values of the formulations are presented in Table 2. Preparation of the formulations is visually presented in Figure 1.

Table 2. Particle size, Polydispersity index and Zeta Potential values

Code	Particles Size (nm)	PDI	Zeta Potential (mV)
NP-1 Blank	181.77 ± 2.38	0.12 ± 0.06	-15.47 ± 0.23
NP-1	196.33 ± 0.65	0.11 ± 0.02	-15.60 ± 0.44

*Results given as Mean± Standard Deviation (**Mean ± SD**), **PDI**: polydispersity index, **nm**: nanometer, **mV**, milivolt

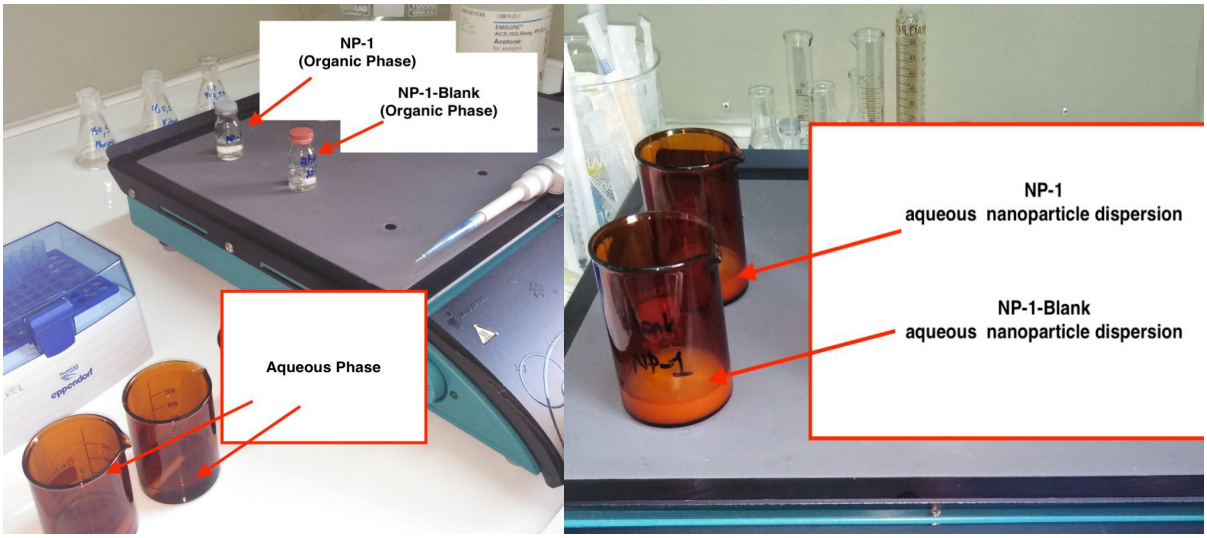

Figure 1. Preparation of Formulations

4. Discussion

As seen in Figure 1, the formulations were developed without any aggregation or any problems. Characterizations of nanoparticles are primarily evaluated with particle size, particle size distribution (polydispersity index: PDI), and zeta potential. The relevant information is presented in Table 2. Particle size obtained in the blank formulation was 181.77 nm while particle size in the Vitamin A palmitate-loaded nanoparticles was 196.33 nm. In particle size analysis, it is important to note that particle size increases with active substance loading. Particle size growth has been reported in the literature when the nanoparticles are loaded with drug active substance (Şenel and Öztürk, 2019; Ilkan and Özdemir, 2017).

PDI value which defines particle size distribution is in the range of 0.01 and 0.7 for monophasic systems; value higher than 0.7 is indicative of a very wide particle size distribution and the value close to zero means narrow particle size distribution (Öztürk and Aygül, 2020). When the PDI results are discussed in this literature information, it can be said

that blank and Vitamin A palmitate loaded PLGA nanoparticle formulations are monodisperse.

When Table 2 is examined, negative zeta potential values are seen in PLGA nanoparticles. The zeta potential was observed as -15.47 and -15.60 mV in blank PLGA nanoparticle and Vitamin A palmitate loaded nanoparticles, respectively. PLGA in neutral environment has negative surface potential attributed to terminal carboxyl groups, and this can be confirmed by the zeta potential of the negative obtained in PLGA nanoparticles (de Lima et al., 2018).

5. Conclusion

PLGA nanoparticles were prepared for dermal delivery of Vitamin A Palmitate nanoprecipitation technique. Particle size, PDI and zeta potential values of formulations prepared confirmed the successful preparation of Vitamin A Palmitate into PLGA nanoparticles. Nanoparticle formulations seem to be promising for dermal delivery of Vitamin A Palmitate for dermacosmetic use. The solid structure of the nanoparticles will be elucidated in the later stages of the study. After the completion of in vitro dissolution studies of nanoparticles, their wound healing potential and antiaging benefit will be examined at the cellular level.

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