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Nanoparticle Betacarotene Formulated in Cetyl Alcohol, Glycerine, Stearic Acid and TEA as Based Cream

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Abstract: The effectiveness cream nanobetacorotene (nanosuspension) had been evaluated. This research aims to ensure which one between nanobetacarotene that was better to be produced as a cream after 28 -day observation. The manufacture of nanoparticles is carried out by the ionic gelation low energy method. The characteristics of the nanoparticles tested include particle size and distribution, zeta potential, nanoparticle morphology, encapsulation efficiency The prepared concentrations betacarotene were 0.1%, 0.3%, and 0.5% with in based cream. Cream tested included pH, homogeneity, spreadly, and testing of irritation during 28 days observation: Nanoparticle preparation produces nano suspension in the form of a clear, some -sticky, and odorless solution. The morphology of particle nanoparticles is in the form of square, rectangular and some around shapes, the average value of particle size 187.5 nm; PI 0,288; potential zeta 10 mV; and encapsulation efficiency was 90%. Findings indicate that 0.5 % of nanobetacarotene were more favorable effective formulated cream. None irritating to arm respondent up to 28 days observation.

Keywords: creams; particle size; potential zeta, nanobetacarotene

I. Introduction

Over the last century, there has been a dramatic change in the nature of therapeutic, biologically active molecules available to treat disease. Therapies have evolved from extracted natural products towards rationally designed biomolecules, including small molecules (Katz and Baltz, 2016). The use of potent drugs which target specific organs, cells or biochemical pathways, necessitates new tools which can enable controlled delivery and dosing of these therapeutics to their biological targets from the macro to nano-scale (Declassian, 2019).

β-Carotene is one of the main carotenoid compounds and is an active compound that contributes significantly to human health, i.e., as a pro-vitamin A, an antioxidant, and an anticancer agent. Unfortunately, β-carotene is unstable to light, heat, and oxygen (Xu et al, 2020; Boon et al, 2010; Aburjai and Nathsheh 2003). To improve the stability of β-carotene, numerous researchers have tried to encapsulate β-carotene in various matrices to produce liquid or solid products that are easier to be handled (Burton at al, 2021). One of the studied due to extracted of betacarotene was doing by Taswin et al, (2021) and Mangunsong et al, (2020).

Beta-carotene is a precursor of vitamin A. It is the pigment responsible for the orange color of carrots and it is found in many other fruits and vegetables. Beta-carotene is a precursor of, and can be synthesized from, vitamin A. Beta-carotene used in cosmetics and personal care products is prepared synthetically or obtained from natural sources. (Bohn et al., 2019, von Lintig 2020). Some of betacarotene has been studied to improve its stability (Liu et al. 2022).

The field of nanotechnology has grown over the last two decades and made the transition from the benchtop to applied technologies. Nanoscale-sized particles, or nanoparticles, have emerged as promising tools with broad applications in drug delivery, diagnostics, cosmetics and several other biological and non-biological areas. The use of nanotechnology in medicine and more specifically drug delivery is set to spread rapidly (Bayda et al, 2019). These advances also lead to questions about nanoparticle safety (Fiume et al., 2020; Farokhzad, 2009).

Despite considerable efforts to understand the toxicity and safety of these nanoparticles, many of these questions are not yet fully answered. Nevertheless, these efforts have identified several approaches to minimize and prevent nanoparticle toxicity to promote safer nanotechnology. Accordingly Betacarotene nanoparticle need to explore .(Lestari et al., 2020) (Mangunsong et al., 2020).

In cosmetics and personal care products, beta-carotene is used in the formulation of aftershave lotions, bath products, cleansing products, makeup, hair conditioners, shampoos, skin care products and suntan products. Beta-carotene imparts an orange color to cosmetics and personal care products. It also enhances the appearance of dry or damaged skin by reducing flaking and restoring suppleness (Kusbandari & Susanti, 2017). One of the cosmetics preparation was cream, cream preparation can be used for many

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purposes (Blanco-Fernandez, 2021). Nanoemulsions are biphasic dispersion of two immiscible liquids: either water in oil (W/O) or oil in water (O/W) droplets stabilized by an amphiphilic surfactant. These come across as ultrafine dispersions. However there is still relatively narrow insight regarding development, manufacturing, fabrication and manipulation of nanoemulsions. This fenomenom which primarily stems from the fact that conventional aspects of emulsion formation and stabilization only partially apply to nanoemulsions. In general deficiency sets up the premise for current develop (Singh Y,et al 2017).

Cream is one of the semi-solid pharmaceutical preparations, to be chosen that is easier to manufacture. Using a cream base that matches the properties of the efficacious ingredients. The cream type can be in the form of O / W or W / O which contains efficacious ingredients that are suitable for the purpose of use (Santini et al, 2015; Singh Y, et al 2017). The nanosystems were introduced in the model formulations-cream, tonic, and gel, and confirmed by TEM or SEM to analysis morphology and size (Lewinska et al, 2021).

Efficacious materials can be in the form of plant extracts, chemicals, minerals or other suitable materials or nanoparticle preparations. In this study, the basic ingredients of the cream betacarotene were selected with own consideration and from the results of literature studies. Beta-carotene is a phytochemical compound of the terpenoid group that has properties as an excellent anti-oxidant that can be used as an external drug. Beta-carotene is mainly derived from carrots isolated by its own method without organic solvents (Tawin et al. 2021: Mangunsong et al. 2020)

Creams are the most common types of delivery system used for emollients and moisturizers. The complete definition for a “cream” is suggested as an emulsion semisolid dosage form that contains >20% water and volatiles and/or <50% hydrocarbons, waxes or polyethylene glycols as the vehicle for external application to the skin. They enable a wide variety of ingredients to be quickly and conveniently delivered to the skin. On the base of a structural and functional definition, creams are emulsions of water in oil (oily creams) or oil in water (vanishing creams), in which the active agent is dispersed between the oil and water phases according to formula partition coefficient. Exposure to nanoparticles for medical purposes involves intentional contact or administration understanding the properties of nanoparticles and their effect on the body is crucial before clinical use can occur. For nanoparticles cream betacarotene to move into the clinical area, it is important that nanotoxicology research uncovers and understands how these multiple factors influence the toxicity of nanoparticles into the skin so that their undesirable properties can be avoided by tested into the arm. The aim of this study was to explore nanobetacarotene cream formulation and its characteristic.

II. Experimental Section

2.1 Materials

Chitosan, TPP, Sodium Alginate, and β-carotene were purchased from Sigma Aldrich. Glacial acetic acid, glycerine and absolute ethanol were purchased from E.Merck. Cetyl alcohol, Stearic acid, Triethanolamine, Methylparabene, distilled water, Purchase from Bharata, Ltd and Co. Betacarotene for cream extracted by own method from carrot. All materials were used as received without further purification.

The manufacture of nanoparticles was carried out using the low-energyionic gelation method. The fabrication of beta-carotene nanosuspension using the ionic gelation method with aeration (low energy) sodium alginate and calcium chloride techniques. The characteristics of the tested nanoparticles included particle size and distribution, zeta potential, nanoparticle morphology, as well as encapsulation efficiency.

2.2 Matrix Dispersion

For this purpose, betacarotene was extracted with calcium chloride, chitosan solution was prepared by dissolving chitosan in acetic acid (1% v/v). The alginat dispersion was prepared by mixing sodium alginate in water, and stir to develop. While, TPP solution was prepared by dissolving TPP in distilled water. After all solutions prepared, 20-mL of TPP solutions as concentration (3% (w/v) were added to 1% (w/v) of alginat dispersion as described in Table 1. Afterwards, certain amount of volume (alginat:chitosan) of cationic solution (1% w/v chitosan) was added to the TPP-alginat mixture and was mixed using magnetic stirrer. When the microprecipitation steps were completed, β-carotene encapsulated in the alginate/chitosan/TPP matrices were then formed

2.3 Microprecipitation of Beta-carotene

Performed according to the other research with slight modifications.

As much as 50 -mL of matrix mixture described above were heated and stirred in water bath at 90 °C for 10 min, followed by adding 50 mL -Betacarotene dispersion in ethanol (5 mg/100 mL) dropwise under magnetic stirring. The mixtures were allowed to cool to room temperature, then the additional 50-mLof β-carotene in ethanol (5 mg/100 mL) were added accompanied by

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continuous stirring. After centrifugation (3000 ×g, 10 min), the microprecipitation products were then dried in freeze-dryer for 24 hours, crushed, and sieved. The yield of microprecipitation product was used to form cream formulated.

2.4 Cream Formulated

Cream, we referred to Sahu et al., (2011) The nanobetacarotene formulated was formulated into cream dosage at various concentrations namely F1 (0.1%), F2 (0.3%), and F3 (0.5%). Cream was performed by weighing each of the ingredients used. The oil phase was made by heating stearic acid and cetyl alcohol until they melted in a porcelain dish. During the heating process, we churned the two ingredients until they were homogenous at 70°C above a water bath. The water phase was conducted by dissolving triethanolamine, glycerin, methylparaben, and nanobetacarotene formulated in a porcelain dish and stirring them over a water bath at 70 ° C. Distilled water was heated over a water bath at a temperature of 70 ° C. The water phase and the ethanol nanobetacarotene formulated were transferred to a hot mortar and added to the oil phase, then stirred slowly. Distilled water was gradually added up to 100 mL. The mixture of the oil phase and the water phase was stirred until cool, and a homogeneous cream mass was then formed. The formula for the respective cream of nanobetacarotene formulated was tested for its chemical and physical properties of cream. Characteristic test of the physical properties of cream in general (Taswin et al.. 2021).

2.5 Cream stability test

The three creams were stored at three different temperatures, namely low temperature (5±2°C), room temperature, and high temperature (40±2°C) for 28 days. During the storage period, organoleptic observations, pH checks, and globule diameter measurements were carried out each of 7,14,28 days while viscosity and cream consistency measurements were carried out in the first day (0) and last (28 days) which were stored at room temperature.

III. Result

Table 1. Nanoparticle Betacarotene Time to Ultrasonicator Used

Formula	F1	F2	F3
Betacarotene	100 mg	100 mg	100 mg
Time to Ultrasonicator	2(Minute)	3 (Minute)	5 (Minute)
Chitosan	0,1%	0,5%	1%
Na Alginate	0.2 %	0.2 %	0,2 %
NaTPP	0.5 %	0.5 %	0,5 %
Ethanol	50 mL	50 mL	50mL

Table 2. Cream Dosage Formula Nanobetacarotene

No.	Ingredient	FI (% b/b)	FII (% b/b)	FIII (% b/b)
1	Betacarotene	0.1	0.3	0.5
2	Cetyl alcohol	2	2	2
3	Stearic acid	12	12	12
4	Triethanolamine	3	3	3
5	Glycerine	8	8	8
6	Methylparabene	0.2	0.2	0.2
7	Distilled water	ad 100	ad 100	ad 100

Table 3: Organoleptic and Homogeneity Tests

Formula	Color	Odor	Softness	Homogenized
F 1	Soft pink	Betacarotene taste	Soft	Homogene
F2	Soft pink to Orange	Betacarotene taste	Soft	Homogene
F3	Soft Orange	Betacarotene taste	Soft	Homogene

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Table 4. pH and spread ability tests

No. Formula	pH	Spread ability area
F 1	5.5	3.8
F2	5.4	3.7
F3	5.6	3.8
Average	5.5	3.76

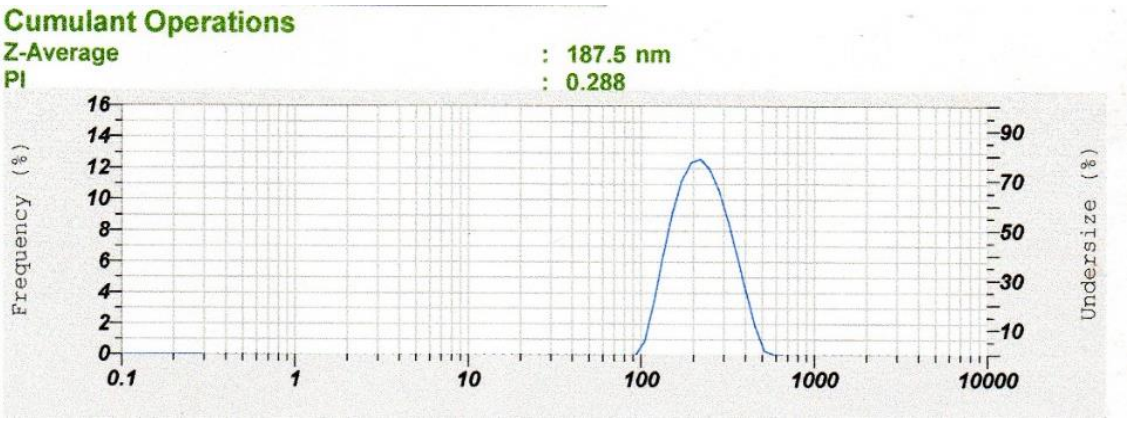

Figure 1 Particle Size of Betacarotene Average 187.5 nm

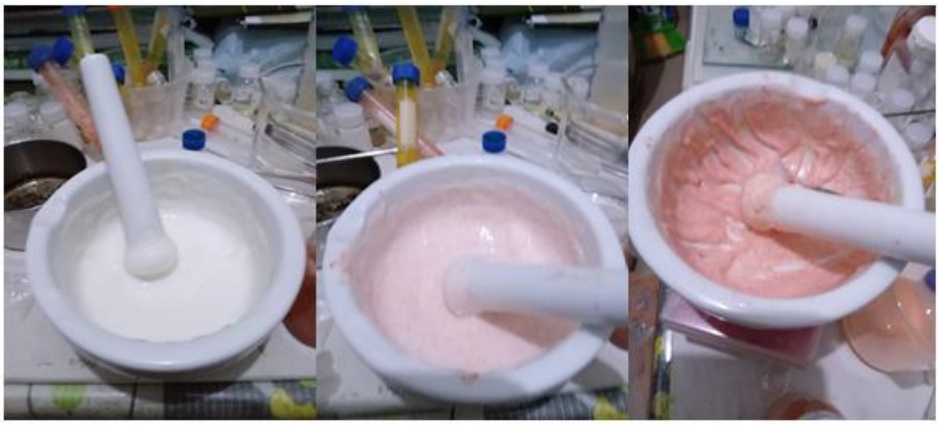

Figure. 2. a) Based Cream, b) 0,3 % nanobetacarotene Cream and c) 0,5% nanobetacarotene Cream

Figure 3. Cream Nano Betacarotene 0,5% in 28 days observation.

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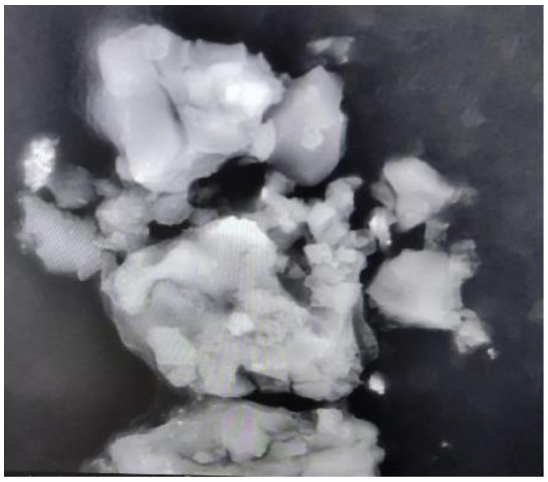

Figure 4 , Morphology Nanobetacarotene, SEM, Size in 5 µm , square, rectangular and some around shapes

Figure 5. The Arm Tested of Respondent For Allergic Tested in 15, 30, 60, 120, 240, 360 Minutes Observed.

IV. Discussion

As the purpose of this study was to determine the physical stability of a cream containing nanobetacarotene formulated with varying concentrations of 0.5%, 0.3%, and 0.1% in the same base composition in 28 days observation, that perform characteristics, physical stability, morphology of nanobetacarotene formulated. This research was conducted in three stages, namely the stage of making nanobeta-carotene, and its characteristics, formulated cream, and the evaluation stage of the cream. The initial evaluation which included organoleptic observations, homogeneity observations (Figure 1, 2, 3 and 4), Formulated and pH measurements (Tabel 1, 2 ,3 and 4), determination of flow properties, and observed of stability.

The particle size of developed nanoparticles was determined employing HORIBA PS100 analyzers of particle size. The suspension was diluted with double deionized water for the measurement of polydispersity index (PDI) and particle size see figure 1). The surface charge of BC-Encapsulation was measured by diluting the suspension ten times at an electric field of 20.24 V/cm to have crystal figure 4. The morphological attributes of BC- encapsulation were studied using field emission scanning electron microscopy (FE-SEM). The carbon-coated grids were covered with a drop of diluted nanosuspension and further subjected to 300 Å gold coating using a sputter coater. Samples were visualized at an accelerating voltage of 10 kV and × 2500 magnification. Percent drug efficiency (%EE) and percent drug loading (%DL) were determined using direct lysis method (full data not found).

From the results, the initial evaluation of nanobetacarotene cream formulated were performed, physical stability tests were carried out on the three creams containing nanobetacarotene for 28 days observation, namely physical stability tests of the creams at low temperature storage (5 ± 2°C), room temperature, and high temperature (40 ± 2 °C). Figure 2. We found that there is no change physically observation of cream in 28 days observation.

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Beta carotene has also studied by Sun et al. (2022) encapsulated form and its stability (Borba et al, 2019). Comparing to this studied, nanobetacarotene preparation has been already finished produced in based cream with formula in Table 1 and 2. Due to pharmaceutical preparation need to observed and analysis and confirm that preparation were useful to continued or even needed for new confirmation (Gamble et al., 2015). The main critical role also was in the sonication of the formula to produce the nanoparticle size. Sonication procedure is needed to make more smaller the particle into the nano size of the material in the study. Consuming of the time to sonication has been used in this study 1 to 5 minutes to looking for which one of the time is better to produced nano size due to Zeta potensial and % Efficiecy (Castillo-Peinado Lde L, et al., 2016)

Nanobetacarotene has been studied in based cream in this work. Producing in stable state during 28 days observed. Contain with based formulated Tabel 3. Cream is a semi-solid dosage form containing one or more drug ingredients dissolved or dispersed in a suitable base material. This preparation is a semisolid preparation from an emulsion consisting of a mixture of an oil phase and an aqueous phase (Figure 2). Creams are generally less viscous and lighter than ointments, so they are preferred over ointments. Generally creams spread easily and, because they are oil-in-water emulsions, they wash off much easier than most ointments. Cream is considered to have charm greater aesthetics because of its non-greasy nature and its ability to penetrate quickly into the skin (Ansel, 1989). In this study showed well based cream preparation due to formula (Tabel 2). The analysis of nanobetacorotene in cream formulated showed (size, polydispersity, Zeta potential, and stability) that nanoemulsion has a matrix, morphology confirm by SEM (Figure 4) and size up to 220 nm (Figure 1). Due to Lewiska 2021 (size, polydispersity, Zeta potential, and stability) of the nanosystems were introduced in the model formulations-cream, tonic, and gel, and confirmed by TEM. The analysis showed that nanoemulsion has a spherical morphology and size 220-300 nm, while levan nanoparticles had irregular shapes independently of the use of matrix and with particle size (130-260 nm).

In this studied we chose nanobetacarotene as active ingredient based cream as topical used, in cosmetics creams are the most common types of delivery system used for emollients and moisturizers (Hu and He, 2021). They enable a wide variety of ingredients to be quickly and conveniently delivered to the skin (Zhang, et al. 2023). By structural characteristics, creams are opaque, viscous, ranged from non-greasy to mildly greasy texture and tend to evaporate or be absorbed when rubbed onto the skin. In comparison with ointments, creams are significantly less greasy, less viscous, less hydrating and more spreadable being used for their moistening and emollient properties Nanoemulsion refer to Singh et al., (2017).

In Table 4 of this study perform the pH of Cream preparation, refer to Blaak and Staib (2018) reviewed that skin barrier regeneration and antimicrobial response, are related to the acidic nature of the skin surface pH (ss-pH). Epidermal barrier functions due to pH. The epidermal acidification is known to be fragile and it is commonly accepted that cosmetic products, can induce significant changes in ss-pH. As a consequence, epidermal barrier function and skin microflora are affected negatively. For cosmetic-relevant skin conditions, skin disorders and specific consumer groups, maintaining of the acidic ss-pH is beneficial for epidermal physiology and cutaneous microflora. Due to this context, cleansing and skin care products with a pH level of 4.0-5.0 may be helpful and fit in to this studied.

As an emulsifier and hardening agent in topical preparations (creams), cetyl alcohol is used. Cetyl alcohol can increase the viscosity of the cream and increase the stability of the preparation. Cetyl alcohol is white flakes or granules, has a characteristic odor and is tasteless. This material is very soluble in 95% ethanol and ether. As a hardener, general concentration used is 2-10% and as an emulsifier concentration of 2-5%. It was well established that there was a predominant and stable α-crystalline gel structure, formed with sucrose fatty acid ester (S1670) and cetyl alcohol, in the pseudo quarter-phase system (Zhou, 2023).

Humectants Glycerin, is used in topical and cosmetic formulations, the use of humectants aims to maintain skin moisture, besides that it also plays a role in maintaining the water content of the preparation by reducing water evaporation during use so that cream is easier to spread and form scale in packaged containers can be avoided. Glycerin, propylene glycol and sorbitol can be used as humectants). In topical and cosmetic formulations, glycerin is commonly used as a humectant and emollient. Glycerin is a clear, colorless, odorless, viscous and hygroscopic solution. This material is slightly soluble in acetone; practically insoluble in benzene, chloroform and oils; Miscible with ethanol, methanol and water. The concentration of glycerin which is commonly used as a humectant can reach 30% (Shekunov 2006).

Cream stability, is defined as the ability of a drug or cosmetic product to persist within the specifications applied throughout the period of storage and use to ensure the identity, strength, quality and purity of the product. The definition of a stable cosmetic preparation is a preparation that is still within acceptable limits during the period of storage and use, where the properties and characteristics are the same as those they had when they were made (Simoes 2019). Before their use in pharmaceuticals and cosmetics the evaluation of particle, the measurement of nanoparticle size, and size distribution, is important to the development of pharmaceutical nanoparticle products and their manufacturing processes, physicochemical properties of organoleptic agents (Patil et al 2018). In this work we report on the use, dynamic light scattering, differential centrifugal sedimentation, particle tracking analysis, and tuneable resistive pulse sensing to measure different of samples. The techniques rely on different physical principles to measure nanoparticle size (Figure 3 and 4).

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Physical instability of the preparation is characterized by the presence of discoloration or appearance of color, odor, change or separation of phases, emulsion rupture, deposition of suspension or caking, change in consistency, crystal growth, gas formation, and other physical changes Commonly used organoleptic agents in pharmaceutical and cosmeceutical formulations, their associated instabilities, and probable approaches to overcoming (Patil et al.2018). The stability of an emulsion is characterized by the absence of coalescence of the inner phase, the absence of creaming, and the appearance, odor, color, and other good physical properties. The physical instability of an emulsion or suspension can be influenced by factors that affect the chemical stability of the emulsifying agent (emulsifier), suspending agent, antioxidant, preservative, and active ingredient (Patil et al. 2018). Referring to an article Tran, (2022) natural is not always better as well as can be allergic, therefore is still need to evaluate before used, due to this statement and cosmetics assessed (Garg et al., 2017: Kim, 2023). We conduct to test allergy to respondent using the nanobetacarotene cream preparation, compare to González-Muñoz P et al. (2014); Hu and He (2021). The sample tested into the arm of respondent can be seen in Figure 5.

V. Conclusion

From this study we come to conclusion that the manufacture of nanoparticles is carried out by the ionic gelation low energy method has successfully produced. The characteristics of the nanoparticles tested include particle size and distribution, zeta potential, nanoparticle morphology, encapsulation efficiency The best concentrations nanobetacarotene were 0.5% with in based cream as usual. Cream tested included pH, homogeneity, spreadly, and testing of irritation over 28 days observation: Nanoparticle preparation produces nano suspension in the form of a clear, some -sticky, and odorless solution. The morphology of particle nanoparticles is in the form of square, rectangular and some around shapes, the average value of particle size 187.5 nm; PI 0,288; potential zeta 10 mV; and encapsulation efficiency was 90%. Findings 0.5 % of nanobetacarotene were more favorable effective formulated cream with none of irritating to arm respondent over 28 days observation suggest more evaluation in morphology and to prolong serial period of observation.

Conflict of interest statement

The authors declare no conflict of interest.

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References

1. Aburjai T, Natsheh FM, 2003, Plants used in cosmetics. .Phytother Res. 2003 Nov;17(9):987-1000. doi: 10.1002/ptr.1363.PMID: 14595575 Review.
2. Bayda S, Adeel M, Tuccinardi T, Cordani M, Rizzolio F.2019. The History of Nanoscience and Nanotechnology: From Chemical-Physical Applications to Nanomedicine. Molecules. 2019 Dec 27;25(1):112. doi: 10.3390/molecules25010112.PMID: 31892180
3. Blaak J, Staib P, 2018. The Relation of pH and Skin Cleansing. .Curr Probl Dermatol. 2018;54:132-142. doi: 10.1159/000489527. Epub 2018 Aug 21.PMID: 30130782 Review.
4. Blanco-Fernandez B, Castaño O, Mateos-Timoneda MÁ, Engel E, Pérez-Amodio S.2019 Nanotechnology Approaches in Chronic Wound Healing. Adv Wound Care (New Rochelle). 2021 May;10(5):234-256. doi: 10.1089/wound.2019.1094. Epub 2020 Jun 2.
5. Bohn T, Desmarchelier C, El SN, Keijer J, van Schothorst E, Rühl R, Borel P. 2019. β-Carotene in the human body: metabolic bioactivation pathways - from digestion to tissue distribution and excretion.Proc Nutr Soc. 2019 Feb;78(1):68-87. doi: 10.1017/S0029665118002641.PMID: 30747092.
6. Boon CS, McClements DJ, Weiss J, Decker EA.2010. Factors influencing the chemical stability of carotenoids in foods. .Crit Rev Food Sci Nutr. 2010 Jun;50(6):515-32. doi: 10.1080/10408390802565889.PMID: 20544442 .
7. Borba CM, Tavares MN, Macedo LP, Araújo GS, Furlong EB, Dora CL, Burkert JFM.2019. Physical and chemical stability of β-carotene nanoemulsions during storage and thermal process..Food Res Int. 2019 Jul;121:229-237. doi: 10.1016/j.foodres.2019.03.045. Epub 2019 Mar 20.PMID: 31108744.
8. Burton GW, Mogg TJ, Riley WW, Nickerson JG. 2021. β-Carotene oxidation products - Function and safety. Food Chem Toxicol. 2021 Jun;152:112207. doi: 10.1016/j.fct.2021.112207. Epub 2021 Apr 20.PMID: 33891992.
9. Castillo-Peinado Lde L, Luque de Castro MD.2016. The role of ultrasound in pharmaceutical production: sonocrystallization J Pharm Pharmacol. 2016 Oct;68(10):1249-67. doi: 10.1111/jphp.12614. Epub 2016 Jul 27.
10. Delcassian D, Patel AK, Cortinas AB, _Langer R.2019. Drug delivery across length scales J Drug Target 2019 Mar;27(3):229-243 doi: 10.1080/1061186X.2018.1438440. Epub 2018 Feb 20.
11. Farokhzad OC, Langer R. 2019. Impact of nanotechnology on drug delivery. ACS Nano. 2009 Jan 27;3(1):16-20. doi: 10.1021/nn900002m.PMID: 19206243 .

ISSN No. 231-2705 | DOI: 10.51244/IJRSI | Volume X Issue VI June 2023

12. Fiume MM, Bergfeld WF, Belsito DV, Hill RA, Klaassen CD, Liebler DC, Marks JG Jr, Shank RC, Slaga TJ, Snyder PW, Gill LJ, Heldreth B.2020. Safety Assessment of Monoglyceryl Monoesters as Used in Cosmetics. .Int J Toxicol. 2020 Nov/Dec;39(3_suppl):93S-126S. doi: 10.1177/1091581820966951.PMID: 33203266.
13. Gamble JF, Tobyn M, Hamey R. 2015. Application of image-based particle size and shape characterization systems in the development of small molecule pharmaceuticals. J Pharm Sci. 2015 May;104(5):1563-74. doi: 10.1002/jps.24382. Epub 2015 Feb 17.PMID: 25690940.
14. Garg T, Agarwal S, Chander R, Singh A, Yadav P.J.2017. Cosmet Dermatol. 2018 Feb;17(1):95-100. doi: 10.1111/jocd.12359. Epub 2017 Jun 1.PMID: 28568892.
15. Han J, Guenier Anne-Sophie, Salmieri, S., Lacroix M 2008. .Alginate and chitosan functionalization for micronutrient encapsulation J Agric Food Chem . 2008 Apr 9;56(7):2528-35. doi: 10.1021/jf703739k. Epub 2008 Mar 7.
16. Hu X, He . 2021. A review of cosmetic skin delivery. J Cosmet Dermatol. 2021 Jul;20(7):2020-2030. doi: 10.1111/jocd.14037. Epub 2021 Mar 9.PMID: 33655674 .
17. Juwita, A.P., Yamlean, P.V.Y., Edy, H.J., 2013. Formulasi Krim Ektrak Etanol Daun Lamun (Syringodium isoetifolium) 2(02), 8–13.
18. Katz L, Baltz RH.J . 2016. Natural product discovery: past, present, and future.Ind Microbiol Biotechnol. 2016 Mar;43(2-3):155-76. doi: 10.1007/s10295-015-1723-5. Epub 2016 Jan 6.PMID: 26739136.
19. Kim KB, Kwack SJ, Lee JY, Kacew S, Lee BM.2021. Current opinion on risk assessment of cosmetics. .J Toxicol Environ Health B Crit Rev. 2021 May 19;24(4):137-161. doi: 10.1080/10937404.2021.1907264. Epub 2021 Apr 8.PMID: 33832410 .
20. Kusbandari, A., & Susanti, H. (2017). Beta Carotene Content And Free Radical Scavenging Activity Of Cantaloupe (Cucumis melo var. Cantalupensis L.) Extract Against DPPH (1,1-diphenyl-2-picrylhydrazyl) USING UV-VISIBLE. Journal of Pharmaceutical Sciences and Community, 14(1), 37–42.
21. Lestari, A. D. N., Siswanta, D., Martien, R., & Mudasir, M. (2020). Synthesis, characterization, and stability evaluation of β-carotene encapsulated in starch-chitosan/tripolyphosphate matrices. Indonesian Journal of Chemistry, 20(4), 929–940. https://doi.org/10.22146/ijc.50449.
22. Lewińska A, Domżał-Kędzia M, Kierul K, Bochynek M, Pannert D, Nowaczyk P, Łukaszewicz M. 2021. Targeted Hybrid Nanocarriers as a System Enhancing the Skin Structure. Molecules. 2021 Feb 18;26(4):1063. doi: 10.3390/molecules26041063.PMID: 33670519.
23. Liu S, Zhang J, Fu R, Feng H, Chu Y, Huang D, Liu H, Li C, Ma C, Abd El-Aty AM. 2021. Improved stability and aqueous solubility of β-carotene via encapsulation in self-assembled bioactive oleanolic acid nanoparticles. .Food Chem. 2022 Mar 30;373(Pt B):131498. doi: 10.1016/j.foodchem.2021.131498. Epub 2021 Oct 30.PMID: 34753075.
24. Matthew J Zirwas. 2019. Contact Dermatitis to Cosmetics Clin Rev Allergy Immunol, 2019 Feb;56(1):119-128. doi: 10.1007/s12016-018-8717-9.
25. Murrukmihadi, M., Ananda, R., Handayani, T.U., 2012. Sediaan Krim Ekstra Etanolk Bunga Terhadap Sifat Fisik Dan Aktifitas Antibakteri Pada Staphylococcus aureus Effect of Carbomer 934 and Cetyl Alcohol Addittion as Emulsifier in Ethanolic Extract Hibiscus (Hibiscus rosa-sinenis L.) Cream on the Physical. Majalah Farmaseutik, 8(2), 152–157.
26. Mangunsong, S., Taswin, M., & Natarajan, S. B. (2020). Determine β-carotene in carrot (Daucus carota L.) by using HPLC and GC-MS. IOSR Journal Of Pharmacy, 10(12), 21–27. www.iosrphr.org
27. Patil A, Bhide S, Bookwala M, Soneta B, Shankar V, Almotairy A, Almutairi M, Narasimha Murthy S.2018. Stability of Organoleptic Agents in Pharmaceuticals and Cosmetics.
28. AAPS PharmSciTech. 2018 Jan;19(1):36-47. doi: 10.1208/s12249-017-0866-2. Epub 2017 Sep 12.PMID: 28900868 .
29. Paithankar, V. V, 2010 "Formulation and evaluation of herbal cosmetic preparation using safed musli," International Journal of PharmTech Research, vol. 2, no. 4, pp. 2261–2264, 2010.
30. Santini, B., Zanoni, I., Marzi, R., Cigni, C., Bedoni, M., Gramatica, F., Palugan, L., Corsi, F., Granucci, F., & Colombo, M. (2015). Cream formulation impact on topical administration of engineered colloidal nanoparticles. PLoS ONE, 10(5), 1–14. https://doi.org/10.1371/journal.pone.0126366.
31. Sahu A. N., Jha, S.and. Dubey S. D, 2011 "Formulation and evaluation of curcuminoid based herbal face cream," Indo Global Journal of Pharmaceutical Sciences, vol. 1, no. 1, pp. 77–84, 2011.
32. Simões A , Veiga F Vitorino C. 2019. Developing Cream Formulations: Renewed Interest in an Old Problem. J Pharm Sci. 2019 Oct;108(10):3240-3251. doi: 10.1016/j.xphs.2019.06.006. Epub 2019 Jun 16.
33. Shekunov BY, Chattopadhyay P, Tong HH, Chow AH.2007. Particle size analysis in pharmaceutics: principles, methods and applications. .Pharm Res. 2007 Feb;24(2):203-27. doi: 10.1007/s11095-006-9146-7. Epub 2006 Dec 27.PMID: 17191094.
34. Singh Y, Meher JG, Raval K, Khan FA, Chaurasia M, Jain NK, Chourasia MK.2017. Nanoemulsion: Concepts, development and applications in drug delivery..J Control Release. 2017 Apr 28;252:28-49. doi: 10.1016/j.jconrel.2017.03.008. Epub 2017 Mar 6.PMID: 28279798.

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35. Sun Y, Tang W, Pu C, Li R, Sun Q, Wang H.2022. Improved stability of liposome-stabilized emulsions as a co-encapsulation delivery system for vitamin B_2, vitamin E and β-carotene. .Food Funct. 2022 Mar 7;13(5):2966-2984. doi: 10.1039/d1fo03617c.PMID: 35194623.
36. Tran JM, Comstock JR, Reeder M. 2022. Natural Is Not Always Better: The Prevalence of Allergenic Ingredients in "Clean" Beauty Products. J.Dermatitis. 2022 May-Jun 01;33(3):215-219. doi: 10.1097/DER.0000000000000863. Epub 2022 Mar 7.PMID: 35256558.
37. Taswin, M., Mangunsong, Sonlimar, Azza Hanif Harisma Wahyu Dwi, N., Syafie, Mardliyati, E., & Natarajan, S. B.2021. Characterization of Nanoparticle-encapsulation of ß-carotene Isolated from Daucus carota. International Journal of Pharmaceutical Research, 13(03), 831–835. https://doi.org/10.31838/ijpr/2021.13.03.173.
38. von Lintig J.2020. Eat Your Carrots! β-Carotene and Cholesterol Homeostasis. J Nutr. 2020 Aug 1;150(8):2003-2005. doi: 10.1093/jn/nxaa189.PMID: 32747944
39. Wren S, Minelli C, Pei Y, Akhtar N,. 2020. Evaluation of Particle Size Techniques to Support the Development of Manufacturing Scale Nanoparticles for Application in Pharmaceuticals J Pharm Sci . 2020 Jul;109(7):2284-2293. doi: 10.1016/j.xphs.2020.04.001. Epub 2020 Apr 9.
40. Xu P, Chukhutsina VU, Nawrocki WJ, Schansker G, Bielczynski LW, Lu Y, Karcher D, Bock R, Croce R. 2020. Photosynthesis without β-carotene.mElife. 2020 Sep 25;9:e58984. doi: 10.7554/eLife.58984.PMID: 32975516.
41. Zhou J, He X, Hu Q.A. 2023. Sucrose Fatty Acid Ester-mixed Emulsifier as Stabilizer of Emulsion Systems. J Oleo Sci. 2023 Jun 1;72(6):623-633. doi: 10.5650/jos.ess23001. Epub 2023 May 11.PMID: 37164691.
42. Zhang P, Wang Y, Liu Y, Wu Y, 2022. Ouyang Improved stability of β-carotene by encapsulation in SHMP-corn starch aerogels.J.Food Chem. 2023 Apr 16;406:135040. doi: 10.1016/j.foodchem.2022.135040. Epub 2022 Nov 23.PMID: 36462356.