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REVIEW: REVIEW ARTICLE LIPID-BASED NANOTECHNOLOGY

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ABSTRACT

Nanotechnology is defined as engineering the creation of materials, functions, and devices on the nanometer scale. Nanoscience is increasingly developing and becoming a part of various fields, such as electronics, materials, and biology. Lipid nanoparticles are a major application in nanotechnology. In formulas II and III, smaller results were obtained compared with the other formulas. Based on the results of this study, it can be concluded that the nanostructured lipid carrier system with solid lipid poloxamer and stearic acid with liquid soybean oil lipids obtained good characteristics, and each test met the range. From the explanation above, it can be concluded that lipid-based nanotechnology has great potential in various fields such as medicine, cosmetics, and agriculture. Its use can provide great benefits such as increasing the effectiveness of drug administration, increasing the absorption of nutrients in food, and developing cosmetic products. which one is safer and more effective. To compare several types of nanoparticle methods, such as Liposomes, Neosomes, Etosomes, SLN, and NLC for selection of the lipid base, namely NLC. It is important to ensure that the use and development of this technology are safe and beneficial for humans and the environment.

Keywords : Nanotechnology, Nanoparticles, Lipid-Based Nanoparticles

INTRODUCTION

Nanotechnology is defined as the engineering of materials, functions, and devices on the nanometer scale. Along with technological developments, the use of nanotechnology is increasingly widespread and is becoming a part of various fields, such as electronics, materials, biology, health, energy, and the environment (Dwandaru 2012). It consists of the development of nanotechnology at the nanometer scale, usually 0.1 to 100 nm. Nano comes from the Greek word "Nanos" which means dwarf or very small. Nanoscience is related to the study of molecular and atomic particles (Sarika Nikam, 2014).

Nanoparticles, which have properties that are different from those of larger materials, are one of the main applications of nanotechnology. The special properties of nanoparticles offer many potential applications in the medical, environmental, energy, and other fields.

Even though it still requires further research and development, the use of nanotechnology opens up new opportunities to improve the quality of human life and provide solutions to various global problems (Avilia Dhiar Aryani 2022).

Lipid-based nanotechnology is a promising field for the development of various applications, especially in the fields of medicine and pharmacy. Lipids can form nanostructures, such as Solid Lipid Nanoparticles (SLN), micelles, and liposomes, which have potential for targeted drug delivery, bio-imaging, sensors, and early disease diagnosis. Lipid-based nanoparticles have been widely applied in various pharmaceutical formulations such as SLN hydrocortisone acetate. The unique properties and characteristics of these materials at the nanometer scale have opened a new era in nanotechnology, especially in the development of innovative drug delivery systems. Thus, lipid-based nanotechnology offers

great potential for improving the effectiveness of medical treatment and diagnosis (Dwina Rahmi 2010).

Lipid nanoparticles have a size–50-100 nm where lipids are the main carriers and are stabilized by surfactants and additional polymers. Lipid nanoparticles are a large group that includes solid lipid nanoparticles, nanostructured lipid carriers, nanoemulsions, and vesicular nanosystems. Lipid nanoparticles have better penetration into the skin membrane because they contain lipids as carriers, which can more easily penetrate the epidermis layer (Anggraeni et al., 2023).

RESEARCH METHODS

This research is qualitative research using the literature study method by searching for references to theories relevant to the cases or problems found by collecting data from systematic search studies of computerized databases (Google Scholar) in the form of research journals and this review article was compiled. Based on scientific articles that reviewed the development of nanotechnology in the last 10 years (2012 -2023). The articles included nanotechnology, lipid bases, liposomes, niosomes, estosomes, transfersomes, solid lipid nanoparticles, and nanostructured lipid carriers. References used were taken from Scopus, PubMed, Elsevier, NCBI. This technique is carried out with the aim of uncovering various theories relevant to the problem being studied as a reference material in discussing the research results.

Table I. Journal Reference Table Used In This Article

Writer	Title	Year
Andriani, Rina, Irmayani Jubir, Vica Aspadiah, And Adryan Fristiohady.	"Journal Review: Utilization of Etosome as a Patch Dosage Form."	2021
Anggraeni, Dila, Marita Kaniawati, and Ganardi Jafar	"Nanotechnology Approach for Delivery of Active Pharmaceutical Ingredients in Acne Vulgaris Therapy."	2023
Avilia Dhiar Aryani, And Hilda Aprilia Wisnuwardhani.	"Literature Study of the Synthesis of Copper Nanoparticles Using Plant Extract Bioreductants with Antioxidant Activity."	2022
Dian Aditya Putra, Komang, GA Desya Pradnyaswari, And Eka Indra Setyawan	"Review of the Article on the Potential of Nanostructured Lipid Carrier (Nlc) Using the Active Ingredient of the Herbal Extract of Gotu Kola (Centella Asiatica (L.) Urb.) as a Topical Anti-Photoaging Gel Preparation."	2022
Dwandaru, Wipsar Sunu Brams.	“Applications of Nanoscience in Various Areas of Life: Nanotechnology.”	2012
Ilhamsyah, Re Septian, Annisa Dewi Nugrahani, And Ade Firman Kurniawan	“Clustered Regularly Interspaced Short Palindromic Repeats- Associated Library.”	2018
Kurnia, Dwi Febrianty, A Fitri Annisa Isa, Siti Nurmila Putri, And Isriany Ismail	"The Effect of Using Nonionic Surfactants and Methods on Niosome System Characteristics"	2023
Kurniasari, Dessy, And Sri Atun	"Manufacture and Characterization of Temu Kunci (Boesenbergia Pandurata) Ethanol Extract Nanoparticles in Various Chitosan Composition Variations."	2017
Lopes, RM, MM Gaspar, J.	“Liposomes Versus Lipid	2014

Pereira, CV Eleutério, M. Carvalheiro, AJ Almeida, And MEM Cruz.	Nanoparticles: Comparative Study Of Lipid-Based Systems As Oryzalin Carriers For The Treatment Of Leishmaniasis.”	
Nurleni, Novi, And Iskandarsyah	"Nanoparticle Formulation with Azelaic Acid Ethosomal Vesicles as Anti-Acne."	2020
Okta Dody Muzuka, Muhammad, Adeltrudis Adelsa Danimayostu, And Siti Jazimah Iswarin	"Pharmaceutical Journal Of Indonesia Test Of Ethosome Antioxidant Kaffir Lime Leaves Extract (Citrus Hystrix DC) As Skin Anti-Aging Using The Dpph Antioxidant Method Test Of Ethosome Kaffir Lime Leaves (Citrus Hystrix DC) Extract As Skin Anti-Aging With D."	2018
Purwanto, Ungsari Rizki Eka, Lilies Wahyu Ariani, and Anastasia Setyopuspito Pramitaningastuti.	“Anthocyanin Liposome Serum Formulation from Red Dragon Fruit Peel (Hylocereus Polyrhizus) for Antiaging.”	2019
Ramadon, Delly, And Abdul Mun'im	"Utilization of Nanotechnology in New Drug Delivery Systems for Natural Products."	2016
Rochman, M Fatchur, Aditya Darmawan, and Pramudya Wardhana	“Nanostructured Lipid Carriers System Solid Lipid Poloxamer And Stearic Acid With Liquid Lipid Soybean Oil.”	2022
Rosalina, Ajeng Illastria	“Drug Delivery Through the Skin: Liposome Vesicle Technology and Its Analogues.”	2023
Salunkhe, Sachin S., Neela M. Bhatia, Vikram S. Kawade, And Manish S. Bhatia.	“Development Of Lipid Based Nanoparticulate Drug Delivery Systems And Drug Carrier Complexes For Delivery To Brain.”	2015
Sarika Nikam, Mayura Chavan, And Padmini Sharma	“Solid Lipid Nanoparticles: A Lipid Based Drug Delivery.”	2014
Triana, Siahaan, Parsaoran.	"Journal of Chemical Science and Applications Preliminary Study on Encapsulation of Vitamin C in Liposomes"	2017

RESULTS AND DISCUSSION

Nanotechnology

Nanotechnology (Dwandaru 2012) is defined as engineering in the creation of materials, functions, and devices on the nanometer scale. Nanotechnology is an interesting field of development. In the microscopic world, physical, chemical, and biological properties change drastically. In addition, the magnetic, electrical, and optical properties of the material are unique. Various important biological mechanisms exist in this microscopic world. In addition, it would be interesting to create mechanical devices of microscopic sizes. Thus, there is a critical length scale at which drastic changes in the properties occur at the microscopic scale.

Figure 1. Mechanical properties depending on particle size.
[Source: (Dwandaru 2012) Reworked]

Figure 1 It can be observed from Figure 1 that the best (maximum) mechanical properties occur when the particle size is very fine, approaching the nanometer size. The larger the particle size, that is on the micrometer scale and above, the desired mechanical properties actually decrease. Meanwhile, particles smaller than the nanometer scale produce amorphous material. Another interesting physical property is the optical properties of nanomaterials. These optical properties depend on the particle size. This can be observed from Figure 2 below.

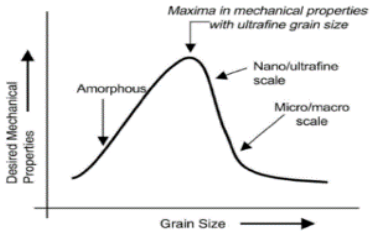

Figure 2. The optical Properties of Nanomaterials Depend on Their Particle Size. The Larger The Particle Size (Arrow To The Right), The UV Test Emission Will Shift Towards The Red (The Wavelength Is Larger)
[Source: (Dwandaru 2012)]

The magnetic properties of nanomaterials can be used for future medical technologies. Nanoparticles smaller than the blood vessels can be used to guide certain drugs to their targets in the body.

First, nanoparticles were injected into the drug particles. Then, using magnetic field control outside the body, the drug particles can be controlled until they reach the diseased tissue. This can be observed in Figure 3. In addition, these nanoparticles can be used for attenuating therapy by inserting nanomaterials into disease cells and then applying magnetic fields to the nanomaterials.

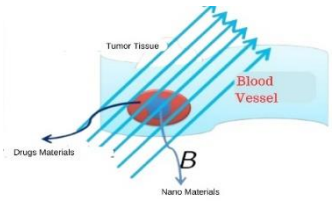

Figure 3. Nanomaterials Incorporated Into Medicinal Substances. The Magnetic Properties Of Nanoparticles Are Used To Direct Drugs To Specific Tissues
[Source: (Dwandaru 2012)]

Special Discussion on Lipd-Based Nanotechnology: Etosomes, Niosomes, Liposomes, SLN, NLC

Utilizing developments in pharmaceutical technology, namely the Novel Drug Delivery System (NDDS). Several carrier systems are included in NDDS, such as nanovesicles (liposomes, phytosomes, ethosomes, and transfersomes), nanoparticles, microspheres, micro/nanoemulsions, and micelles, or by modifying the solubility of the flavonoid compound itself, for example, by making cocrystals with coformers. The operators mentioned above can be grouped into several groups, namely phospholipid-based carrier systems, such as liposomes, ethosomes, transfersomes, and phytosomes, and lipid-based carrier systems, such as micro/nanoemulsions and Solid Lipid Nanoparticles (SLN).

Liposomes. Liposomes are artificial vesicles that are composed of phospholipids and cholesterol. Liposomes have been used as carriers for active substances in medicine. The size of liposomes varies from nanometers to micrometers, and generally ranges from 25 nm to 2.5 µm. Liposomes are spherical particles that encapsulate the solvent fraction, allowing it to diffuse into the interior. Liposomes consist of one, several, or many concentric membranes. Liposomes are formed from polar fat compounds and are characterized by lipophilic and hydrophilic parts in one molecule. Polar lipids aggregate and form colloidal particles when interacting with water. When depicted transversely (Figure 4), the hydrophilic part is directed towards the water and the lipophilic part is directed towards the center of the vesicle, forming a lipid bilayer membrane.

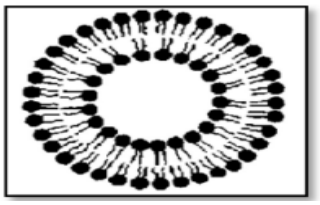

Figure 4. Cross-section of liposomes
[Source: (Ramadon and Mun'im 2016) has been reworked]

Liposomes can uniformly encapsulate both hydrophilic and lipophilic compounds. Hydrophilic compounds are absorbed in the center of the liposome, and fat-soluble compounds are collected in the fat part. Liposomes are usually formed from phospholipids, which are commonly used to alter the pharmacokinetic profile of drugs, natural compounds, vitamins, or enzymes. Liposomes have been extensively studied as natural compounds. Due to their unique properties, liposomes can be used to improve the performance of herbal products by increasing solubility, BA, intracellular uptake, and pharmacokinetic and biodistribution profiles (Ilhamsyah et al., 2018).

Liposomes as NDDS can improve the therapeutic activity and safety of drugs, especially by delivering drugs to the site of action and regulating drug levels at therapeutic concentrations over a long period of time. The main advantages of using liposomes are that they can increase solubility, high biocompatibility, ease of manufacture, and flexible nature, meaning that they can be used as carriers for hydrophilic, amphiphilic, or lipophilic drug substances; simple modulation of pharmacokinetic characteristics simply by changing the bilayer composition; and can be used for targeted delivery systems.

One example of the application of liposomes for herbal products is in the journal entitled "Development of liposomal Ginsenoside Rg3". Optimization of the formulation and evaluation of its anticancer effect explains why ginsenoside is a natural compound with anticancer activity but has low solubility in water. In his research, he optimized the ginsenoside liposome formula with 33 factorial designs using Response Surface Method (RSM) software. Based on the optimization results, ginsenoside Rg3 liposomes were prepared by thin layer hydration using egg phosphatidylcholine and cholesterol. Bioavailability test results showed that ginsenoside Rg3 liposomes provided a better pharmacokinetic profile than the regular ginsenoside Rg3 solution. In addition, the inhibition of tumor growth was observed by measuring the tumor volume after administering several

doses of liposomes and ginsenoside solution. The results showed that liposomes at a dose of 3.0 mg/kg provided the best inhibitory activity.

1) Etosome

The etosome is a carrier system in the form of soft and elastic vesicles with the main components being phosphophilide, alcohol (ethanol or isopropyl alcohol) at quite high concentrations (20-45%), and water. Etosomes were developed by Touitou and colleagues in 1997. Etosomes are attractive carriers because of their ability to penetrate the skin owing to their high deformability. The physicochemical properties of ethosomes can be used as carriers to deliver active compounds through the skin in quantities and depths better than those of conventional liposomes. In addition, ethosomes can be used to deliver hydrophilic, lipophilic, or amphiphilic drugs.

In general, the structure of ethosomes is similar to that of liposomes, namely in the form of lipid bilayer vesicles with gaps in their core, as shown in Figure 5.

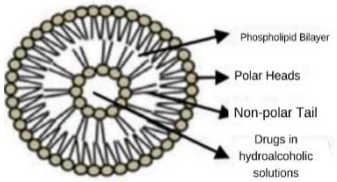

Figure 5. Illustration of ethosome diagram
[Source: (Nurleni and Iskandarsyah 2020) has been reprocessed]

The difference with liposomes is that the constituent components use high concentrations of ethanol. Etosomes can also be smaller in size and have greater entrapment efficiency than conventional liposomes, thereby increasing the stability of the resulting vesicles. Ethosomes can be used as slow-release preparations. The size of ethosomes varies from 10 to 1000 nm, depending on the manufacturing method, composition, and technique of using tools such as sonicators.

Etosomes are non-invasive carriers that can deliver drugs deep into the skin or into the systemic circulation. High deformability was obtained because the constituent components were phospholipids and ethanol. Phospholipids are vesicle-forming materials in the ethosome system. Phospholipids that can be used to make ethosomes are quite diverse; for example, phosphatidylcholine (PC), hydrogenated PC, or phosphatidylethanolamine (PE), with a concentration range of 0.5 -10%. Phospholipids can come from eggs and soybeans, and are semi-synthetic or synthetic.

In ethosomes, ethanol can also increase the penetration power of the drug because ethanol can disrupt the structure of the lipid double layer in the skin, which increases membrane permeability and changes the ability to dissolve materials from the lipid double layer in the stratum corneum (MPOC, Lia Dwi Jayanti, and Brier 2020). Ethosomes and glycol derivatives such as propylene glycol can also be added to the formula. Propylene glycol is used to increase skin penetration. To increase the stability of ethosomal vesicles, cholesterol can also be added at a concentration of 0.1 -1%.

When compared with other carrier vesicles, etosomes have several advantages, namely: Etosomes can increase drug penetration through the skin for dermal or transdermal purposes; they can carry drug molecules with diverse physicochemical properties, ranging from hydrophilic, lipophilic, or amphiphilic compounds; their constituent components are safe and have been approved for use in pharmaceutical and cosmetic preparations; in its development there are no risks such as the toxicological profile of each component that makes up ethosomes. Generally ethosomes are given in semisolid dosage form (gel or cream) thereby increasing patient compliance, in its management, this is a non-invasive

system, making it on a large scale is quite easy because it does not require complicated manufacturing techniques.

However, ethosomes also have several weaknesses, such as the ability to absorb limited amounts of drugs and only carry a low daily dose of drugs.

Etosomes are often used to improve percutaneous penetration of natural compounds. Etosome ammonium glycyrrhizinate was prepared by the cold method using phospolipone 90 as a basic vesicle material. The results of the in vitro penetration test showed that ammonium glycyrrhizinate prepared in the form of ethosomes provided the highest amount of penetration compared with hydroalcoholic solutions, aqueous solutions, and ethosome-ethanol mixtures. From this study, it was proven that ethosomes were able to increase the penetration of ammonium glycyrrhizinate, as shown in Figure 6. The anti-inflammatory test results also showed that ethosomal ammonium glycyrrhizinate provided the highest erythema inhibition for 4 hours as in Figure 6.

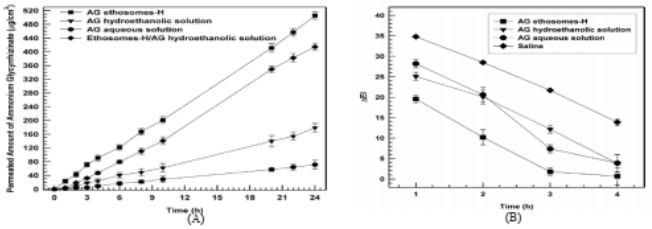

Figure 6. (A) In Vitro Penetration Test Results and (B) Anti-Inflammatory Test Results of Ammonium Glycyrrhizinate on Various Vehicles.
[Source: (Ramadon and Mun'im 2016)]

Ethosomal Test

Table II. Ethos Azelaic Acid Optimization Formula

Material Name	Concentration (%)		
	EF1	EF2	EF3
Assam Azelat	10	10	10
Fofolipon 90	10	10	10
Ethanol	30	35	40
Propylene glycol	2	2	2
Phosphate Buffer pH7.4	up to 100	up to 100	up to 100

Information: EF1 = Ethosomal formula 1; EF2 = Etosome Formula 2; EF3 = Etosome Formula 3
[Source: (Nurleni and Iskandarsyah 2020) has been reprocessed]

In this study, optimization of the azelaic acid ethosome formulation was carried out by comparing several variations in ethanol concentrations (30%, 35%, and 40%). Based on research conducted by (Nurleni and Iskandarsyah 2020) variations in ethanol concentration in ethosomes can affect the adsorption capacity of the active substance, particle size, polydispersity index, zeta potential and penetration ability of the preparation. The results of the azelaic acid ethosome suspension using the thin-layer or classical hydration method are shown in Figure 7.

Figure 7. Azelaic Acid Etosome from Various Ethanol Concentrations (30%, 35% and 40%)
[Source: (Nurleni and Iskandarsyah 2020) has been reprocessed]

Optimized ethosomes consist of phospholipids (Phospholipon 90 G), alcohol, propylene glycol, and buffer. The phospholipid used is Phospholipid 90 G which is a hydrogenated phospholipid derived from soybeans. Soybean phospholipids were chosen as the main ingredient for preparing ethosome agar. The resulting product does not produce an unpleasant odor when egg yolk phospholipids are used.

The conclusion of research that has been carried out in formulating nanoparticles with ethosome vesicles containing azelaic acid as an anti-acne agent with several variations in ethanol concentration using the classical method or thin layer hydration can be formulated into a good ethosome suspension (Nurleni and Iskandarsyah 2020).

2) Phytosome

Phytosomes are a technology that has been developed for drug formulations and nutraceutical products that contain active compounds from natural ingredients (herbs) that are hydrophilic by forming complexes of active compounds (phytoconstituents) in phospholipids. Making phytosomes aims to increase drug absorption to increase the bioavailability and efficacy of drugs. The formation of natural compounds with phospholipid molecules has been widely developed as a potential carrier system that is capable of increasing the bioavailability of extracts or active compounds from hydrophilic natural ingredients. The characteristics of phospholipids that resemble the properties of human cell membranes make this system highly compatible with human physiological systems.

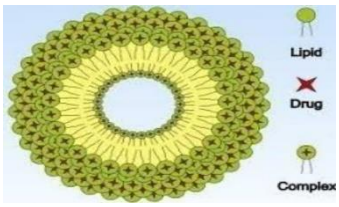

Figure 8. Cross-section of Phytosomes and Interactions of Phytosomes With Biological Membranes
[Source: (Ramadon and Mun'im 2016) has been reworked]

The application of phytosomes in herbal products is still under development to increase the absorption and solubility of a substance. Other applications of phytosomes, for example, include slowing down the release of drugs (Ramadon and Mun'im 2016). Developing NDDS for curcumin compounds in the form of phytosomes trapped in chitosan microspheres (Cur-PS-CMs). This is motivated by the physicochemical properties of curcumin, which has low solubility and is rapidly eliminated from the body. With this formula, it is hoped that the bioavailability of curcumin can be increased because the release is extended. Cur-PS-CMs were prepared by encapsulating Cur-PSs in chitosan microspheres using ionic gelation. The results of the in vitro release test for 5 hours showed that Cur-PS-CMs were slower (39-43%) in releasing curcumin than curcumin microspheres (Cur-CMs) (59-61%) alone. In addition, the half-life of curcumin in the form of Cur-PS-CMs was longer (3.16 hours) than that of microspheres (1.73 hours) and curcumin phytosomes (2.34 hours).

These results prove that CurPS-CMs provide advantages compared with curcumin microspheres or single phytosomes (Ramadon and Mun'im 2016).

3) Transfersomes

Transfersomes are lipid vesicles with the best deformability among the nanovesicles. Transfersomes are generally used topically. These vesicles consist of phospholipids and an Edge Activator (EA), a single-chain surfactant. EA plays a role in increasing the flexibility and deformability of transfersomes so that they can easily pass through the stratum corneum, as shown in Figure 5. Several types of EA that are often used include sodium cholate, sodium deoxycholate, Span 60, Span 65, Span 80, Tween 20, Tween 60, Tween 80 or dicalcium glycyrrhizinate. Transfersomes can pass through the skin through the mechanism of osmotic pressure differences. Transfersomes consists of 10-25% surfactant and 3-10% solution or hydroalcohol.

Transfersomes have several advantages: they are biocompatible, biodegradable, easy to make, can protect drugs from environmental degradation, can deliver drugs through narrow gaps between cells, and have been used for various materials such as peptides, proteins, analgesics, and natural ingredients. ingredients. compound compound. However, transfersomes also have several limitations; for example, they are difficult to produce on a large scale, the carrier system is unstable to oxidation, and they cannot carry high daily doses of drugs (Ramadon and Mun'im 2016).

4) Niosomes

Niosomes are vesicular delivery agents consisting of nonionic surfactants, cholesterol and charge inducing agents (Anggraeni, Kaniawati, and Jafar 2023). Meanwhile (Kurnia et al. 2023Niosomes are assystemsdelivery system bilayersbilayefulfills that fulfills the requirements for a topical dose delivery system. This system can help active ingredients penetrate the skin barrier membrane and has good stability as a carrier system.

Niosome Assay

Nosomes are generally divided into 8 methods: passive adsorption, thin film hydration, ether injection, reverse phase evaporation, double membrane extrusion, microfluidation, sonication, bubble method, active adsorption, and transmembrane pH gradient. The thin layer hydration method is the conventional method most often used because it is easier. Based on the standard size of the vesicles, niosomes can be divided into three groups. Namely Small Unilamellar Vesicles (0.025-0.05 µm), large unilamellar vesicles (>0.10 µm), and Multilamellar Vesicles (>0.05 µm) (Kurnia et al. 2023). .

5) Etosome

Etosomes are ethosomal vesicles of varying sizes, ranging from micrometers (µm) to nanometers (nm). The size depends on the composition, manufacturing method, and techniques used for tools such as sonicators (Andriani et al. 2021). Other researchers have found that Etosomes are a carrier system in the form of soft and elastic vesicles with the main components being phospholipids, alcohol in fairly high concentrations (20-45%), and water. High ethanol concentrations make ethosomes more elastic and flexible, and can increase penetration by disrupting the lipid bilayer structure of the skin (Nurleni and Iskandarsyah 2020).

Etosome Test

Etosomes were prepared using a cold method. Lecithin, extract, and cholesterol were dissolved in 85% room-temperature ethanol in a closed container with vigorous stirring using an overhead stirrer at a speed of 506 rpm. Propylene glycol was added during stirring at room temperature. Aquades (lecithin, extract, cholesterol, 85% ethanol, propylene glycol) were added to the mixture and stirred for 20 minutes at 20,000 rpm until homogeneous in a closed container. The size of ethosomal vesicles was reduced by sonication for 45 minutes.

Based on the vesicle size results, Formulas 1, 2, and 3 had vesicle sizes of 17.086 ± 28.491 µm, 52,872 ± 42,553 µm, and 27,489 ± 38,634 µm, respectively. Formula 1 has the smallest vesicle size (Figure 9).

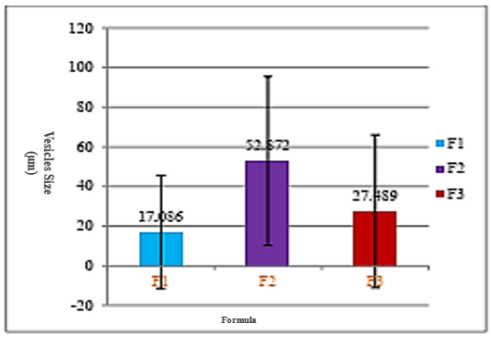

Figure 9. **Graph of The Size of F1, F2 and F3 Vesicles**
[Source: (Okta Dody Muzuka, Adelsa Danimayostu, and Jazimah Iswarin 2018)]

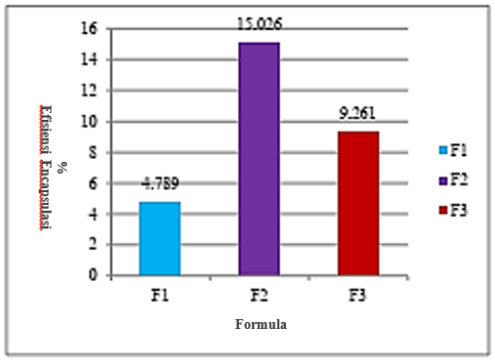

Figure 10. **Percentage of F1, F2 and F3 Traps**
[Source: (Okta Dody Muzuka, Adelsa Danimayostu, and Jazimah Iswarin 2018)]

If vesicles measuring > 10 µm penetrate the skin surface, 3-10 µm will concentrate in the hair follicles, and vesicles measuring < 3 µm will penetrate the stratum corneum. Based on the PSA results obtained, the average vesicle sizes for formulas 1, 2, and 3 were 17.086 ± 28.491, 52,872 ± 42,553, and 27,489 ± 38,634 µm. The results showed that the average vesicle size penetrated the stratum corneum, and the vesicle size did not match the expected specifications, namely 50-200 nm. There are several factors that cause differences in vesicle size, including material composition, sonication, and stirring speed.

In the study conducted, the entrapment efficiency value in formula 3 had a smaller entrapment percentage compared to formula 2 because of the influence of ethosome production at the sonication stage. Tsemperature affects vesicle size.30 The effect of temperature on vesicles shows that soy lecithin has a transition temperature point. Damage to the lipid membrane structure can occur at higher temperatures. 31 In this study, the temperature used during sonication was the lowest temperature in the device, namely 40 °C, while the temperature needed to concentrate the lipid phase in water required room temperature to form a gel phase. The temperature during sonication is anticipated by adding ice to the sonicator container, but the temperature is not monitored so that if the ice temperature starts to rise, the formation of vesicles in the sonication process is disrupted (Okta Dody Muzuka, Adelsa Danimayostu, and Jazimah Iswarin 2018).

6) Liposomes

Liposomes are micro- or nanosized vesicles containing amphiphilic phospholipids arranged in concentric bilayers in a water carrier. Conventional liposomes consist of phospholipids and cholesterol (Rosalina 2023). Another article states that liposomes Liposomes are a drug delivery system, where their amphilic nature allows the dissolution or encapsulation of drugs, both hydrophobic and hydrophilic. Liposomes are good drug delivery systems that can be used topically. Several studies have shown that liposomes are a good drug delivery system for topical preparations (Purwanto, Ariani, and Pramitaningastuti 2019).

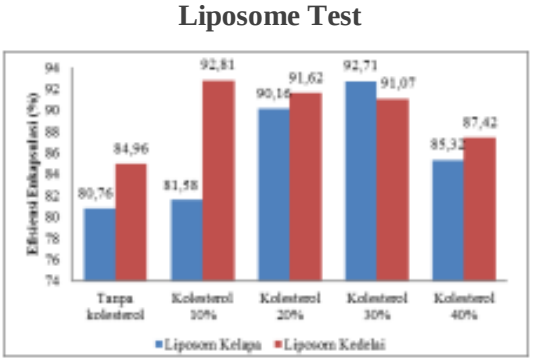

Figure 11. Encapulation Efficiency Values For Coconut and Soybean Liposomes
[Source: (Triana, Siahaan 2017)]

Coconut liposomes showed the highest encapsulation efficiency value at a cholesterol concentration of 30%, namely 92.71%. This encapsulation efficiency increased by 11.95% compared to that of coconut liposomes without the addition of cholesterol. The highest encapsulation efficiency value was found in soybean liposomes with a cholesterol concentration of 10% (92.81 %). The encapsulation efficiency was increased by 7.85%. The addition of cholesterol increased the encapsulation efficiency of coconut liposomes to a greater extent than soy liposomes. These data indicate that cholesterol interacts better with the coconut phospholipid bilayer than with soybean phospholipids. Coconut phospholipids have short acyl chains with fewer strong interactions between chains, allowing cholesterol to more easily place itself on the phospholipid membrane. As a result, cholesterol strengthens the interaction between its acyl chains, so that vitamin C encapsulation in coconut liposomes is maximized (Lopes et al. 2014).

The encapsulation efficiency of coconut liposomes was 80.76%. The addition of cholesterol to the liposome membrane affects encapsulation efficiency. The addition of 30% cholesterol increased the encapsulation efficiency to 92.71%. Temperature affects the ability of coconut liposomes to store vitamin C. Storage at 5°C reduces the leakage of coconut liposomes (Triana, Siahaan 2017).

7) Solid Lipid Nanoparticles (SLN).

Solid Lipid Nanoparticles (SLNs) are a relatively new class of lipid-based nanocarriers consisting of a lipid matrix (Salunkhe et al. 2015).

Solid Lipid Nanoparticles (SLN) are particulate-type carrier systems consisting of solid fat dispersed in a water medium in the presence of a surfactant as an emulsifier with an average particle size of 50-1000 nm.

SLN can be used in topical, transdermal, oral, or parenteral delivery systems. The main objective of designing SLNs as a particulate drug delivery system is to reduce particle size, increase absorption, and control drug release so that they can reach a specific site of action at an optimal release rate and dosage regimen (Kurniasari and Atun 2017).

SLN testing

SLN are prepared by emulsification by precipitating a mixture of fats into an o/w emulsifier. The lipophilic formula was then dissolved in water and an organic solvent (cyclohexane). The organic solvent was then evaporated to obtain fat microparticles. This microparticle fat is stored again until nanoparticles are produced.

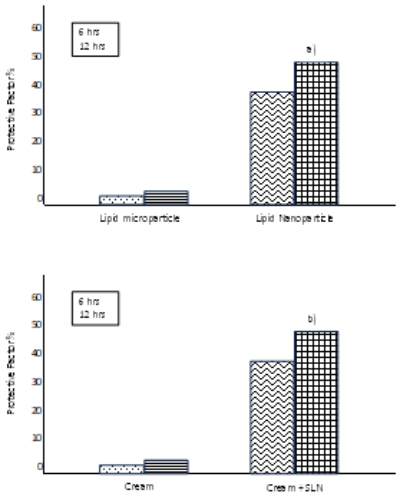

Figure 12. (a). Comparison of Protection Factors of Microparticles (2 µm) and nanoparticles (200 nm) (b). Comparison of Protection Factors From Sunlight Without and Smeared With SLN.
[Source: (Dwina Rahmi 2010)]

Figure 12 shows that the use of nanoparticles was more efficient than that of microparticles. In

Figure 12, it can be seen that cream containing SLN is more protective than cream without SLN.

Solid Lipid Nanoparticles (SLN), which use essential fatty acids as the main raw material, are increasingly in demand to overcome the side effects of using mineral and polymer nanoparticles in cosmetics/medicines. SLN have been introduced and developed as colloidal systems. SLN are produced using several HSH/USG, HPH, and SE methods. Among these methods, HPH is the most widely used by researchers and industry to produce SLN (Dwina Rahmi 2010).

8) NLC

The nanostructured lipid carrier (NLC) system is the development of a carrier system based on Solid Lipid Nanoparticles, which has the weakness of a low diffusion rate resulting in a long release time, high water content resulting in crystallization in the system, and ultimately a decrease in the solubility and release of bioactive compounds. sudden (Rochman, Darmawan, and Wardhana 2022).

The most popular topical preparations are semi-solid dosage forms such as creams, ointments, and gels. However, these creams and ointments have a weakness when applied: they leave a film layer that is difficult to clean. In a previous study, it was reported that the combination of NLC with a gel base was able to provide better skin permeability as well as the lowest rheological properties, stability, and toxicity. In addition, the gel is also reported to provide benefits for the skin, such as thixotropic, easy to spread, easy to clean, does not leave stains, is acceptable, and is long lasting. The gel base, which is composed of gelling agent components, also acts as a penetration enhancer to increase the absorption of the active ingredients into the skin. So it can be interpreted that the use of the NLC system and its incorporation into the gel base will increase the penetration of the active substances used synergistically (Dian Aditya Putra, Desya Pradnyaswari, and Indra Setyawan 2022).

NLC Testing

This study was conducted to determine the NLC system formulation using solid lipid poloxamer and stearic acid with liquid lipid soybean oil with three comparison formulations

in order to determine the physical characteristics of a good NLC system by measuring particle size, polydispersity index, pH, and viscosity test. The NLC system is the development of a carrier system based on Solid Lipid Nanoparticles, which has the disadvantages of a low diffusion rate, resulting in a long release time, high water content, resulting in crystallization in the system, and ultimately reducing the solubility of the bioactive. compound. and an explosive discharge occurred. Suddenly.

This study aimed to determine whether the NLC system made from solid poloxamer fat and stearic acid with liquid soybean oil fat has good physical properties and can be used as a drug delivery system for lipophilic drugs so that it can reach the target.

Table III. NLC System Formula

Formulasi	Konsentrasi (% b/b)					
	FI	FII	FIII	FIV	FV	FVI
Minyak Kedelai	3	2	1	3	2	1
Poloksamer	3	4	5	-	-	-
Asam Stearat	-	-	-	3	4	5
Tween 80	23	23	23	23	23	23
Propilenglikol	10	10	10	10	10	10
Aquadest add	100	100	100	100	100	100

[Source: (Rochman, Darmawan, and Wardhana 2022)]

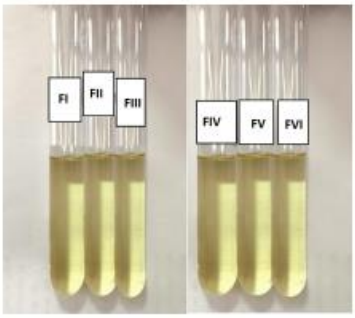

Figure 13. NLC system of Poloxamer Solid Fat (FI, FII, FIII) and Stearic Acid (FIV, FV, FVI) With Soybean Oil Liquid Fat
[Source: (Rochman, Darmawan, and Wardhana 2022)]

Table IV. Particle Size Test Results

Formula	Nilai Ukuran Partikel (nm)			Rata – rata ± SD
	R1	R2	R3	
I	650,2	909,1	706,9	755,4± 111,12
II	13,0	12,0	11,2	12,0 ± 0,74
III	9,6	11,2	11,3	10,7 ± 0,78
IV	288,9	198,4	224,7	237,3 ± 38,011
V	356,8	356,8	413,5	214,7 ± 26,822
VI	728,3	794,0	1018,8	215,7 ± 121,066

[Source: (Rochman, Darmawan, and Wardhana 2022)]

The NLC system then continues with particle size testing. The particle size test results of the six formulas listed in Table IV produced a particle size of <1000 nm, indicating that the particle size of the three formulas was within the particle size range of the NLC system, namely 10-1000 nm. In formulas II and III, smaller results were obtained compared with the other formulas.

Based on the results of this study, it can be concluded that the nanostructured lipid carrier system with solid lipid poloxamer and stearic acid with liquid soybean oil lipids obtained good characteristics, and each test was in accordance with the range (Rochman, Darmawan, and Wardhana 2022).

CONCLUSION

From the explanation above, it can be concluded that lipid-based nanotechnology has great potential in various fields such as medicine, cosmetics, and agriculture. Its use can provide great benefits such as increasing the effectiveness of drug administration, increasing the absorption of nutrients in food, and developing safer and more effective cosmetic products. To compare several types of nanoparticle methods, such as Liposomes, Neosomes, Etosomes, SLN, and NLC for selection of the lipid base, namely NLC. needs to be done to ensure that the use and development of this technology is carried out safely and is beneficial for humans and the environment.

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