Sun International Journal of Engineering and Basic Sciences
Nano Carrier as a Cosmetic Delivery System

Rohmawati Hidayah*, Widji Soeratri, Noorma Rosita

Department of Pharmaceutical, Faculty of Pharmacy, Airlangga University,
 Dharmawansa Dalam, Surabaya 60286, East java, Indonesia.

***Corresponding author: E-Mail: rohmawatihidayah@gmail.com, Tel: +6283830524095**

ABSTRACT

The purpose of this review is to discuss nanoparticles for topical use of cosmetics. Topical use is introduced long ago for the purpose of various levels (on the surface of the skin, epidermis, dermis and hypodermis). In the use of cosmetics and dermatology nanoparticles have the advantage of increasing the penetration of drugs on the skin, controlling the delay of drug release, improving drug adherence to the skin and improving drug stability. Nanoparticles reviewed in this paper are lipid nanoparticle and vesicle. The expectation of cosmetic products on the market can improve the profit / risk ratio for topical use.

KEY WORDS: Cosmetic Delivery System, NLC, SLN, Liposome, Transfersome, Vesicle, Penetration.

1. INTRODUCTION

The skin is the largest organ part of the human body, which contacts the external environment and covers body surface between 1.5 and 2.0 m². From a pharmaceutical point of view, the skin offers a variety of drug delivery routes because drug delivery through the skin has more advantages, such as avoiding first-pass metabolism, controlling drug release for a certain period of time, reducing side effects associated with systemic toxicity, and relieving pain (Wiechers, 2008).

There are several routes for penetrated compounds into the skin, namely intracellular routes, intercellular routes and appendageal routes. The intracellular route in which the penetrated compound passes the cell into the deeper layers of the skin, the compound prefers routes with small hydrophilic molecular sizes, whereas the intercellular route is the route by which the compound can penetrate into the skin through the extracellular lipids, fatty acids, and cell liquids and its location between cells. Many compounds choose to use lipophilic routes, the last route is the appendageal route is a route that utilizes the oil glands and hair follicles. This route is interesting for the delivery of nanoparticles into the skin and the appendages route can work as a depot for drugs that work with slowed drug release (Rattanapak, 2013).

Nanotechnology is a study with dimensions of 1-100 nm materials, which include nanotechnology disciplines including biomedicine, optics, electronics, chemistry, engineering, consumer goods, food and cosmetics. Nano medicine and nanodermatology dominate nanoparticulate drug delivery systems and have been accepted as new dermatologic treatments, a few years ago the FDA in America granted permission for some new therapies for skin diseases. Nanoparticles used in cosmetics include nanoemulsion, nanocrystal, micelles, polymer nanocapsule, niosome, liposome, nanostructure lipid carrier, solid lipid nanoparticles, dendrimer, fullerenes, and carbon nanotubes. (Naseri, 2015) on cosmetics and dermatology, nanoparticles improve drug stability, control delay in drug release and enhance drug adherence with the skin.

Solid Lipid Nanoparticles (SLN): Solid Lipid nanoparticles (SLN) introduced in 1990, is a colloid carrier to regulate drug delivery systems through the development of emulsions, liposomes, microparticle polymers and nanoparticles, with an average size of 40-1000 nm, solid lipid nanoparticles with composition solid lipids or solid lipid mixtures prepared in lieu of emulsion m/a (liquid lipids) (Pardeike, 2009). Solid lipid nanoparticles have several advantages including: Enabling controlled drug release and drug targeting, improving drug stability, enabling the incorporation of lipophilic and hydrophilic drugs, making it easy on a large scale, however SLN has some disadvantages such as low entrapment capacity and drug release system during the storage period (Pezeshki, 2014).

Nanostructure Lipid Carrier (NLC): Nanostructure lipid carrier (NLC) is the second generation of SLN. NLC is a development of SLN (Lipid Solid Nanoparticles) aimed at overcoming the shortcomings of SLN. Nanostructure lipid carrier (NLCs), a nanoparticle fat base with diameters measuring less than 100 nm, and is a new drug delivery system for lipophilic active ingredients with high solubility. Nanostructure lipid carrier (NLC) is prepared using a mixture of liquid lipids and solid lipids in a certain amount. A solid lipid mixture should be prepared in a 70:30 ratio with a liquid lipid in a ratio of up to 99:1, in this mixture should be observed oil content at the time of drop point melting (Pardeike, 2009). In addition to the solid and liquid lipids, other components added to the NLC are surfactants added to stabilize the nanoparticles formed on the system and prevent the incorporation of particles during storage (Naseri, 2015).

NLC is introduced for the use of medicines and cosmetics, and more than 40 products are available in the cosmetics market. Excess NLC has good penetration into the skin, low irritation, imparts occlusive effect on the skin, improves skin hydration, increases bioavailability of active ingredients in the skin and improves chemical stability on a topical formulation. Topical NLCs employed on the skin work to form films, the film works occlusive to prevent water loss from evaporated skin, the occlusal level on the skin based on particle size, small particle size, will result

in a small amount of water evaporating from the skin where large particle size causing excess water evaporation (Loo, 2013).

Type for Nanostructure Lipid carrier (NLC) can be seen in the picture below:

Figure.1. SLN with different crystallization with Type NLC. Type 1 imperfect matrix, type II multiple W/O/W. Type III amorphous non crystallization (Muller, 2002)

NLC type 1 is defined as an imperfect type crystal model. The structural difference between the solid and liquid lipids leads to imperfections of the formation of crystals to form larger spaces to occupy drug molecules.

NLC type II is defined as an amorphous model because it is made when mixing certain lipids that cannot crystallize a gain after homogenization. The lipid used is a solid lipid with an amorphous form. In the absence of crystallization, the tendency of the drug to get out of the system can be reduced.

NLC type III is defined as multiple models. This model has been developed to increase the load capacity as a medicine. Multiple type is a type of NLC where this drug where the soluble drug in liquid lipids is more.

Stratum corneum provides a range of barrier for Transdermal delivery to medications and stratum corneum containing corneocytes embedded in intracellular lipid matrix in ceramide, free fatty acids and cholesterol. Some approaches used in transdermal delivery systems are using conventional vesicular.

Conventional Vesicles As Skin Delivery System:

Vesicles: Vesicles are hollow colloidal particles, containing amphillic molecules, amphillic molecules containing polar hydrophilic clusters and hydrophobic groups, molecules can be formed due to a bilinear concentric (multi lamellar vesicle) concentric that surrounds the number of water compartments. Both water-soluble and water-insoluble compounds can become entangled in the vesicle. Hydrophilic compounds can become entangled in the compartment of internal compounds. While lipophilic compounds may be entangled in bilayer vesicles or partitioned between bilayers and aqua phases (Loans and jokes, 2008). Various lipid and surfactant variations can be used to prepare vesicles, especially those most composed by phospholipase or nonionic surfactants. Vesicles are preferred as liposome and noisome or nonionic surfactant vesicles. And the composition of the vesicle affects physicochemical characters such as size, lamellar and bilayer elasticity. The physicochemical characteristics will significantly alter the effectiveness of the vesicle as a skin delivery system (Loan and Joke, 2008).

Liposomes: Liposomes are vesicle microscopic which contain one or more concentric lipid bilayer, separated by aqueous phase or aqua buffer with a diameter between 80 nm to 10 μ m. Liposome (also called phospholipid vesicle) was first described by Bangham (1965). Such a vesicle containing one or more phospholipid bilayer membranes may trap both the hydrophilic and lipophilic drug molecules. For small uni lamellar vesicle (SUV) (10-100nm) or uni lamellar (100-3000nm) and if more than one bilayer as multi lamellar vesicle. Larger liposomes move quickly to the blood circulation. Liposome is unique in that it has the ability to accommodate different drug physicochemical characteristics such as polarity, and size (Bansal, 2012). Liposomes can work as carriers of drug molecules, proteins, nucleotides and plasmids and potentially as ophthalmic. The main components of the liposome membrane are dipalmitoyl phosphatidylcholine (DPPC, PC or EPC-egg phosphatidylcholine). Although some compounds are added to improve the stability or structure of other compounds. Two compounds were added: dipalmitoyl phosphatidylglycerol (DPPG or PG) and cholesterol. Cholesterol has the effect of making the membrane less permeable as it tends to fill the whole (Bansal, 2012).

Figure.2. Basic structure of vesicular systems

Cubosomes: Cubosomes are discrete, submicron, nanostructured particles of bi continuous cubic liquid crystalline phase. Recent research activities on the use of cubosome in personal care product varied from skin care to hair care and antiperspirants. L'Oreal and Nivea is trying to use cubosome particles as oil-in-water emulsion stabilizers and pollutant absorbents in cosmeceuticals (Lohani, 2014).

Novel Type Vesicle As Carrier Delivery:

Transfersome: Transfersome resembles liposomes morphologically but differs in function, transfersome more elastic. Transfersome is used as a carrier for small molecules, peptides, proteins and vaccines both *in vivo* and *in vitro*. The transfersome is concentrated through the pores of the stratum corneum, which is smaller in size under the skin in its intact form. This is because of its elastic properties (Bansal, 2012). Transfersome passes through the SC pore of approximately 1-10 liposome diameter, can be penetrated intact on the skin. Transfersome contains phosphatidylcholine (PC) and surfactant (edge activator) and also contains at least one aqua compartment that surrounds the lipid bilayer. Sodium cholate, Span 80, Tween 80, oleic acid, and dipotassium glycyrrhizinate are used as edge activators. For transdermal delivery of DNA, DOTAP (positive molecule) as the component used to make transfersome. Several investigations reported extended transfersome release and improved *in vivo* biologic activity.

Ethosome is a carrier of phospholipid liposomes containing high ethanol content (20-45%) despite the ethanol inter digitative effect on lipid bilayers, but high concentrations of ethanol may be detrimental to liposome formulations; recently ethanol can only be found at low concentrations in liposome formulations of 7% up to 10% for 14% transfersome, as conventional liposomes we know as drug delivery in the outer layer of the skin, ethosome shows increased permeation across the SC barrier. Ethosome is penetrated in the skin and promotes a deeper delivery of the skin. Ethome is a non-invasive delivery. Investigate the effects of phospholipids and the ethanol concentration of the size is distributed on the ethosome vesicle. At an ethanol concentration of 20% -45%, the vesicle size improves by lowering the ethanol concentration of a large size in a preparation containing 20% (193-8nm) ethanol and the smallest size containing 45% (103-9 nm) of ethanol. Ethanol gives a negative charge and improves the stability of the vesicle. Hydrophilic and hydrophobic chemicals can be trapped in ethosome and hydrophobic chemical trapping efficiency higher than hydrophilic chemicals ethosome systems are easy to prepare, non-irritant and the main ones contain phospholipids and ethanol, a compound commonly found in the manufacture of drugs. Ethosome structures are unique and trapped and carriers pass through the skin with higher lipophilic molecules such as cannabinoids, testosterone and minoxidil as cationic drugs such as propranolol and trihexphenidyl which can enhance the delivery of molecules by skin and cell membrane by ethosome carriers and research opportunities to develop new therapeutic improvements.

Application Nanoparticle:

Sunscren: Sunscreen is used to protect the skin from the harmful effects of sun exposure, the material used for sunscreen Zinc oxide (ZnO) and titanium dioxide (TiO₂) are materials to protect against sun damage. In the study (Wissing and Muller, 2001; 2002; Muller, 2002). SLN can act as a physical UV blockers themselves and are able to improve the UV protection in combination with organic sunscreens such as 2- hydroxy-4-methoxy benzophenone which allows a reduction of the concentration of the UV absorbers. This is where nanoparticles come in. Improved sunscreens are just one of the many innovative uses of nanotechnology. Sunscreen products using nanoparticles of ZnO or TiO₂ are transparent, less greasy, and less smelly and have increased aesthetic appeal (Lohani, 2014).

Increase of skin hydration and elasticity: The reduction of transepidermal water loss (TEWL) caused by occlusion leads to an increase in skin hydration after the dermal application of SLN, NLC or formulations containing them. An *in vivo* study showed that SLN-containing o/w cream increased the skin hydration more than the conventional o/w cream (Dubey, 2012). An increase of skin penetration was reported for coenzyme Q10-loaded SLN and NLC compared to nanoemulsion and liquid paraffin or isopropanol respectively, performing a tape stripping test (Dingler, 1998; Pardeike and Muller, 2007). Using the fluorescence dye Nile red as a marker, it could be shown by Teeranachaideekul (2008), that the penetration depth and the amount of penetration into the skin depends on the oil content used in NLC

Antiaging products are the main cosmeceuticals in the market are manufactured by nanotechnology. L'Oreal has employed nanotechnology in products such as Revitalift anti-wrinkle cream which contains nanosomes of Pro-Retinol A, and claims that it instantly return the skin and reduces the appearance of wrinkles. Application of retinol can increase epidermal water content, epidermal hyperplasia, and cell renewal while enhancing collagen synthesis (Lohani, 2014).

2. CONCLUSION

Both nanoparticle and vesicle lipid nanoparticle carrier systems have been developed for topical applications of cosmetics and pharmaceuticals, as well as scale up, qualification and validation, simple technology, low cost, tolerability etc., nanoparticle carrier systems also have benefits, increases in skin hydration, modified release,

increase of skin penetration associated with a targeting effect and avoidance of systemic uptake. In addition to the most important nanotechnology offering excellent business and research.

REFERENCES

- Andre O, Barel Marc Paye, Howard Maibach I, Handbook of Cosmetic Science and Technology, Informa Healthcare USA, 2009, 797-807.
- Bangham A.D, Standish M.M, Watkins J.C, Diffusion of univalent ions across the lamellae of swollen phospholipids, J. Mol. Biol., 13, 1965, 238–252.
- Bansal S, Chandan Prasad Kashyap, Geeta Aggarwal and SL Harikumar, A comparative review on vesicular drug Delivery system and stability issues, IJRPC, 2 (3), 2012.
- Dubey Prabhu P and Kamath J.V, Nano Structured lipid carriers, A Novel Topical drug delivery system, International Journal of PharmTech Research, 4 (2), 2012, 705-714.
- Honewell loan and Joke A, Bouwstra, Vesicle as Too for Transdermal and Dermal Delivery, Drug delivery technology, 2, 2005, 67-74.
- Indu Kaur P, Alka Garg, Anil Singla K, Deepika Aggarwal, Vesicular systems in ocular drug delivery, Elsevier, International Journal of Pharmaceutics, 2004, 1–14.
- Kupferman A, Ryan W.J.J, Leibowitz H.M, Prolongation of antiinflammatory effect of prednisolone acetate, Influence of formulation in higher viscosity gel, Arch, Ophthalmol, 1981, 2028–2029.
- Lohani Alka, Anurag Verma, Himanshi Joshi, Niti Yadav and Neha Karki, Nanotechnology-Based Cosmeceuticals, ISRN Dermatology, 2014.
- Loo CH, Basri M, Ismail R, HLN Lau, Tejo BA, Kanthimathi M.S, Hassan H.A, Choo YM, Effect of compositions in nanostructured lipid carriers (NLC) on skin hydration and occlusion International Journal of Nanomedicine, 8, 2013, 13–22.
- Muller R.H, Olbrich C, Neue Adjuvantien in der Impfstofftechnologie, Pharmazeutische Biotechnologie W, Verlagsgesellschaft, Wissenschaftliche Verlagsgesellschaft, Stuttgart, 2000, 283–302.
- Muller R.H, Pardeike J, Petersen R, Hommos A, C Lipid nanoparticles (NLC) as novel carrier for cosmetics-special features & state of commercialisation, SOFW-J, 5, 2007, 14–20.
- Naseri Neda, Hadi Valizadeh, Parvin Zakeri-Milani, Solid lipid nanoparticles, Production, characterization and applications, Adv Pharm Bull, 5 (3), 2015.
- Pardeike J, Aiman Hommos, Rainer H, Muller, Lipid nanoparticle (LN, NLC) in cosmeic and pharmacheutical, International Journal Of Pharmaceutics, 366 (1-2), 2009, 170-184.
- Pezeshki1 Akram, Babak Ghanbarzadeh, Maryam Mohammadi, Isa Fathollahi, Hamed Hamishehkar, Encapsulation of Vitamin A Palmitate in Nanostructured Lipid Carrier (NLC)-Effect of Surfactant Concentration on the Formulation Propertie, Adv Pharm Bull, 4 (2), 2014, 563-568.
- Rattanapak Teerawan, PhD Thesis, Transcutaneous immunization using lipid colloidal systems and microneedles, University of Otago, New Zealand, 2013.
- Teeranachaideekul, Eliana B, Souto B, Varaporn B, Junyaprasert Rainer H, Muller B, Cetyl palmitate-based NLC for topical deliveryof Coenzyme Q10-Development, physicochemical characterizationand *in vitro* release studies European Journal of Pharmaceutics and Biopharmaceutics, 67, 2007, 141–148.
- Weichers JW, Skin Delivery System Vesicle as Skin Delivery Vehicle, Allured, USA, 2008, 205-226.
- Wissing S.A, Muller R.H, Solid lipid nanoparticles (SLN)—a novel carrier for UV blockers, Pharmazie, 56, 2001, 783–786.
- Wissing S.A, Müller R.H, Solid lipid nanoparticles as carrier for sunscreens, *in vitro* release and *in vivo* skin penetration, J. Control. Release, 81, 2002, 225–233.