INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Paper

A Review: Formulation And Evaluation of Glycerosomes of Anti-Fungal Drug

S. S. Gotpagar*, A. H. Hosmani, I. D. Gonjari, S. V. Potdar, B. S. Gaikwad, S. J. Momin, R. A. Tambe

Department Of Pharmaceutics, Government College of Pharmacy, Karad.

ARTICLE INFO

Published: 29 Jan. 2025
Keywords:
Fungal infection, Glycerosomes, Anti-Fungal Drugs, Topical medication delivery, Drug delivery system.
DOI:
10.5281/zenodo.14764924

ABSTRACT

Skin fungal infections are among the most common dermatological conditions in the globe. Because of its benefits, which include directing medications to the infection site and lowering the possibility of systemic adverse effects, topical therapy is a desirable option for treating cutaneous infections. Nowadays, antifungal medications are typically applied topically as traditional cream and gel formulations. Drugs must be able to pass through the target skin layers at the right concentrations for that treatment to be successful. Nonetheless, the stratum corneum, the skin's outermost layer, acts as a strong barrier to prevent medications from penetrating the skin's deeper layers. Glycerosomes are new drug delivery vehicles made up of different proportions of phospholipids, cholesterol, water, and glycerol. Glycerosomes are improved liposomes designed for transdermal and topical medication delivery. Glycerol serves as a penetration enhancer and edge activator in these formulations. These drug delivery methods exhibit enhanced fluidity, stability, penetration, and entrapment. This review paper discusses the advantages of glycerosomes for topical antifungal treatment. This page provides a thorough analysis of glycerosomes, emphasising preparation techniques, assessment methodologies, benefits, and drawbacks based on published research.

INTRODUCTION

Fungal infections can range from minor skin and nail disorders like athlete's foot and ringworm to the fatal infectious illness.[1]. Ringworm, also known as dermatophytosis, typically presents as a sequence of rapidly growing, irritating lesions that can appear anywhere on the skin. These lesions primarily target the stratum corneum of keratinised tissues and hair fibers, which causes the fiber structure to autolyze, causing the hair to break off and causing alopecia. [2,3] Mycoses are fungal skin infections that can cause systemic,

***Corresponding Author:** S. S. Gotpagar
Address: *Department Of Pharmaceutics, Government College of Pharmacy, Karad.*
Email ✉: sharayugotpagar@gmail.com
Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

subcutaneous, or superficial illnesses. Fungal skin infections are common all over the world. Subcutaneous mycosis is the result of the infection's initial confusion at the skin's surface, which then spreads to the deeper layer of the skin as a result of desquamation. The World Health Organization states that skin conditions are a major cause of deformity, disability, and suffering. [4,5] In emerging and underdeveloped countries, an estimated 40 million people have experienced fungal diseases. Fungal infections can spread quickly and seriously because they impair immune function. [6,7]. Onchomycosis and tinea are frequently caused by dermatophytes. Additionally, one of the most common superficial cutaneous fungal diseases is Candida.[8]. When the immune system is compromised, candida can even infiltrate deeper tissues and the blood, resulting in potentially fatal systemic candidiasis. [9,10]

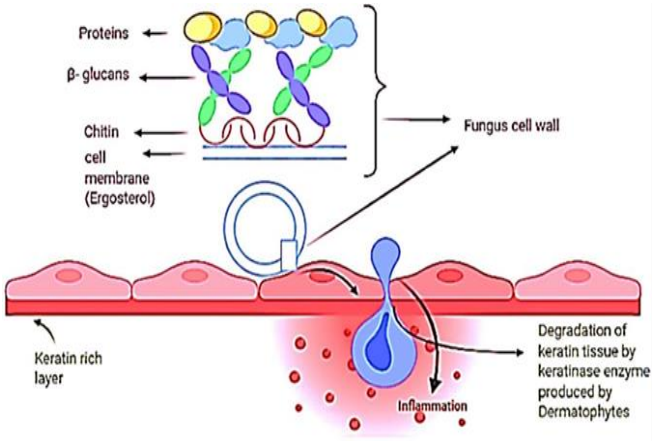
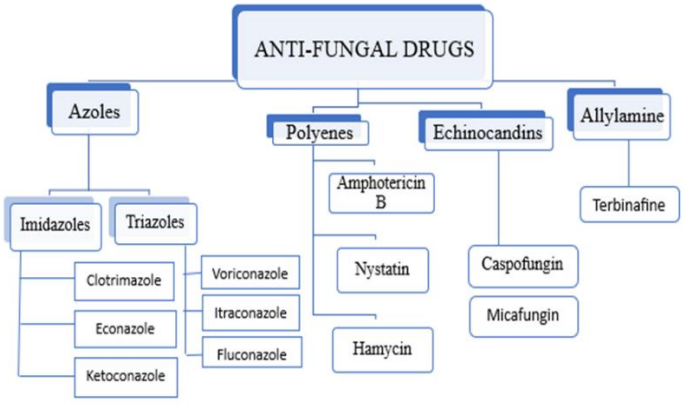


Fig. 1 Schematic illustration of Tinea Pedis pathophysiology (dermatophytosis; Figure from Navkiranjeet et al, 2021 [11]

Many types of skin infections caused by dermatology have been treated with various topical antifungal agents. Topical antifungals fall into three primary classes: azoles, polyenes, and allylamine/benzylamines.[10]



Topical medication delivery methods are widely utilized to treat local skin conditions. One potential benefit of applying medications topically is that they can be delivered at the site of action for a longer amount of time. It avoids the risk and inconvenience of intravenous (IV) therapy, as well as issues with absorption and pH changes. It also avoids the first pass metabolism. [12,13]. The stratum corneum, the epidermis' outermost layer, is the main obstacle to medication penetration through the skin, nevertheless. A medication with a low molecular weight (≤ 500 Da), strong

lipophilicity, and low dose effectiveness is appropriate for transdermal administration. The development of innovative drug delivery systems (NDDS) to increase permeability and decrease the stratum corneum barrier has received a lot of interest in recent decades. [14,3] Drug penetration through the target tissue determines how well a topical antifungal treatment works. Therefore, the skin should have the appropriate amounts of medication concentration.[10]. Understanding the structure of the skin is essential for that. The human skin is a well-structured membrane with three major layers: the epidermis, dermis and hypodermis.[10]

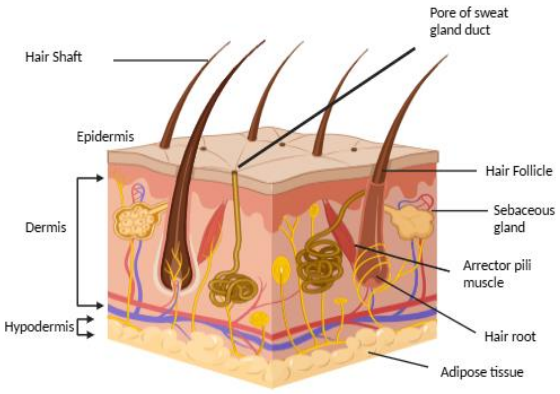


Fig.2 Human Skin

A. Epidermis: Cells of the epidermis's epithelium. These cells can be identified as both living and dead. The younger, rapidly dividing cells at the base of the epidermis push the older cells forward. The epidermis is not directly supplied with nutrients by blood vessels. It is well nourished by the underlying dermis's extensive vascular network, which permits the necessary chemicals to permeate here. Desmosomes connect epidermal cells in a very strong way. Intracellular keratin filmates and desmosomes come into contact. Keratin filmates produce keratin. In the cytosol, keratin cells congregate and crosslink with one another as they mature. The following cell types can be found in the epidermis:

1. In the epidermis, Keratinocytes make about 95% of the cells in the epidermis
2. The basal layers of the epidermis include melanocytes, which are cells that produce pigment.
3. Merkel cells are situated in the epidermis' basal layer and are a component of the amine precursor and decarboxylation system.
4. Langerhans cells are significant immune cells that are present in the middermis. [15,16]

Epidermis consists of five layers, namely from inside to outside;

- Stratum Germinativum (basal layer)
- Stratum Spinosum
- Stratum Granulosum
- Stratum Lucidum
- Stratum Corneum

•Stratum Corneum: This outermost layer provides mechanical protection for the skin. It acts as a barrier to stop the loss of water. It contains coenocytes. These cells die as a result of the pressure because they lose their nuclei. A protein called keratin-A is present in cells and prevents water from evaporating. [16,17]

• Stratum Lucidum: Cells of the stratum lucidum are flattened epithelial. Shiny character is present in the cells. This mainly occurs on the palms and

soles. The stratum lucidum is the name given to the layer because it resembles a shiny zone.

• Stratum Granulosum: Granular cells, a thin layer consisting of two to five rows of compressed rhomboid cells, make up the stratum granulosum [18]. The cytoplasm contains keratohyalin granules. It generally appears in the palm and soles and stops water loss.[16]

•Stratum Spinosum: Because it has spinous cells that mimic spines, the stratum spinosum is also referred as prickle cell layer. They also contain keratin filaments.

• Stratum Germinativum: The stratum germinativum is composed of polygonal cells on the borders and columnar or cuboidal epithelial cells in the deeper areas. In addition to glands and keratin structures made from these layers, it contains keratocytes going through mitosis. [19,20]

B. Dermis: The epidermis' beneath, the dermis is characterised by a thick network of collagen that provides the skin its strength and a thick network of fibers that allow the skin to stretch. The dermis together with epidermis receive nourishment from dermal blood vessels. When it comes to tracking body temperature, the dermis is essential. The senses of pressure and pain are provided by some nerves. The dermis is 3 to 5 mm in thickness. Elastin fibers, blood vessels, nerves, lymphatic cells, sweet glands, and an interfibrillar gel of glycosaminoglycan, salt, and water make up the dermis. The dermis' cell types include:

1. Fibroblasts: These are cells that produce collagen.

2. Scavenger cells: These are called macrophages.

3. Mast cells: These cells are in charge of eosinophil interactions and immunological responses. [21]

The dermis serves as a vital link to the other layers of the skin. The integrity of the epidermis, hair follicles, and skin glands can all be impacted by changes in the dermal metabolism.

C. Hypodermis: The hypodermis is the skin's deepest layer. It's the layer of skin that comes into contact with the deeper tissues of the body, such bone and muscles. Though they are encased in the epidermis, sweat glands, hair follicles, and sebaceous glands all have their origins in the dermis. Sweat glands apply a thin salt solution to the skin's surface. The skin is cooled by the evaporation of this fluid, which helps to balance body and skin temperatures. Sweet glands can be found all over the body. The number of dilutions (sweat) produced depends on the temperature, the degree of heat-producing skeletal muscle activity, and several emotional factors. Sebum is the product of the sebaceous glands. Hair follicles discharge sebum, an oily material, onto the skin.[16]

Routes Of Drug Permeation Through Skin: Three primary routes of skin absorption are [22,23,16]

1) Primary Transcellular: The chemical elements are carried into and out of the cell membrane by keratin-packed coenocytes.

2) Secondary Intercellular: The molecules go through the lipid-rich extracellular space, passing around coenocytes.

3) Thirdly, the Transappendageal: The system is maintained by sebaceous glands, hair follicles, and sweat glands.

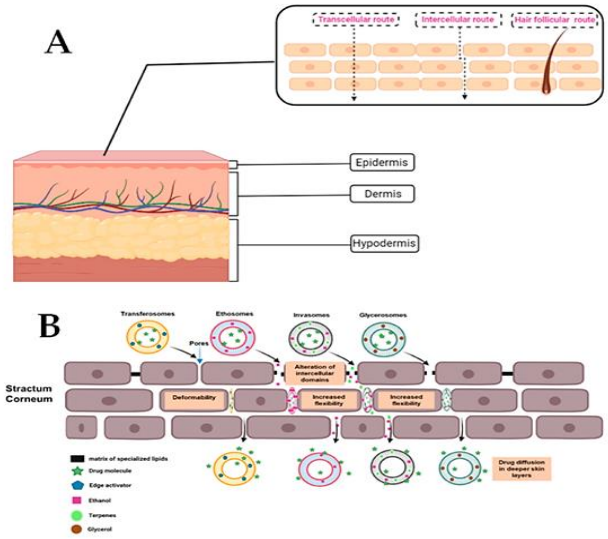


Fig.3 Graphic illustration of structure of the skin and pathways for skin penetration of nanoparticles (A) and the mechanisms involved in advanced vesicular skin penetration (B). [24,25] Even though antifungal drugs come in a number of standard dosage forms, including creams, gels, and the like, they didn't seem to be able to adequately address the many negative effects of antifungals, including toxicity, drug-drug interactions, and decreased water solubility of systemic antifungal agents [26]. Therefore, novel methods of delivery are vitally needed to address these issues. Nanoparticles, Sonophoresis, microneedles, patches, and vesicular drug delivery systems are some of the methods being employed for topical drug delivery. Vesicular drug delivery methods seem to be the most promising of these tactics. [27]. In order to localize the medication in the skin and deeper tissues, a specifically made carrier with enhanced penetration and permeation across the stratum corneum may be helpful in treating cutaneous fungal infections. [28,5]

Glycerosomes:

Bangham created these highly structured phospholipid complexes for the first time in 1965. These systems are hence referred to as Bangham bodies [29,30,31] Numerous vesicular systems, including as liposomes and niosomes, have been developed that offer regulated and targeted drug release [32]. However, these vesicles typically lose their efficacy in drug administration because of low entrapment efficiency, instability, etc. To get over these restrictions, novel vesicular formulations including ethosomes and transferosomes have been developed. Ethosomes have a high ethanol content, which increases the drug's penetration into the skin by making it more flexible and deformable. However, the ethosomes' high ethanol content has unfavourable effects. By altering the fluidity of lipid bilayers, Manca et al. created a novel method to improve the vesicular characteristics of these systems. Glycerosomes are the name given to these vesicular structures [33]. These carriers are completely approved for topical distribution because they don't contain any hazardous materials. [34,27] With their higher glycerol content, glycerosomes (GMs) offer a novel way to alter the liposome bilayers' fluidity, improving their effectiveness as a topical drug delivery vehicle. Various phospholipids and 20–30% (v/v) non-toxic glycerol make up GMs.[35]. Glycerol serves as a penetration enhancer and edge activator in these formulations. Glycerosomes' physical stability is greatly enhanced by increasing their quantity by 10, 20, or 30%. [36,24]. These adaptable vesicular carriers can include a variety

of substances, such as cholesterol, which improves the lipid bilayer's stability. In order to reduce vesicle aggregation and modify the electrical charge of the vesicular surfaces, basic or acidic lipid molecules can be added. The same methods used to produce regular liposomes can also be used to produce GMs. These vesicles' glycerol content raises the compactness index, which improves the permeability and penetration of therapeutic skin. As a barrier in the aqueous phase, cholesterol increases the stability of GMs and maintains the integrity of the lipid membrane.[35]

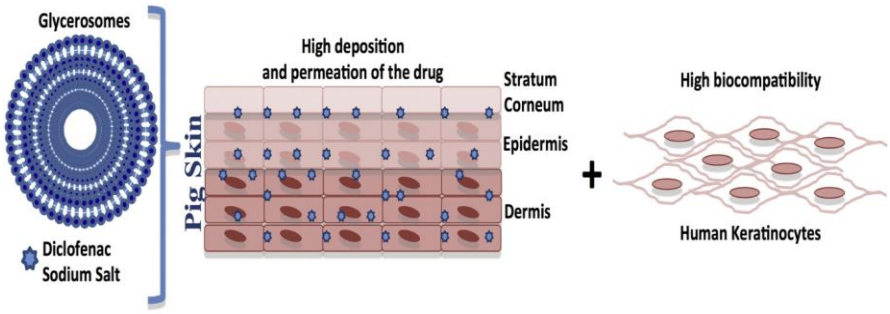


Fig. 4 Glycerosomes [38]

GMs have recently been suggested for use in inhalable delivery systems as well as intranasal, topical, and transdermal drug delivery. [37-41]. These glycerosomes have lately shown promise in a number of therapeutic domains, including skin conditions and inflammatory and infectious disorders. [42,43,24]. The ability of glycerosomes to entrap drugs that are hydrophilic and hydrophobic makes them a promising method for delivering drugs. [44]

Methods Of Preparation of Glycerosomes: [45] Commonly used methods of preparation of glycerosomes are as follows:

1. **Thin film hydration technique**:

Lipid is in an organic solvent, dissolved and then dried to create a lipid film using the thin film hydration process. By adding aqueous medium, the resulting film is hydrated above the lipid's transition temperature. The dispersion is agitated mechanically. The medicine to be encapsulated is introduced to aqueous hydration buffer if it is hydrophilic, and to the lipid film if it is lipophilic. This process for creating MLVs was initially described by Bangham et al. Glycerol in water can be used as the hydration medium to create glycerosomes.

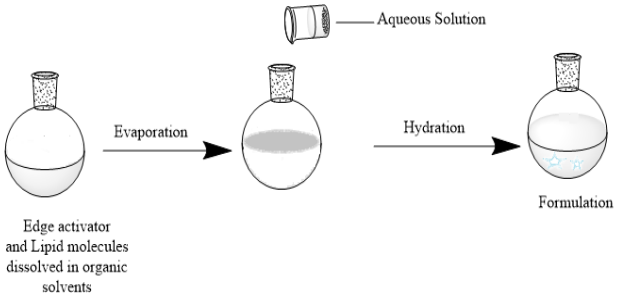


Fig. 5 Thin Film Hydration

2. **Solvent spherule method:**

Phospholipids are combined with an organic solvent and subsequently dissolved in an aqueous media using the solvent spherule process. Spherules of lipids with organic solvents (o/w emulsion) are then produced by vortexing or stirring the aforementioned combination for one hour under low vacuum. On a water bath, the spherules undergo controlled evaporation. to remove organic solvents and produce MLVs

3. Sonication:

This technique involves sonicating MLVs. A probe sonicator or a bath sonicator is used to do the sonication. The procedure is conducted in an inert atmosphere. This approach has a number of problems, including the rejection of big molecules, compound degradation, and a decrease in encapsulation efficacy.

4. Solvent injections method, ether injection method:

This technique, which involves dissolving lipids in a diethyl ether/ether methanol combination, was described by Watkins. After that, these are injected into a heated aqueous solution that contains the substance that has to be encapsulated. It is important to keep the heated aqueous phase above the ether's boiling point. During encapsulation, a temperature of 55 to 65° is typically maintained. Injection should proceed slowly rather than quickly. Ether evaporates when it comes into contact with a heated aqueous phase, creating unilamellar vesicles. This method's drawbacks include the limited yield of heterogenous liposomes and the exposure of the chemicals to be encapsulated to organic solvents and high temperatures.

5. Ethanol injection method:

Batzri and Korn first described the ethanol injection technique in 1976. This technique involves dissolving lipid in ethanol and forcing it through a tiny opening—which may be a syringe—in an excess of water. When injecting an ethanolic lipid solution into an aqueous media, the pace should be such that the two are completely mixed. For phospholipids to disperse in water and for ethanol to be immediately diluted in a hydration medium, the two must be well mixed. The primary benefit of this technique is that, by injecting a lipid solution that has been dissolved in ether in water, tiny liposomes smaller than 100 nm can be produced without the need for sonication or extrusion. Additionally, diluted and homogeneous liposomes are produced. The restriction resulting from lipid solubility in ethanol limits the amount of ethanol that can be added to aqueous media, which in turn limits the amount of lipid that can be added to ethanol. This is one of the drawbacks of the ethanol injection method. Although it can be eliminated by dialysis, ethanol stays in liposomes.

6. Calcium-induced fusion method:

Using this procedure, SUVs undergo fusion when calcium (Ca2+) is added, creating LUVs. Large planar lamellae are created during fusion, and these eventually develop into cochleate cylinders. To create LUVs, these are further combined with EDTA and undergo additional transformation. EDTA keeps the membrane fluid and aids in the restoration of negative charge.

7. Freeze-thaw method:

This technique uses the freezing and thawing process. Only charged phospholipid mixtures, or those with both positive and negative charges, can be employed with the freeze-thaw approach. It can also be applied to phospholipids that are naturally crude. We quickly freeze and then thaw small unilamellar liposomes. LUVs are then produced by sonicating them. Following freezing and thawing, the bilayers of SUVs fuse, forming LUVs as a result of this process. The production of liposomes using this technique is decreased by higher liposome concentration or increased ionic strength.

Advantages Of Glycerosomes [45]:

1. Nontoxic and safe topical medication delivery technology.

2. Transition temperatures are not necessary for the production of glycerosomes.
3. Unlike traditional liposomes, they can develop at ambient temperature (30 or 25°).
4. They function as edge activators and penetration enhancers, improving medication penetration in the stratum corneum and delivering it to the inner layers of skin.
5. Unlike traditional liposomes, glycerol, which is viscous by nature, evenly distributes on the skin and does not allow the active pharmaceutical ingredient to leak [46].
6. Glycerosomes also alter and enhance the skin layer's plasticity. These lessen the barriers to transdermal medication transport and raise the stratum corneum's water content.[47]
7. Glycerosomes have the ability to alter the arrangement of hydrophilic phospholipid chains and the manner in which other system vesicles behave in relation to one another. Given that glycerosomes can alter the system's dielectric constant, this is feasible. [48] These vesicles are special because they have the ability to function as both the elastic and penetration enhancing. [47,49]

Disadvantages Of Glycerosomes:

1. Glycerol increases particle size and decreases drug release in vesicles [50,37].
2. The viscosity of glycerosomes may lengthen the time it takes for vesicles to travel from the formulation to the skin's surface, but it also improves stability [48].

Evaluation Parameters of Glycerosomes:

1. Particle size analysis:

A Zetasizer can be used to examine the polydispersity index (PI) and particle size analysis of glycerosome preparation. This approach is called photon correlation spectroscopy [37,38,47,52] or dynamic laser light scattering [51,27]. For this, a Malvern zetasizer is typically utilized [37,38,47,52].

2. Vesicle formation:

SEM (scanning electron microscopy), TEM (transmission electron microscopy), and cryo-TEM are used to validate vesicle formation [51, 52]. The materials are first stained with 1% phosphotungstic acid in TEM before being examined using an electronic microscope. Coating the samples on a carbon rod and immersing it in ethane at its melting temperature is how cryo-TEM works. The TEM is then used to investigate these.

3. Determination of deformation index:

This involves creating glycerosomal preparations that can pass through a membrane extruder with a particular pore size and employing an extruder to do so at a particular pressure. The membrane's hole size needs to be less than the average phospholipid vesicle size. Flexible vesicles that can readily flow through skin pores are necessary for penetration into the skin. Since glycerol is thought to form these kinds of vesicles, the deformation index is computed to determine if glycerol may form vesicles with the ability to alter shape. [47]

4. Determination of entrapment efficiency (%):

Entrapment efficiency is calculated using various methods. Manca et al. [38,47,51,52] have employed the dialysis technique. They sorted the formulations that are entrapped from those that are not after passing the formation of glycerosomes from the dialysis tube of 12,000 to 14,000 Dalton. They were then tested for the presence of drugs. Entrapment is calculated using the formula acquired drug content/initial drug content×100, which compares the percentage of drug obtained after dialysis to that taken prior to dialysis.

5. Determination of penetration:

The degree of glycerosome penetration into the epidermal layer can be ascertained with the use of this evaluation criteria. This can be accomplished ex vivo. It aids in figuring out how well drugs penetrate the epidermis. This is accomplished by using a Franz diffusion cell. Animal skin is positioned with the stratum corneum of skin

towards the donor side between the donor and receptor compartments. Following the application of the glycerosome preparations to the skin (stratum corneum) at specific intervals, the medium accumulated within the receptor compartment side is removed and replaced with new medium. It is examined for drug content using an appropriate technique (HPLC or UV). The skin is separated from the Franz diffusion cell once all of the samples have been delivered. The layers are sonicated once the epidermis and dermis have been separated, and the drug concentration is then ascertained [37,38,47,52].

6. Determination of drug release in vitro:

Glycerosome drug release in vitro is measured using a dialysis bag. This process involves adding 1 millilitre of glycerosome preparation to a dialysis bag and submerging the bag in phosphate buffer. Samples are removed at specific times and subjected to either UV or HPLC analysis [37].

7. Determination of fluidity:

Lipid bilayer fluidity is assessed by differential scanning colorimetry (DSC) investigations. This technique aids in figuring out the phospholipids' transition temperature. According to some reports, phospholipids' transition temperature reveals how they interact with other chemicals. The addition of glycerol causes a change in the transition temperature, which further supports the idea that the glycerosomes are more fluid.[45]

8. Determination of stability:

Using a Zetasizer to measure the zeta potential provides information about the stability of the preparation as well as the charges that may be present on the surface of glycerosomes as a result of the addition of charged species in the formulation. The formulation is more stable when the zeta potential is negative.[45]

CONCLUSION:

To sum up, glycerosomes are new vesicular structures made of different amounts of glycerol. By altering their arrangement, glycerol functions as a modulator for the skin layers. It can transport the medication to deeper skin tissues while avoiding the skin barriers' layers. Due to its capacity to improve skin penetration, increase drug entrapment in vesicles, and create more flexible and fluid vesicles, it is mostly utilized for topical drug delivery. It has been established that glycerosomes can encapsulate hydrophilic as well as lipophilic drugs. Consequently, it resolves the issues of permeability and solubility with antifungal medications.

ACKNOWLWDGEMENT:

We are thankful to our research guide for providing us valuable guidance. Also, we are thankful to the principle of Government College of Pharmacy, Karad for allowing us to publish this article and gave us other facilities.

REFERENCES

1. Vicente, María Francisca, et al. "Microbial natural products as a source of antifungals." Clinical microbiology and infection 9.1 (2003): 15-32.
2. Sahoo, Alok Kumar, and Rahul Mahajan. "Management of tinea corporis, tinea cruris, and tinea pedis: A comprehensive review." Indian dermatology online journal 7.2 (2016): 77-86.
3. Reza, Mohammad Irshad, et al. "Formulation of ketoconazole loaded nano dispersive gel using swollen micelles technique and its in vitro characterization." Int J Pharm Pharm Sci 10 (2018): 162-6.
4. Garg, Abhinava, et al. "Recent advances in topical carriers of anti-fungal agents." Heliyon 6.8 (2020).
5. Johl, Shaanya, and Sayani Bhattacharyya. "Novel Deformable Vesicle for the Transdermal Delivery of Terbinafine Hydrochloride-Formulation and Cytotoxic Evaluation." Ind. J. Pharm. Edu. Res 58.1 (2024): 1-10.

6. Ameen, Mahreen. "Epidemiology of superficial fungal infections." Clinics in dermatology 28.2 (2010): 197-201.
7. Havlickova, Blanka, Viktor A. Czaika, and Markus Friedrich. "Epidemiological trends in skin mycoses worldwide." Mycoses 51 (2008): 2-15.
8. Zhang, Alexandra Y., William L. Camp, and Boni E. Elewski. "Advances in topical and systemic antifungals." Dermatologic clinics 25.2 (2007): 165-183.
9. Verma, Poonam, and Kamla Pathak. "Nanosized ethanolic vesicles loaded with econazole nitrate for the treatment of deep fungal infections through topical gel formulation." Nanomedicine: Nanotechnology, Biology and Medicine 8.4 (2012): 489-496.
10. Güngör, Sevgi, et al. "New Formulation Strategies in Topical Antifungal Therapy." Journal of Cosmetics Dermatological Sciences and Applications, vol. 03, no. 01, 2013, pp. 56–65, doi:10.4236/jcdsa.2013.31a009.
11. Kaur, Navkiranjeet, et al. "A review on antifungal efficiency of plant extracts entrenched polysaccharide-based nanohydrogels." Nutrients 13.6 (2021): 2055.
12. Haneefa, KP Mohammed, et al. "Emulgel: An advanced review." Journal of pharmaceutical sciences and research 5.12 (2013): 254.
13. Ranga, P. M., et al. "Formulation and in vitro evaluation of ciprofloxacin loaded topical emulgel." Int J Pharm Chem Sci 1.1 (2012): 237-242.
14. Shirsand, S. B., et al. "Formulation and evaluation of Ketoconazole niosomal gel drug delivery system." International journal of pharmaceutical investigation 2.4 (2012): 201.
15. Sherwood, L., and Human Physiology. The Skin Microflora and Microbial Skin Disease. Vol. 6, 2007.
16. Sharma, G. S., et al. "A REVIEW ON PHARMACEUTICAL GELS." Ymerdigital.com, https://ymerdigital.com/uploads/YMER2112F7.pdf. Accessed 27 Dec. 2024.
17. Gad, S. C. Pharmaceutical Manufacturing Handbook: Production and Processes. Vol. 5, John Wiley & Sons, 2008.
18. Vollmer, B. Polymer Chemistry. Springer Science & Business Media, 2011.
19. Jones, D. Pharmaceutics-Dosage Form and Design". Pharmaceutical Press, 2008.
20. Jeganath, S., and E. Jeevitha. "Pharmaceutical Gels and Recent Trends-A Review." Research Journal of Pharmacy and Technology 12.12 (2019): 6181-6186.
21. El Maghraby, Gamal M., Brian W. Barry, and AC18572392 Williams. "Liposomes and skin: from drug delivery to model membranes." European journal of pharmaceutical sciences 34.4-5 (2008): 203-222.
22. Yang, Kerong, et al. "Antimicrobial hydrogels: promising materials for medical application." International journal of nanomedicine (2018): 2217-2263.
23. Loydva, N. G., and H. C. Popovich. Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems. Lippincott Williams & Williams, 2011.
24. Akombaetwa, Nakamwi, et al. "Current advances in lipid nanosystems intended for topical and transdermal drug delivery applications." Pharmaceutics 15.2 (2023): 656.
25. Sala, M., et al. "Lipid nanocarriers as skin drug delivery systems: Properties, mechanisms of skin interactions and medical applications." International journal of pharmaceutics 535.1-2 (2018): 1-17.
26. Soliman, Ghareb M. "Nanoparticles as safe and effective delivery systems of antifungal agents: Achievements and challenges."

International journal of pharmaceutics 523.1 (2017): 15-32.
27. Rani, Deepika, et al. "Formulation, design and optimization of glycerosomes for topical delivery of minoxidil." Research Journal of Pharmacy and Technology 14.5 (2021): 2367-2374.
28. Bhattacharyya, Sayani, Avik Si, and Subhabrata Ray. "Liposomes as a skin delivery system for cosmeceuticals." Nanocosmeceuticals. Academic Press, 2022. 209-235.
29. Biju, S., et al. "Vesicular systems: an overview." Indian journal of pharmaceutical sciences 68.2 (2006).
30. Srikanth, K., M. Nappinnai, and V. R. M. Gupta. "Proniosomes: A novel drug carrier system." Research Journal of Pharmacy and Technology 3.3 (2010): 709-711.
31. Saraf, Swarnlata, et al. "Sphingosomes a novel approach to vesicular drug delivery." Research journal of pharmacy and technology 4.5 (2011): 661-666.
32. Kamboj, Sunil, et al. "Vesicular drug delivery systems: a novel approach for drug targeting." brain 1.11 (2013).
33. Manca, M. L., M. Fadda, and G. Orsini. "Glycerosomes and thereof use in pharmaceutical and cosmetic preparation for topical applications." EP2010/001428 (2014).
34. Zaru, M., et al. "Glycerosomes and Thereof Use in Pharmaceutical and Cosmetic Preparation for Topical Applications." US2012/0141565, 2012.
35. Alam, Md Shabbir, et al. "Quality by design-optimized glycerosome-enabled nanosunscreen gel of rutin hydrate." Gels 9.9 (2023): 752.
36. Manca, Maria Letizia, et al. "Glycerosomes: Investigation of role of 1, 2-dimyristoyl-sn-glycero-3-phosphatidycholine (DMPC) on the assembling and skin delivery performances." International Journal of Pharmaceutics 532.1 (2017): 401-407.
37. Salem, Heba F., et al. "Formulation design and optimization of novel soft glycerosomes for enhanced topical delivery of celecoxib and cupferron by Box–Behnken statistical design." Drug development and industrial pharmacy 44.11 (2018): 1871-1884.
38. Manca, Maria Letizia, et al. "Glycerosomes: Use of hydrogenated soy phosphatidylcholine mixture and its effect on vesicle features and diclofenac skin penetration." International journal of pharmaceutics 511.1 (2016): 198-204.
39. Naguib, Marianne J., et al. "Investigating the potential of utilizing glycerosomes as a novel vesicular platform for enhancing intranasal delivery of lacidipine." International Journal of Pharmaceutics 582 (2020): 119302.
40. Melis, Virginia, et al. "Inhalable polymer-glycerosomes as safe and effective carriers for rifampicin delivery to the lungs." Colloids and surfaces B: Biointerfaces 143 (2016): 301-308.
41. Salem, Heba F., et al. "Glycerosomal thermosensitive in situ gel of duloxetine HCl as a novel nanoplatform for rectal delivery: in vitro optimization and in vivo appraisal." Drug Delivery and Translational Research 12.12 (2022): 3083-3103.
42. Moolakkadath, Thasleem, et al. "Preparation and optimization of fisetin loaded glycerol based soft nanovesicles by Box-Behnken design." International journal of pharmaceutics 578 (2020): 119125.
43. Younes, Nihal Farid, and Basant Ahmed Habib. "Augmented local skin accumulation efficiency of sertaconazole nitrate via glycerosomal hydrogel: Formulation, statistical optimization, ex vivo performance and in vivo penetration." Journal of Drug Delivery Science and Technology 72 (2022): 103364.

44. Singh, Ragini, et al. "A Discursive Review of Recent Development and Patents on Glycerosomes." Recent Patents on Nanotechnology 17.3 (2023): 183-189.
45. Gupta, Priya, Rupa Mazumder, and Swarupanjali Padhi. "Glycerosomes: Advanced Liposomal Drug Delivery System." Indian journal of pharmaceutical sciences 82.3 (2020).
46. Oku, Naoto, and Robert C. Macdonald. "Formation of giant liposomes from lipids in chaotropic ion solutions." Biochimica et Biophysica Acta (BBA)-Biomembranes 734.1 (1983): 54-61.
47. Manca, Maria Letizia, et al. "Glycerosomes: A new tool for effective dermal and transdermal drug delivery." International journal of pharmaceutics 455.1-2 (2013): 66-74.
48. Vitonyte, Justina, et al. "Bifunctional viscous nanovesicles co-loaded with resveratrol and gallic acid for skin protection against microbial and oxidative injuries." European Journal of Pharmaceutics and Biopharmaceutics 114 (2017): 278-287.
49. Barichello, José Mario, et al. "Combined effect of liposomalization and addition of glycerol on the transdermal delivery of isosorbide 5-nitrate in rat skin." International journal of pharmaceutics 357.1-2 (2008): 199-205.
50. Zhang, Kai, et al. "Essential oil-mediated glycerosomes increase transdermal paeoniflorin delivery: Optimization, characterization, and evaluation in vitro and in vivo." International journal of nanomedicine (2017): 3521-3532..
51. Manca, Maria Letizia, et al. "Nanoincorporation of curcumin in polymer-glycerosomes and evaluation of their in vitro–in vivo suitability as pulmonary delivery systems." RSC advances 5.127 (2015): 105149-105159.
52. Manca, Maria Letizia, et al. "Improvement of quercetin protective effect against oxidative stress skin damages by incorporation in nanovesicles." Colloids and Surfaces B: Biointerfaces 123 (2014): 566-574.

HOW TO CITE: S. S. Gotpagar*, A. H. Hosmani, I. D. Gonjari, S. V. Potdar, B. S. Gaikwad, S. J. Momin, R. A. Tambe, A Review: Formulation and Evaluation of Glycerosomes of Anti-Fungal Drug, Int. J. of Pharm. Sci., 2025, Vol 3, Issue 1, 2418-2429. https://doi.org/10.5281/zenodo.14764924