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Research Article

A Review on Novel Drug Delivery Systems for Various Skin Diseases

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Abstract

Millions of people worldwide suffer from skin conditions such psoriasis, acne vulgaris, atopic dermatitis, and superficial fungal infections. Oral and topical formulations are the mainstays of conventional treatment techniques; however, both have serious drawbacks, such as low bioavailability, systemic side effects, insufficient skin penetration, and decreased patient compliance. Drug penetration into deeper skin layers is inhibited by the stratum corneum, a highly ordered and selective permeability barrier. Novel drug delivery systems (NDDS), especially vesicular carriers including liposomes, niosomes, ethosomes, and transferosomes, have been thoroughly studied in an effort to get around these restrictions. These systems limit systemic toxicity, offer controlled release, increase cutaneous and transdermal penetration, and improve drug stability.

The limitations of oral and traditional topical treatments, the structure and barrier function of the skin, and the function of vesicular systems in dermatological treatment are all critically discussed in this paper. The better penetrating effectiveness of transferosomes is highlighted in a comparative analysis of various carriers.

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KEYWORDS: Vesicular drug delivery, topical therapy, liposomes, niosomes, ethosomes, transferosomes, psoriasis, acne vulgaris.

1. INTRODUCTION

Comprising over 16% of the body weight, the skin is the biggest organ in the human body and acts as a multipurpose protective barrier between the internal and exterior environments[1]. It maintains water balance, controls thermoregulation, stops microbial invasion, and offers mechanical protection. Despite its accessibility, the skin's strong barrier qualities make it difficult to transfer drugs effectively into and through it.

Long-term medication is frequently necessary for dermatological disorders such psoriasis, acne vulgaris, atopic dermatitis, and fungal infections[2]. Despite their widespread use, topical and oral routes have significant drawbacks that impair treatment results. While traditional topical preparations frequently do not permeate past the superficial epidermis, oral medication exposes patients to systemic side effects and first-pass metabolism[3].

Novel drug delivery systems that improve drug penetration, retention within epidermal layers, and systemic exposure have been developed as a result of recent advancements in pharmaceutics. Vesicular systems have shown promise as carriers for dermatological treatment among these.

2. Structure of Skin and Barrier Function

There are three main layers to the skin:

- The epidermis
- The dermis
- The hypodermis

The layers that make up the epidermis are the base layer, stratum spinosum, stratum granulosum, and stratum corneum. The primary barrier to through the skin is the outermost stratum corneum.

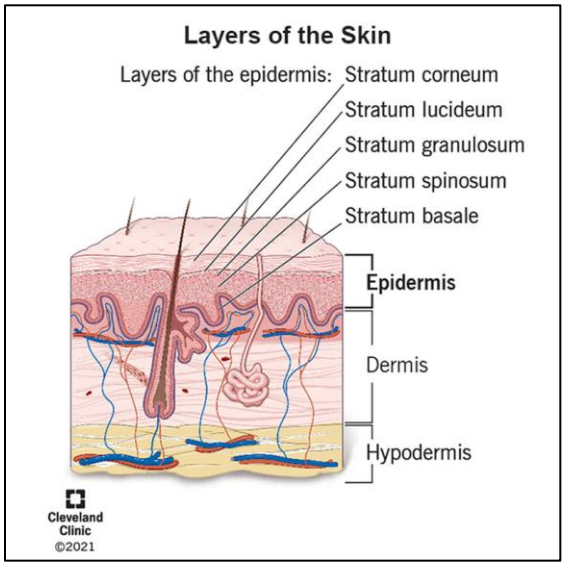

Figure 1. Structure of the skin and drug penetration pathways. **Source**: Cleveland Clinic 2021

The stratum corneum has a "brick and mortar" structure, with corneocytes (bricks) embedded in a lipid matrix (mortar) mostly made of free fatty acids, cholesterol, and ceramides. While the tightly packed keratin network inhibits lipophilic medications, this lipid structure limits the diffusion of hydrophilic substances. There are three ways that drugs can enter the skin:

1. The intercellular route
2. The transcellular route
3. The transappendageal route

However, molecules that weigh more than 500 Da typically show poor penetration; this is known as the "500 Dalton rule."

3. Oral Drug Delivery in Dermatology

For the treatment of moderate to severe dermatological diseases, oral medication delivery is still essential. Medications like systemic antifungals for dermatophytosis, isotretinoin for severe acne, and methotrexate for psoriasis are frequently recommended. [9]

Oral administration is advantageous for widespread disease involvement because it guarantees systemic dispersion through circulation. In situations where topical therapy is not enough, it is very helpful.

4. Limitations of Oral Therapy

Oral treatment has a number of disadvantages despite its therapeutic efficacy:

- The liver's extensive first-pass metabolism lowers the bioavailability of drugs[10]
- Irritation and ulceration of the digestive tract
- Hepatotoxicity, particularly with prolonged usage Nephrotoxicity
- Suppression of the immune system
- Interactions between drugs

Systemic exposure is frequently superfluous for localized skin conditions and raises the possibility of negative consequences." Furthermore, because of cumulative toxicity, long-term oral medication may decrease patient adherence.[11]

5. Rationale for Topical Therapy

Topical drug delivery offers several advantages over systemic administration:

- Localized activity at the pathological location
- A decrease in systemic adverse effects
- Steer clear of the liver's first-pass metabolism
- A lower dosage is needed.
- A higher level of patient compliance

Topical therapy offers a logical and focused approach because many dermatological problems are limited to surface tissues.[12]

6. Limitations of Conventional Topical Formulations

Creams, ointments, gels, and lotions are examples of traditional dose forms that frequently fall short of achieving sufficient drug concentration in deeper skin layers.

Among the main restrictions:

- The stratum corneum is little penetrated.
- Sweating or bathing causes drugs to be removed quickly.
- Short stay
- Absorption that varies
- The possibility of irritation[13]

The creation of sophisticated vesicular carriers has been prompted by these difficulties

7. Vesicular Novel Drug Delivery Systems (NDDS)

Vesicular systems are small carriers with an aqueous core surrounded by bilayers of lipids or surfactants. By interacting with skin lipids, they can enhance penetration and encapsulate both hydrophilic and lipophilic medications[14].

7.1 Liposomes

Liposomes are spherical vesicles with an aqueous core surrounded by phospholipid bilayers.[15]

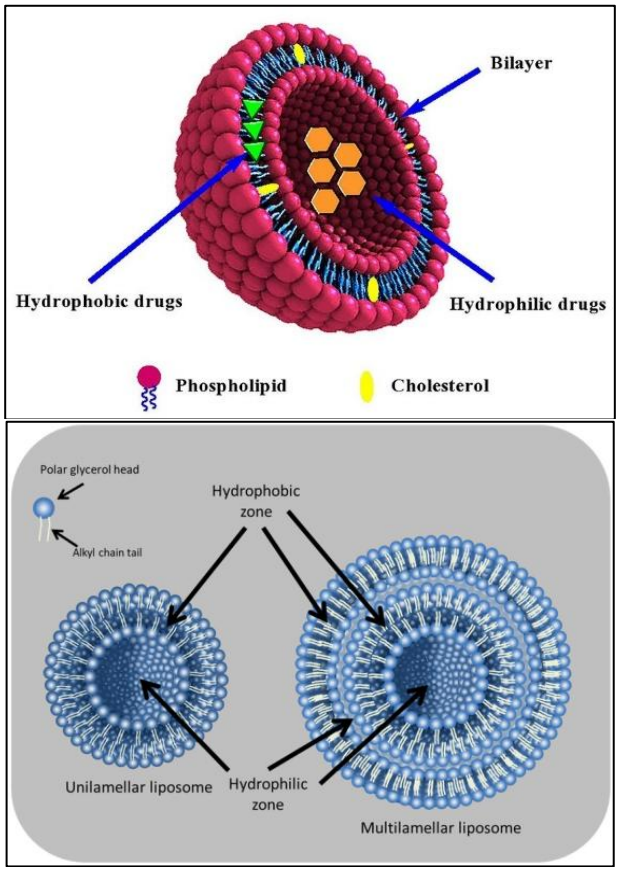

Figure 2: Structural representation of liposomes.

The mechanism Drug distribution is improved by liposomes via:

- Combination with lipids in the stratum corneum
- Improving skin moisture
- Improving the retention of drugs in the epidermal layers[16]

Advantages

- The ability to be biocompatible
- The capacity to transport lipophilic and hydrophilic medications
- A decrease in systemic toxicity

Limitation

- Insufficient deep penetration
- Stability of the body
- Phospholipid oxidation

7.2 Niosomes

Niosomes are vesicles made of cholesterol and non-ionic surfactants.[17]

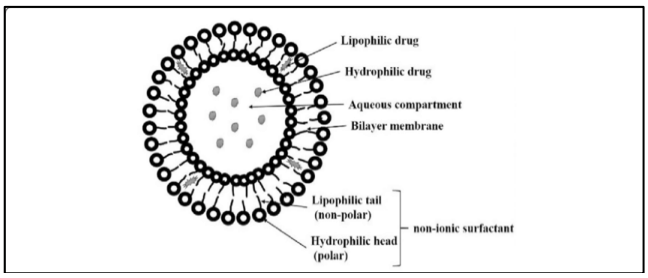

Figure 3: Structural representation of niosomes.

Advantages

More stable chemically than liposomes
Cost-effective production
Controlled release capability[18]

Limitations

Vesicle aggregation
Drug leakage during storage

7.3 Ethosomes

Ethosomes are phospholipid vesicles containing high ethanol concentration (20–45%) [19].

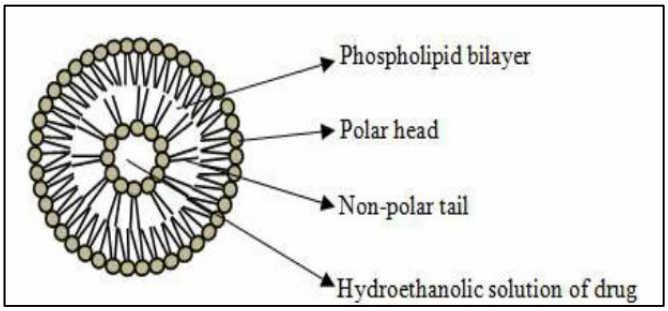

Figure 4: Ethosome penetration mechanism.

Ethanol disrupts lipid packing in the stratum corneum, increasing membrane fluidity and enhancing drug permeation[20].

Limitations
High ethanol content may cause skin irritation or dryness.

7.4 Transferosomes
Transferosomes are ultra-deformable vesicles composed of phospholipids and edge activators such as surfactants[21].

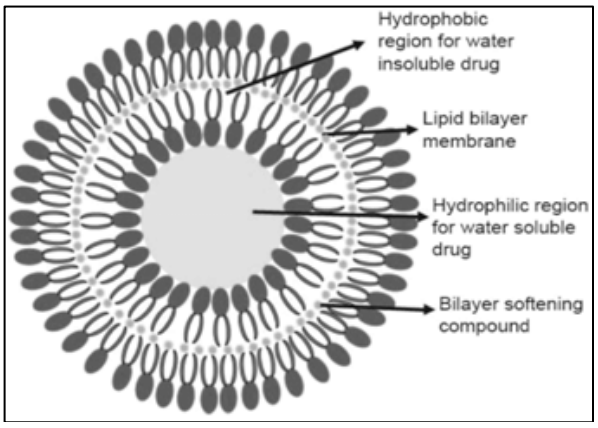

Figure 5: Transferosome structure and deformability.

Mechanism
Transferosomes penetrate through intact skin by squeezing through narrow intercellular channels driven by hydration gradients[22].

Advantages
- High deformability
- Superior penetration capability
- Enhanced dermal and transdermal delivery Improved drug retention

8. Why Transferosomes are better
Transferosomes exhibit greater elasticity compared to conventional liposomes and niosomes. Unlike ethosomes, they do not rely on high alcohol concentration to enhance permeation. Their ultra-flexible structure enables them to traverse pores much smaller than their own diameter[23].
Studies have demonstrated enhanced delivery of corticosteroids, NSAIDs, and antifungals using transferosomal formulations compared to conventional vesicles[24].

9. Comparative Evaluation of Vesicular Systems

Parameter	Liposomes	Niosomes	Ethosomes	Transferosomes
Composition	Phospholipids	Surfactant + Cholesterol	Phospholipid + Ethanol	Phospholipid + Edge Activator
Penetration	Moderate	Moderate	High	Very High
Stability	Moderate	High	Moderate	Moderate
Irritation	Low	Low	Moderate	Low
Deformability	Low	Low	Moderate	Very High

Transferosomes demonstrate the highest penetration efficiency among these systems.

10. CONCLUSION
The management of dermatological disorders remains challenging due to the barrier properties of the skin and limitations of conventional therapies. While oral therapy is effective in severe cases, it carries significant systemic risks. Conventional topical formulations often fail to achieve adequate dermal penetration.
Vesicular drug delivery systems such as liposomes, niosomes, ethosomes, and transferosomes offer promising alternatives. Among them, transferosomes exhibit superior deformability and penetration capability, making them highly suitable for advanced dermatological therapy. Future research focusing on clinical translation and large-scale production will further enhance their therapeutic potential.

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