Archives of Pharmaceutical Sciences and Research E-ISSN0975-2633|PRINTISSN0975-5284
Vol 15 Issue 2 017–030 June 2025 Review Article

TOPICAL LIPID FILM FORMING GELS: PROSPECTS FOR ENHANCED DERMAL DELIVERY

Praghna M.R*, S. Rajarajan, Beny baby, K. Ramesh

Department of Pharmaceutics, Karnataka College of Pharmacy, Bangalore.

ABSTRACT

Dermal drug delivery localizes therapeutic agents at the site of action while minimizing systemic effects, but the skin barrier limits drug penetration. This review explores lipid-based film-forming gels as an innovative approach to enhance drug absorption, particularly for melanoma treatment. Film-forming systems (FFS) create an in situ polymeric film upon application, allowing sustained drug release and improved adhesion. Lipid-based formulations integrate with the skin's lipid matrix, facilitating deeper penetration. Permeation enhancers, liposomes, and nanocarriers further augment drug absorption. Techniques like micro needles, electroporation, and sonophoresis help overcome skin barrier limitations. Recent advancements focus on optimizing film-forming gels for controlled drug delivery. Despite advantages, challenges like formulation stability and variability in skin permeability persist. Future research should refine formulations and integrate advanced technologies for improved therapeutic outcomes. Personalized dermal therapies may revolutionize melanoma treatment, offering more effective and convenient alternatives.

Keywords: Lipid-based film-forming gels, transdermal delivery, electroporation, liposomes.

INTRODUCTION

Malignant tumors known as melanomas appear from melanocytes which function as pigment-producing cells spread through skin and eyes and mucosal membranes. Melanoma stands as the most aggressive type of skin cancer since it readily spreads to other body areas when undetected during early stages. UV radiation along with genetic background and environmental elements work together to form melanoma. Advances in molecular research together with targeted therapies have revolutionized early diagnosis and prognostic assessment and treatment outcomes thus making melanoma a primary focus in current oncological research.

1.Dermal drug delivery

The targeting of drugs for skin lesions through dermal drug delivery approaches maintains minimal drug spread throughout the body system. The medical treatment of skin diseases, including psoriasis, dermatitis, eczema, skin cancer, and microbial infections, requires effective skin drug deposition, according to experts. The barrier capability of the stratum corneum reduces drug penetration to an extent that makes topical treatment suitable only for skin conditions. Successful treatment demands active substances to penetrate specific skin layers with their proper concentration for an adequate period of time [1].

Dermal drug delivery through conventional dosage formats, such as ointments and creams, exhibits unspecific penetration coupled with unreliable drug skin penetration.

2. Melanoma

Melanoma stands as the 19th most common cancer globally and represents one of the most severe medical conditions. Melanocytes produce melanin which results in skin colour through a development process beginning within cell groups known as melanocytes[2]. The uncontrolled proliferation of melanocytes cells produces cancer known as melanoma. Melanoma develops throughout different body parts including mucosal surfaces and uveal tract and leptomeninges[3].

2.1 Pathogenesis

The DNA of skin cells gets damaged by UV rays from both tanning beds and sunlight that results in genetic mutations[4]. Normal cells undergo transformation into abnormal cells because BRAF, NRAS, and PTEN genes develop mutations that cause uncontrolled cell division and melanocyte changes leading to nevus formation (mole)[5,6]. The mutant cells evolve through dysplastic alterations before advancing into radial growth phase (RGP) which then leads to vertical growth phase (VGP) melanoma. The immune system fails to detect melanoma cells because these cells lower their tumor antigen expression while enhancing their check point receptor proteins and drawing immune suppression mechanisms to the cancer site. The cancerous cells spread from their origin to penetrate

nearby tissues and migrate to distant locations in the body including lymph nodes as well as lungs and brain. Melanoma cells become resistant to treatments which causes tumors to advance and return[7,8].

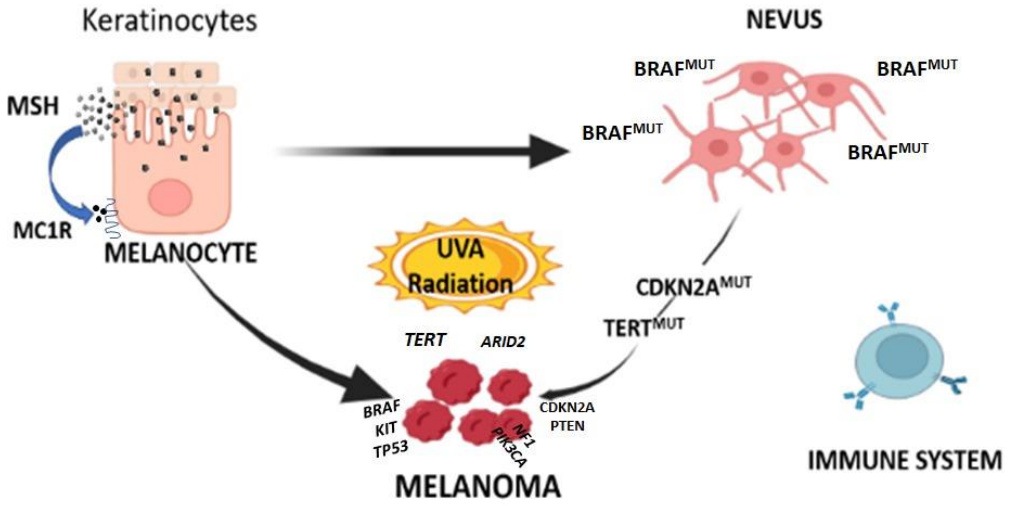

Fig. 1. Pathogenesis Of Melanoma.

2.2 Dermal Drug Delivery For Melanoma Treatment

Melanoma skin cancer needs specific treatment applied to the local area to reduce harmful side effects and enhance treatment success[9]. Dermal drug delivery refers to the direct application of therapeutic agents to the skin for the treatment of melanoma, either topically or through transdermal delivery mechanisms. The therapy employs skin properties to send drugs accurately to tumors without creating the typical side effects that standard chemotherapy creates. Research in dermal drug delivery for melanoma treatment continues to expand due to its access to the skin directly which matters because melanoma begins in this tissue[10,11].

2.3 Mechanisms of Dermal Drug Delivery

1.Topical Drug Delivery

Cellular drug delivery for melanoma treatment requires direct medicinal substance application over the skin surface. Medical practitioners use this treatment approach for flat melanoma cases and blend it with additional therapy methods for invasive tumors.

Topical treatment utilizes the immune-activating drug imiquimod through its ability to stimulate Toll-like receptor 7 against melanoma cells[12,13].

2. Transdermal Drug Delivery

Transdermal systems provide an alternative delivery method by allowing drugs to pass through the skin to reach the blood circulation while skipping the gastrointestinal tract. Continuous drug release combined with enhanced bioavailability through this method proves advantageous for long-term melanoma treatment requiring constant therapeutic doses.

Transdermal systems utilize micro-needles coupled with lipid nano-carriers to boost drug penetration of the skin's protective outer layer[14].

3. Nanoparticle-Based Dermal Delivery

Nanoparticles such as liposomes and micelles and solid lipid nanoparticles remain commonly utilized within dermal drug delivery systems. Medicinal nanoparticles function as carriers to shield anticancer drugs like paclitaxel and doxorubicin while navigating them safely to melanoma locations[15].

The delivery of chemotherapy agents using liposomes proves particularly effective through topical and transdermal routes because liposomes maintain biocompatibility while encapsulating drugs of both hydrophilic and hydrophobic categories[16].

2.4 Advantages of Dermal Drug Delivery for Melanoma Treatment

1. **Localized Treatment:** The localized approach of dermal delivery enables healthcare providers to treat melanoma cells in target areas including cases of superficial disease and advanced stages through combined methodologies[17].

2. **Reduced Systemic Toxicity:** The selective topical application of drugs through skin delivery reduces the overall drug toxicity that occurs throughout the body while helping patients avoid unwanted chemotherapy side effects.

3. **Controlled Release:** The release mechanism of dermal delivery systems enables controlled drug distribution which enhances both therapeutic impact and reduces frequency of medication applications[18].

4. **Ease of Administration:** The delivery method through skin demonstrates easy accessibility because it provides non-invasive care instead of traditional treatments like injection or intravenous therapies which boosts patient drug adherence[19].

2.5 Challenges and Considerations:

1) **Skin Penetration:** The skin's outermost layer, the stratum corneum, acts as a formidable barrier to drug penetration. The drug permeability requires methods including microneedles and chemical enhancers as well as ultrasonication to break through the stratum corneum barrier [20].
2) **Melanoma depth:** Deep or aggressive melanomas typically have reduced sensitivities to topical medications. The tumors might need treatments through the bloodstream or hybrid treatment methodologies[23].
3) **Stability of Formulations:** The stability of drug delivery formulations containing nanoparticles and liposomes which are intended for dermal use requires preservation of active ingredients throughout the storage period until they reach the tumor site[21,22].

2.6.Recent Developments in Dermal Drug Delivery for Melanoma:

Category	Description	Advantages
Topical immune response modifier	Imiquimod is an FDA-approved to TIRM for superficial melanoma.	Stimulates the immune system, leading to the destruction of melanoma cells in early- stage disease.
Microneedle- based drug delivery	Small needles that can penetrate the skin's outer barrier without causing significant pain.	Improve the delivery of anticancer drugs such as piclataxel and imiquimod.
Liposome- Encapsulated chemotherapy	Liposomes Encapsulating chemotherapeutic agents like paclitaxel.	Delivers chemotherapeutic agents directly to melanoma lesions through dermal administration. Improves drug stability and enhance localised tumor targeting.
Lipid nanocarriers	Solid lipid nanoparticles & nanostructured nanocarriers.	Enhances drug absorption and retention in the skin, potentially improving the therapeutic effects of topical treatments.

Table. 1. Recent Developments in Dermal Drug Delivery for Melanoma[24].

2.7 Techniques to enhance dermal drug delivery of topical formulations:

1. Permeation Enhancers: These agents break down tissue barriers in a temporary manner so lipid-based formulations penetrate the skin better.

a. Chemical permeation enhancers

Fatty acids: Lipid bilayers in stratum corneum experience damage from fatty acids such as oleic acid which creates conditions that enhance lipid formulation penetration.

Ethanol and Isopropyl Alcohol: These are responsible for solvation of lipids and reduction of skin barrier function which enables lipid-based formulations to penetrate better.

Surfactants: (Polysorbates, sodium lauryl sulphate) decrease the interface tension between formulations and epidermal skin to facilitate lipid drug penetration.

Dimethyl Sulfoxide: It works as a penetration enhancer because it breaks down skin lipid structures to create better skin permeability.

b. Lipid-Soluble Penetration enhancers:

Phospholipids: The addition of phospholipids leads to better skin permeability while improving both stability and lipid-based formulation absorption.

Cholestrol: The skin penetration abilities of lipid formulations improve when cholesterol gets added because it disrupts the skin's lipid bilayer structure[25].

2. Liposomes and Nanoparticles:

The better skin permeation of drugs results from lipid-based formulations that include liposomes and solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs).

Liposomes: The lipid bilayer vesicles known as liposomes function to encapsulate drugs from both hydrophilic and lipophilic groups thus extending their skin penetration potential and ensuring their stability. The combination of liposomes with skin lipid structures causes them to merge so drugs reach deeper skin layers.

Solid- Lipid nanoparticles: They represent a type of nanoparticle based on solid lipids which provides drug delivery systems that produce sustained drug release and better penetrate through the skin.

Nanostructured lipid carriers: The drug-loading capacity of NLC's exceeds SLN's because they contain both solid and liquid lipid components. NLCs enhance drug delivery to the skin and provide sustained drug release over time[26].

3. Microneedles: The tiny needles in microneedle delivery systems produce microchannels through skin tissue to enhance lipid-based drug delivery. The approach delivers medication underneath the stratum corneum to reach both skin layers: viable epidermis and dermis directly. A classification of microneedles includes multiple varieties.

- Solid Microneedles,
- Dissolvable Microneedles
- Coated Microneedles[27].

4. Sonophoresis (Ultrasound): The application of ultrasound waves in sonophoresis creates tiny skin disruptions that increase the ability of lipid-based formulations to penetrate the skin. During ultrasound therapy the skin's lipid barrier becomes permeable due to cavitation bubble formation which simplifies the passage of lipid formulations[28].

5. Electroporation: The application of short electric pulses to skin results in development of pores in stratum corneum's lipid bilayer through the electroporation process. Such pores facilitate the better delivery of lipid-based formulations through the skin. The application of this technique benefits large lipid molecules along with formulations which struggle to penetrate skin naturally[28].

6. Hydration Techniques (Occlusion): Application of dressings or layers serves as occlusion which promotes skin hydration thus it increases permeability. Moisturized skin creates optimal conditions for lipid-based formulations to penetrate deeper parts of the skin structure. The permeation can be enhanced through combining this delivery method with acceptable systems including liposomes SLNs and NLCs.

7. Thermal and Radiofrequency (RF) Treatment: Skin permeability increases either by exposure to thermal energy or radiofrequency (RF) waves. Heating the skin through appropriate treatments brings about two benefits: it makes pores more open and it raises blood flow levels

to help lipid-based formulations penetrate easily[29].

8. Use of Bioadhesive Systems: Combination of bioadhesive products like hydrogels and polymeric films improves skin retention capability by using them in conjunction with lipid-based formulations. The lengthened skin-formulation contact produced by these systems leads to better drug uptake[30].

CONCLUSION

Proper drug delivery systems (such as liposomes and SLNs and microneedles) together with appropriate permeation enhancers (chemical enhancers and sonophoresis and electroporation) are vital for maximizing lipid-based formulation access through the skin by topical application. Delivery efficiency for skin-targeted therapies improves through the combination of thermal treatment along with occlusion and nanoemulsion or vesicular system methods and techniques.

3. FILM FORMING GELS AS TOPICAL FORMULATION:-

3.1 Introduction:

Film forming system (FFS) is a novel approach that can be used as an alternative to conventional topical and transdermal formulations. It is defined as a non-solid dosage form that produces a film in situ, i.e., after application on the skin or any other body surface.

These systems contain the drug and film-forming excipients in a vehicle, which upon contact with the skin, leaves behind a film of excipients along with the drug upon solvent evaporation. The formed film can either be a solid polymeric material that acts as a matrix for sustained release of the drug to the skin or a residual liquid film which is rapidly absorbed in the stratum corneum[31,32] .

3.2 Mechanism of film formation and permeation:-

The procedure of forming skin films starts with applying liquid formulations containing drugs and solvents together with polymers. The film develops from evaporating the volatile solvents into a transparent layer that results from polymers whose network maintains drug retention. The drug concentration in these systems reaches supersaturation state which boosts pharmaceutical activity by surmounting natural solubility levels and enabling skin permeation. Through its function as a reservoir the film enables controlled drug release that users can either absorb throughout their system or achieve localized effects[33, 34].

The concept of supersaturation can be explained by the modified form of Fick's law of diffusion.

Fick's law of diffusion is given by :-

$$J = \frac{DKCv}{H} \quad \text{–(1)}$$

where:

J = rate of drug permeation per unit area of skin per unit time (flux)

D = diffusion coefficient of drug

Cv = concentration of drug

h = thickness of barrier to diffusion

From this equation, it is clear that the rate of drug permeation across the skin is proportional to the concentration of the drug. However this is true when all the drug is dissolved in the vehicle.

Modified Fick's Law of diffusion:

$$J = \frac{Ad}{\gamma H} \quad \text{- (2)}$$

Where,

α = thermodynamic activity of drug within formulation

γ = thermodynamic activity of drug within membrane

According to this equation, the flux of the drug is directly proportional to the thermodynamic activity of the system, which is related to saturation. However increasing the supersaturation increases thermodynamic instability[35,36].

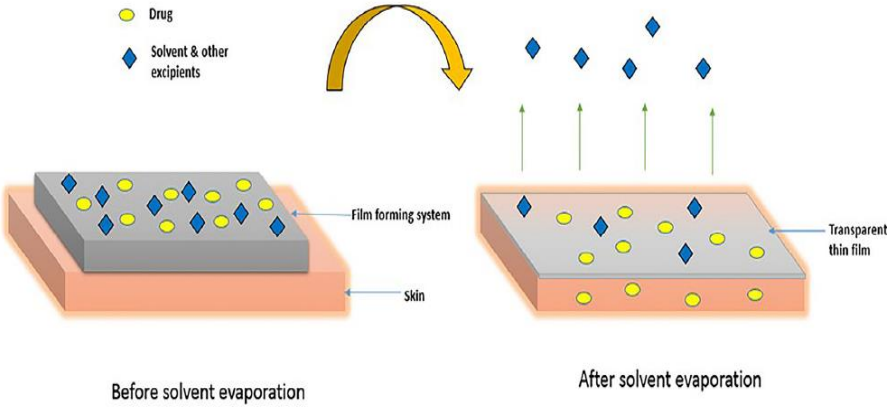

Fig 2: Mechanism of film- formation

3.3 Properties of Film Forming systems:

Transparency: The clear form of FFS creates transparent films that increase patient acceptance because their appearance promotes better compliance to therapy.

Non-greasy and Non-sticky: The films have a non-greasy consistency along with being non-sticky to allow comfortable wearing while not leaving any greasy residue on the skin.

Wipe-off Resistance: The skin-adhesive quality of dried films produces strong attachment which minimizes potential contacts between the skin and outside surfaces.

Long Retention: The duration which FFS stay on skin surfaces extends because of their ability to deliver medications in a sustained way with prolonged therapeutic benefits.

Dose Flexibility: The systems maintain high capabilities for dose adjustments that help doctors provide personalized medication amounts to specific patient needs.

Sustained Release: Through FFS technology the drug release extends over time in a controlled manner that improves treatment results.

Excellent Adhesion: The films demonstrate excellent adherence with the skin because proper contact and effective drug delivery depend on this property.

Reduced Skin Irritation: The designed formulation uses techniques that reduce skin irritation to work perfectly on sensitive skin applications[37, 38, 39].

3.4. Film- Forming Formulations:-

3.4.1 Spray/ Solutions:

Film-forming solutions/sprays consist of volatile solvents that dissolve necessary film-forming polymers together with plasticizers and active ingredients. The skin receives a flexible polymer film when the solvent evaporates from the solution after application. The solutions appear clear or translucent so healthcare providers can visually inspect their application process. These formulations dry rapidly and create a fine even coating on the skin surface[40, 41,42].

3.4.2 Gels:

The semi-solid structure of gels contains polymer chains spread through a liquid base which usually contains water[17]. When applied these solutions create a cooling reaction that improves the comfort of patients. Clear or translucent gels are available in non-greasy formulations that create an attractive appearance. The ability of gels to absorb and retain water lets them hydrate skin successfully[43, 44].

3.4.3 Emulsions:

The mixture of oil and water in emulsions stays stable thanks to emulsifying agents which provides their structure. Such pharmaceutical systems contain dual capabilities to enclose hydrophilic and lipophilic active pharmaceutical substances which expand delivery options. Emulsion formulations exist as two distinct types: when oil remains dispersed within water it becomes O/W while W/O occurs when water exists inside the oil particles. When used in formulating products emulsions yield a smooth texture and deliver enhanced moisturization according to users[45,46].

3.4.5. Patch- No- Patch sytsems:

The drug delivery systems permit sustained medication distribution through customized flexible therapies that eliminate the necessity of adhesive bandages. Doctors design these systems to function as self-adhesive skin attachments

without requiring regular adhesive materials through polymer film-forming properties[47].

3.5. Components of Film- Forming Gels:-

Drug: The active component within the drug works directly on the skin. The drug needs to be both small and oily to penetrate skin easily. The ingredient needs to blend properly throughout the gel base while also operating effectively without causing skin sensitivity. Drugs with reduced sizes deliver their effects more swiftly. The selection of an appropriate drug component enables the gel to become functional for both therapeutic purposes and skincare applications[48, 49] .

1. Film-Forming Polymers: When the liquid dries polymers develop a stretchy adhesive film which sticks to your skin surface. The polymers shape the gel's feel while also ensuring it remains stable on the skin surface. A suitable polymer choice creates gels that both work efficiently and have attractive visual characteristics. The dimension of polymers determines their ability to create high-quality films. Green alternatives gain increasing popularity because they allow us to make environmentally responsible choices[50].

Table 2: Key Polymers used in film-forming formulation[51, 52, 53]:

Polymers	Properties
Carbopol (Polyacrylate)	Water-soluble, pH sensitive
Chitosan (Poly-D-Glucosamine)	Water-soluble at pH < 7
Cross-linked Polymer Layer (XPL)	Adhesive, elastic
Dermacryl 79 (Carboxylates Acryl polymer)	Non-toxic, not irritating, anti-allergic
Ethyl cellulose	Water-insoluble, transparent, elastic, adhesive
Eudragit NE (Ethylacrylate Methyl methacrylate Copolymer)	Water-insoluble, transparent, elastic, adhesive.
Eudragit RL-100 (Polymethacrylate Polymer)	Water-insoluble, transparent, elastic, adhesive
Eudragit RS-100 (Polymethacrylate Polymer)	Water-insoluble, transparent, elastic, adhesive

2. Plasticizers: Using plasticizers in film production allows for creation of soft flexible materials which resist breaking. The gel enjoys comfortable movement due to these materials on your skin surface. You need to keep the usage correct because excessive plasticizer causes stickiness but insufficient application creates cracking. The careful quantity adjustment enables both gel effectiveness and easy wear ability[54,55].

3. Penetration Enhancers:

The drug penetration process becomes simpler because of the addition of penetration enhancers to the system. The drug requires this method to create minimal skin surface openings which enhance its delivery capacity[56]. Different alcohol and oil compounds function as standard enhancers. Users need to benefit from drug delivery without physical discomfort because these enhancement protocols create a comfortable experience[57,58].

4. Solvents:

When applied, solvents combine all the materials in the gel before rapidly disappearing. A skin-top layer forms after solvent evaporation, which maintains the drug ingredients inside it. Solvents mainly use water for its gentle properties, although alternative compounds possess similar effectiveness. When choosing good solvents for gels, they should create a lightweight, clean texture to meet user satisfaction[59, 60].

4. Liposomes As Dermal Drug Delivery:

4.1 Introduction:

Liposomes are naturally formed phospholipid vesicle structures, which incorporate a single or multiple bilayer membranes around a buoyant water-filled interior space[61]. Various industries, such as pharmaceuticals and cosmeceuticals, as well as neutraceuticals, use liposomes as flexible delivery systems for their bioactive compounds[62]. The spherical phospholipid

structures, consisting of natural phospholipids, can capture substances that are either hydrophilic or hydrophobic in nature[63,64]. The drug delivery field displays interest in liposomes because of their ability to deliver substances across biological membranes and their biocompatible nature[65].

4.2 Structural Composition:

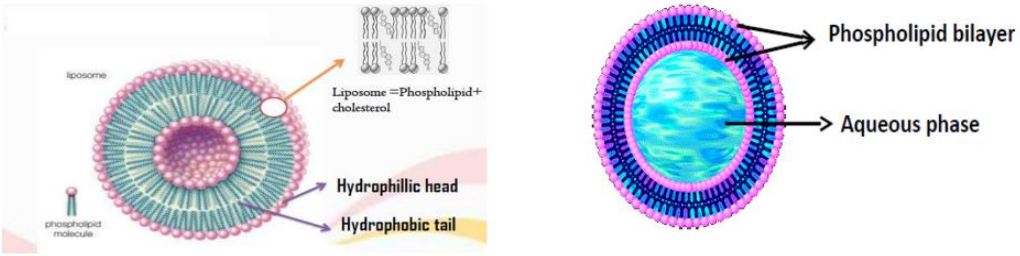

Fig.3. Structure of liposomes.

Liposomal composition depends mainly on the structure of their phospholipid bilayer framework. Key components include:

Phospholipids: The fundamental components that build the bilayer consist of phospholipids. Medical science uses three types of phospholipids for structures namely phosphatidylcholine, phosphatidylethanolamine, and sphingomyelin. Two facing sides of the liposomes serve as hydrophilic "head" groups pointing outward and hydrophobic "tails" facing inward toward the core to form a flexible protective barrier[66, 67].

Cholestrol: Membrane stability and permeability reduction occurs when cholesterol is added into the lipid bilayer which helps maintain fluidity and membrane integrity so liposomes can withstand changes in environmental conditions.

Bioactive compounds: The aqueous core contains bioactive compounds which also include drugs and vitamins and carbohydrates and peptides alongside them. Choosing appropriate encapsulated substances determines both liposomes' operational effectiveness and performance results.

Surface modifiers: The surface of liposomes receives surface modifiers such as polymers (including PEG) and charged molecules for improving biocompatibility while extending circulation duration and enabling targeted delivery functions[68,69,70].

4.3 Methods of Preparation of Liposomes:

1. Thin Film Hydration Method: This method requires dissolving lipids in an organic solvent until the solution evaporates through reduced pressure to create a thin film that can be hydrated with aqueous buffer solution. The buffer solution used for hydration contains hydrophilic drugs and moves above the transition temperature (Tm) of the lipids. The hydration process rate determines drug encapsulation efficiency because slower hydration results in improved efficiency[71, 72].

2. Reverse phase evaporation method: This method involves development of a water-in-oil emulsion using lipids dissolved in organic solvents which are blended with an aqueous phase. Liposomes develop as the organic solvent evaporates from the solution. Liposome formation through this method proves to be an alternative to thin-film hydration by offering superior control over liposome size[73].

3. Detergent Removal Method: Lipids and a high critical micelle concentration (CMC) surfactant are dissolved in an organic solvent. After forming mixed micelles by hydrating the lipid film with an aqueous solution containing drug molecules, the surfactant is removed through dialysis or other techniques. A drawback is that hydrophilic drugs may be lost during surfactant removal[74] .

4. Dehydration-Rehydration Method: This organic solvent-free method involves dispersing

lipids in an aqueous solution containing drug molecules, followed by sonication. The process includes a dehydration step to create a multilayered film, which is then hydrated to form large vesicles. This method is simple but results in high heterogeneity in liposome size.

5. Heating method: This method includes directly hydrating lipids with water followed by at least one hour of heating above the phospholipid Tm which extends up to 100°C in cholesterol-containing solutions. To protect the formulation from coagulation the addition of 3-5% hydrating agents like glycerine or propylene glycol is necessary[75].

6. pH Jumping technique: This technique descends upon phosphatidic acid and phosphatidylcholine solutions to rapidly raise pH values and reduce the result into small unilamellar vesicles from multilamellar vesicles (MLVs). The relative amount of phosphatidic acid and phosphatidylcholine controls the ratio between produced SUVs and LUVs[76].

7. Supercritical Fluidic Method: This method utilizes supercritical carbon dioxide (CO_2) as a solvent alternative to organic solvents for dissolving lipids within its processes. The liposome formation process occurs when fast pressure reduction interacts between the supercritical lipid solution and the continuous water stream flow. The method delivers 5-fold better encapsulation efficiencies during liposome formation, but its productivity is restricted by both high expenses and low yield levels[77, 78].

8. Microfluidic Channel Method: It involves dissolving lipids in ethanol or isopropanol before they are injected into micro-channels filled with an aqueous medium. The continuous mixing process between organic and aqueous solutions creates liposomes through surfactants that prevent solution coagulation. Reproducible liposome characteristics are emerged from this production technique[79,80]

9. Solvent injection method: This technique uses a rapid mixture of lipids together with hydrophobic active agents through an organic solvent into an aqueous solution. During this method an aqueous solution requires a 10-to-20-fold larger excess quantity while vacuum evaporation can remove the organic solvent. The final product usually demonstrates elevated PDI values when produced by this method[81, 82] .

10. Freeze-Thaw Cycles technique: This technique assists in producing liposomes with improved encapsulation efficiency and enhanced structural order through preparation for liposomes. The characteristics of liposomes improve with the aid of freeze-thaw cycles[83].

5.Preparataion Of Lipid Film Forming Gels:

5.1. Preparation of Liposomes:

- **Liposome formulation:** Liposomes are prepared by methods such as the thin-film hydration technique, reverse phase evaporation method or sonication. The formulated liposomes need to match a suitable size range (100-300 nm) when used for topical applications.
- **Characterization**: The encapsulation efficiency and size, along with zeta potential values of liposomes are evaluated through dynamic light scattering (DLS) or electron microscopy[84].

5.2 Preparation of Film-Forming Gel:

Polymer dissolution: Dissolve the film-forming polymer in an appropriate solvent (usually water or a water-alcohol mixture) under stirring.

Viscosity control: The dry film characteristics determine the viscoelasticity, which can be adjusted either with glycerine or propylene glycol or additional plasticizing agents. A drying gel must become solid through forming a film that maintains enough flexibility.

pH adjustment: Some polymers, especially carbopol, need pH adjustment by using NaOH along with other bases to develop their gelling properties.

5.3. Incorporation of Liposomes into Gel:

Slow incorporation: The gel matrix acquisition should receive the prepared liposome suspension through slow and consistent stirring methods. High shear forces should be avoided when incorporating liposomes because they damage the liposomal structure.

Uniform dispersion: Ensure uniform distribution of the liposomes throughout the gel. The mixture needs several minutes of gentle mixing to reach a homogeneous solution.

Cross-linking (optional): Dispersing liposomes into a gel requires the method of slow agent addition when utilizing cross-linkable polymers where a crosslinking agent such as calcium chloride should be added drop-by-drop while mixing to achieve uniform dispersion.

5. Evaluation and Characterization of Lipid Film- Forming Gels:-

6.1. Physical Properties:

Apperance: Visual evaluation of the film-forming gels will focus on their colour appearance and opacity[85].

Viscosity: The Brookfield Viscometer (DV-E model) containing spindle S94 (T-shaped spindle) is ideal for measuring film-forming gel viscosity. An approximate 1g portion of emulgel receives placement on the viscometer plate where it settles for 5-10 minutes to achieve uniform distribution and eliminate air bubbles. Once the settling period ends the spindle needs delicate placement onto the gel-covered plate where the rotation speed should reach 5 rpm. The experimental procedure will be performed under constant temperature conditions at 25°C[86].

Clarity: Visual clarity evaluation is based on observing the colour while determining transparency along with uniformity and consistency[87].

Spreadabiity:

A test for measuring gel spreadability includes placing 0.5 grams of gel material on two smooth glass plates that measured 20 cm by 20 cm. An initial measurement of gel diameter occurred before adding the 200g glass plate for one minute. The authors measured the diameter of the spread gel after they removed the top plate[88].

$$\text{Spreadability} = M \times L / T$$

6.2 Mechanical properties:

- **Phase transition/ Film formation time:**

The measurement of phase transition time begins with depositing 1 gram of film-forming gel on a petri dish while spreading it evenly. A warm 37 °C plate containing a petridish records the duration needed for the gel to dry into a complete film coherently. The trial procedure is performed three times for precision purposes and average transition time results are calculated[89].

Film thickness: The films should be cut in to circular shaped film segments with a 2.0 cm diameter by using scissors . A digital Vernier calliper determines the thickness of each tested film. Five different measurement areas on each film should be used to establish an accurate reading. Readings will be taken for calculating the final thickness average across all measurements[90].

Adhesiveness: The peel adhesion test determines the force limit required to separate skin films after they dry or set on skin surfaces. Testing the adhesive strength against the surface determines the strength of adhesion. A force gauge serves to measure the required force in this examination[91,92].

6.3 Chemical properties:

pH: A digital pH meter checked with standards will be used to measure the gel's pH values[93,94].

Stability studies: Stability studies need to take place under different environmental conditions meant to reflect all the storage and transportation and usage settings that the product might encounter.

Typical conditions include:

Room Temperature (25°C ± 2°C, 60% ± 5% RH): This is considered standard storage.

Accelerated Conditions: Elevated temperature (e.g., 40°C ± 2°C, 75% RH) to simulate long-term storage conditions over a shorter period

Refrigerated Conditions (4°C ± 2°C): To test if the gel remains stable when stored under cold conditions.

Freezing Conditions (-20°C or -40°C): Evaluate freeze-thaw stability.

7. CONCLUSION

The topical film-forming gel concept shows strong promise for enhancing drug delivery into the skin. The unique adaptation works best for patients with melanoma diseases together with various skin-related disorders. Advanced drug delivery systems obtain superior performance than classic ointments and creams because they

enhance drug storage capacity and manage release kinetics and treatment adherence. The stratum corneum barrier can be overcome by different strategies that utilize permeation enhancers with nanoparticles, liposomes, microneedles and nanoparticles.

Succeeding pre-clinical studies indicate the effectiveness of these methods but stability optimization and large-scale manufacturing present major difficulties in their implementation.

The potential applications for transdermal and dermatological therapies in film-forming gels show promise due to the new developments in nanocarrier systems along with improved penetration methods.

8. CHALLENGES

Despite the advances in lipid-based dermal- drug delivery there are multiple challenges that are to be addressed to ensure clinical efficacy, that includes skin barrier limitations formulation stability, drug loading and release efficacy, inter-patient variability & manufacturing & scalability.

9. REFERENCE

1. Badilli U, Gumustas M, Uslu B, Ozkan SA. Lipid-based nanoparticles for dermal drug delivery. In: Grumezescu AM, editor. Organic Materials as Smart Nanocarriers for Drug Delivery. William Andrew Publishing; 2018. p. 369-413.
2. Pachauri A, Chitme H, Visht S, Chidrawar V, Mohammed N, Abdel-Wahab BA, Khateeb MM, Habeeb MS, Orabi MAA, Bakir MB. Permeability-enhanced liposomal emulgel formulation of 5-fluorouracil for the treatment of skin cancer. *Gels.* 2023;9(3):209. doi:10.3390/gels9030209.
3. Lomas, A.; Leonardi-Bee, J.; Bath-Hextall, F. A systematic review of worldwide incidence of nonmelanoma skin cancer. Br. J. Dermatol. 2012, 166, 1069–1080
4. Kim HJ, Kim YH. Molecular Frontiers in Melanoma: Pathogenesis, Diagnosis, and Therapeutic Advances. Int J Mol Sci. 2024;25(5):2984. doi:10.3390/ijms25052984.
5. Liu Y, Sheikh MS. Melanoma: Molecular pathogenesis and therapeutic management. Mol Cell Pharmacol. 2014;6(3):228.
6. Timis T, Bergthorsson JT, Greiff V, Cenariu M, Cenariu D. Pathology and Molecular Biology of Melanoma. Curr Issues Mol Biol. 2023;45:5575–97. doi:10.3390/cimb45070352
7. Adib E, Nassar AH, Akl EW, Alaiwi SA, Nuzzo PV, Mouhieddine TH, Sonpavde G, Haddad RI, Mouw KW, Giannakis M, et al. CDKN2A alterations and response to immunotherapy in solid tumors. Clin Cancer Res. 2021;27(15):4025-35
8. Obrador E, Liu-Smith F, Dellinger RW, Salvador R, Meyskens FL, Estrela JM. Oxidative stress and antioxidants in the pathophysiology of malignant melanoma. Biol Chem. 2019;400(5):589-612. doi:10.1515/hsz-2018-0327
9. O'Donnell, J. S., et al. (2017). "Topical imiquimod therapy for melanoma." *Journal of Immunotherapy*, 40(6), 271-278
10. Park, J. H., et al. (2015). "Transdermal delivery of anticancer drugs for melanoma." *International Journal of Nanomedicine*, 10, 3093-3104.
11. Hong, L., et al. (2018). "Liposome-based drug delivery for melanoma therapy." *Journal of Drug Targeting*, 26(5), 391-405
12. Manikkath J, Sumathy TK, Manikkath A, Mutalik S. Delving deeper into dermal and transdermal drug delivery: Factors and mechanisms associated with nanocarrier-mediated strategies. Curr Pharm Des 2018;24(27):3210–22.
13. Suvarna V, Mallya R, Deshmukh K, Sawant B, Khan TA, Omri A. Novel vesicular bilosomal delivery systems for dermal/transdermal applications. Curr Drug Deliv [Internet]. 2024;21(7):961–77.
14. Lucia M. Lipid-based nanoparticles as carriers for dermal delivery of antioxidants. Curr Drug Metab. 2017;18(5):469–80.
15. Fitriani EW, Avanti C, Rosana Y, Surini S. Nanostructured lipid carriers: A prospective dermal drug delivery system for natural active ingredients. Farmatsiia (Sofia) [Internet]. 2024;71:1–15.
16. Labie H, Blanzat M. Hydrogels for dermal and transdermal drug delivery. Biomater Sci]. 2023;11(12):4073–93.
17. Dudhat K. Emerging trends in transdermal drug delivery: Nanoparticle formulations and technologies for enhanced skin penetration and drug efficiency. Pharm Nanotechnol [Internet]. 2024;
18. Williams AC, Barry BW. Penetration enhancers. Adv Drug Deliv Rev [Internet]. 2012;64:128–37.
19. Vijaykumar, Saikiran, Vr B, Ubaidulla. Formulation challenges in dermal drug delivery systems: A comprehensive review of physicochemical properties and advanced delivery strategies. Int J Drug Deliv Technol. 2024;14(04):1124–9.
20. Nayak D, Rathnanand M, Tippavajhala VK. Navigating skin delivery horizon: An innovative approach in pioneering surface modification of ultradeformable vesicles. AAPS PharmSciTech [Internet]. 2024;25(5):126.
21. Jindal S, Awasthi R, Goyal K, Kulkarni GT. Hydrogels for localized drug delivery: A special emphasis on dermatologic applications. Dermatol Ther [Internet]. 2022;35(11):e15830. http://dx.doi.org/10.1111/dth.15830
22. Kurmi BD, Tekchandani P, Paliwal R, Paliwal SR. Transdermal drug delivery: Opportunities and challenges for controlled delivery of therapeutic agents using nanocarriers. Curr Drug Metab. 2017;18(5):481–95.
23. Nayak BS, Mohanty B, Mishra B, Roy H, Nandi S. Transethosomes: Cutting edge approach for drug permeation enhancement in transdermal drug delivery system. Chem Biol Drug Des [Internet]. 2023;102(3):653–67.
24. Saudagar RB, Gangurde PA. Formulation, development and evaluation of film-forming gel for prolonged dermal

delivery of miconazole nitrate. Int J ChemTech Res. 2017;10(15):282-299.
25. Kahraman E, Güngör S, Özsoy Y. Potential enhancement and targeting strategies of polymeric and lipid-based nanocarriers in dermal drug delivery. Ther Deliv [Internet]. 2017;8(11):967–85.
26. Ramadon D, McCrudden MTC, Courtenay AJ, Donnelly RF. Enhancement strategies for transdermal drug delivery systems: current trends and applications. Drug Deliv Transl Res 2022;12(4):758–91.
27. Nguyen HX, Banga AK. Electrically and ultrasonically enhanced transdermal delivery of methotrexate. Pharmaceutics 2018;10(3):117.
28. Alnaim AS. Nanocrystals in dermal drug delivery: A breakthrough for enhanced skin penetration and targeted skin disorder treatments. Pharmaceutics 2024;16(12).
29. Korkmaz E, Friedrich EE, Ramadan MH, Erdos G, Mathers AR, Scull BP, et al. Potential enhancement and targeting strategies of polymeric and lipid-based nanocarriers in dermal drug delivery. Eur J Pharm Biopharm. 2021;163:174-205
30. Pünnel LC, Lunter DJ. Film-forming systems for dermal drug delivery. Pharmaceutics 2021;13(7):932: http://dx.doi.org/10.3390/pharmaceutics13070932
31. Frederiksen K, Guy RH, Petersson K. The potential of polymeric film-forming systems as sustained delivery platforms for topical drugs. Expert Opin Drug Deliv. 2016;13(3):349- 60.
32. Mcauley WJ, Caserta F, Hoboken NJ. Film-forming and heated systems. In: Donnelly RF, Singh TRR, editors. Novel delivery systems for transdermal and intradermal drug delivery. United States: JohnWiley & Sons; 2015. p. 97–107.
33. Prausnitz, M. R., & Langer, R. (2008). "Transdermal drug delivery." *Nature Biotechnology*, 26(11), 1261-1268.
34. Zurdo Schroeder I. Film forming polymeric solutions as drug delivery systems for the skin, Saarland University, Saarbrücken, Germany, 2007.
35. Khasraghi AH, Thomas LM. Preparation and evaluation of lornoxicam film-forming gel. Drug Invent Today.2019;11(8):1906-1913.
36. Oliveira FF, Menezes LR, Tavares MIB. Film-Forming Systems in Topically Administered Pharmaceutical Formulations. Materials Sciences and Applications. 2020; 11:576-590.
37. Touitou E, Natsheh H, Zailer J. Film-forming systems for delivery of active molecules into and across the skin. *Pharmaceutics.* 2023;15(2):397. doi:10.3390/pharmaceutics15020397.
38. Kokila E, Deattu N, Sunitha PG, Mahalakshmi A, Dhanesh Kumar MR, Chandini A review on novel film-forming systems for topical and transdermal drug delivery. Ijppr. VS. .Human. 2024;30(2):91-111.
39. Abd Kakhar Umar, Maria Butarbutar, Sriwidodo & Nasrul Wathoni (2020) Film-Forming Sprays for Topical Drug Delivery, Drug Design, Development and Therapy, , 2909-2925, DOI: 10.2147/DDDT.S256666
40. Lu W, Luo H,Wu Y. Preparation and characterization of a metered dose transdermal spray for testosterone. Acta Pharm Sin B 2013;3(6):392–399.
41. Umar AK, Sriwidodo S, Maksum IP, Wathoni N. Film-forming spray of water-soluble chitosan containing liposome-coated human epidermal growth factor for wound healing. Molecules. 2021;26(17):5326. doi:10.3390/molecules26175326.
42. Thewanjutiwong S, Phokasem P, Disayathanoowat T, Juntrapirom S, Kanjanakawinkul W, Chaiyana W. Development of film-forming gel formulations containing royal jelly and honey aromatic water for cosmetic applications. Gels. 2023;9(10):816. doi: 10.3390/gels9100816.
43. Vishe A, Wagh H, Waghchaure S, Yadav A, Suse A. Formulation and characterization of film-forming polymeric gel of piroxicam. *Int J All Res Educ Sci Methods.* 2024;12(7):347-356.
44. Saudagar RB, Gangurde PA. Formulation, development and evaluation of film-forming gel for prolonged dermal delivery of miconazole nitrate. Int J ChemTech Res. 2017;10(15):282-299.
45. Abdul Mannan, Masrath Fatima. Film-Forming Emulgel: A Novel Approach for Topical Drug Delivery. Ijppr.Human. 2024 Apr;30(4):548-562.
46. Department of Pharmaceutics, Adarsh Vijendra Institute of Pharmaceutical Sciences, Shobhit University, Gangoh, Saharanpur- 247 341, Uttar Pradesh, India, Bajaj H, Yadav M, B. Chauhan S, Sharma A, C. Pant N, et al. Aceclofenac loaded film forming gels: In vivo study. Indian Drugs [Internet]. 2023;60(06):90–3.
47. Kathe K, Kathpalia H. Film forming systems for topical and transdermal drug delivery. Asian J Pharm Sci. 2017;12(6):487-497. doi:10.1016/j.ajps.2017.07.004
48. Gangurde PK, Patil PS, Pawar SA, Chaudhari PD. Film-forming gels. Int J Pharm Sci. 2024;2(5):1511–7.
49. Bouthillette, M.; Beccati, D.; Akthakul, A.; Ramadurai, N.; Nashat, A.; Langer, R.; Anderson, R.R.; Sakamoto, F.H. A crosslinked polymer skin barrier film for moderate to severe atopic dermatitis: A pilot study in adults. J. Am. Acad. Dermatol. 2020, 82,895–901.
50. de Oliveira FFD, de Menezes LR, Tavares MIB. Film-forming systems in topically administered pharmaceutical formulations. Mater Sci Appl [Internet]. 2020;11(08):576–90. Available from: http://dx.doi.org/10.4236/msa.2020.118038
51. Rosseto HC, de Toledo L de AS, Said dos Santos R, de Francisco LMB, Vecchi CF, Esposito E, et al. Design of propolis-loaded film forming systems for topical administration: The effect of acrylic acid derivative polymers. J Mol Liq [Internet]. 2021;322(114514):114514.
52. Karki, S.; Kim, H.; Na, S.-J.; Shin, D.; Jo, K.; Lee, J. Thin films as an emerging platform for drug delivery. Asian J. Pharm. Sci. 2016,11, 559–574
53. Pudžiuvelytė L, Drulytė E, Bernatonienė J. Nitrocellulose based film-forming gels with cinnamon essential oil for covering surface wounds. Polymers (Basel).
54. Chen Y, Wang J, Xu L, Nie Y, Ye Y, Qian J, et al. Effects of different plasticizers on the structure, physical properties and film forming performance of curdlan edible films. Foods [Internet]. 2024;13(23). http://dx.doi.org/10.3390/foods13233930.
55. Hmingthansanga V, Singh N, Banerjee S, Manickam S, Velayutham R, Natesan S. Improved topical drug delivery: Role of permeation enhancers and advanced approaches.Pharmaceutics.2022;14(12):2818. http://dx.doi.org/10.3390/pharmaceutics14122818
56. Musakhanian J, Osborne DW, Rodier J-D. Skin penetration and permeation properties of Transcutol® in complex formulations. AAPS PharmSciTech [Internet]. 2024;25(7):201. Available from: http://dx.doi.org/10.1208/s12249-024-02886-8

57. Nawaz A, Safdar M, Arshad MS, Rasool MF, Khan GM, Akhlaq M. Formulation development and in vitro permeability of curcumin films using different penetration enhancers. Drug Deliv Lett [Internet]. 2018;8(1). http://dx.doi.org/10.2174/2210303107666171121161647
58. Monica L-L, Jordi G, Francisco F-C. In situ bioadhesive film-forming system for topical delivery of mometasone furoate: Characterization and biopharmaceutical properties. J Drug Deliv Sci Technol [Internet]. 2020;59(101852):101852.
59. Lopes PS, Costa P, Campos PM, Jäger E. Film-forming systems for dermal drug delivery: A review. *Int J Pharm*. 2021;599:120420.
60. Gondane BR, Biyani DM, Umekar MJ. A review of liposomes as a good carrier for transdermal drug delivery system. *World J Pharm Res.* 2022;11(12):2383-2399. doi:10.20959/wjpr202212-25525.
61. Liu G, Hou S, Tong P, Li J. Liposomes: Preparation, Characteristics, and Application Strategies in Analytical Chemistry. *Crit Rev Anal Chem.* 2020;50(6):520-36. doi:10.1080/10408347.2020.1805293.
62. T. Sun, Y.S. Zhang, B. Pang, D.C. Hyun, M. Yang, Y. Xia, Engineered nanoparticles for drug delivery in cancer therapy, Angew. Chem. 53 (2014) 12320–12364.
63. S. Jha, P.K. Sharma, R. Malviya, Liposomal drug delivery system for cancer therapy: advancement and patents, Recent Pat. Drug Deliv. Formulation 10 (2016) 177–183.
64. Delma KL, Lechanteur A, Evrard B, Semdé R, Piel G. Sterilization methods of liposomes: Drawbacks of conventional methods and perspectives. Int J Pharm [Internet]. 2021;597(120271):120271. Available from: http://dx.doi.org/10.1016/j.ijpharm.2021.120271
65. Van der Veen JN, Kennelly JP, Wan S, Vance JE, Vance DE, Jacobs RL. The critical role of phosphatidylcholine and phosphatidylethanolamine metabolism in health and disease. Biochim Biophys Acta [Internet]. 2017;1859(9 Pt B):1558–72. Available from: http://dx.doi.org/10.1016/j.bbamem.2017.04.006
66. Li J, Wang X, Zhang T, Wang C, Huang Z, Luo X, et al. A review on phospholipids and their main applications in drug delivery systems. Asian J Pharm Sci [Internet]. 2015;10(2):81–98. Available from: http://dx.doi.org/10.1016/j.ajps.2014.09.004
67. Nsairat H, Khater D, Sayed U, Odeh F, Al Bawab A, Alshaer W. Liposomes: Structure, composition, types, and clinical applications. Heliyon. 2022 May 1;8(5).
68. Pavelić Z, Skalko-Basnet N, Jalsenjak I. Characterisation and in vitro evaluation of bioadhesive liposome gels for local therapy of vaginitis. Int J Pharm [Internet]. 2005;301(1–2):140–8. Available from: http://dx.doi.org/10.1016/j.ijpharm.2005.05.022
69. Monteiro N, Martins A, Reis RL, Neves NM. Liposomes in tissue engineering and regenerative medicine. J R Soc Interface [Internet]. 2014;11(101):20140459. Available from: http://dx.doi.org/10.1098/rsif.2014.0459
70. Tagrida M, Prodpran T, Zhang B, Aluko RE, Benjakul S. Liposomes loaded with betel leaf (Piper betle L.) ethanolic extract prepared by thin film hydration and ethanol injection methods: Characteristics and antioxidant activities. J Food Biochem [Internet]. 2021;45(12):e14012. Available from: http://dx.doi.org/10.1111/jfbc.14012
71. Al-Amin MD, Bellato F, Mastrotto F, Garofalo M, Malfanti A, Salmaso S, et al. Dexamethasone loaded liposomes by thin-film hydration and microfluidic procedures: Formulation challenges. Int J Mol Sci [Internet]. 2020;21(5):1611. Available from: http://dx.doi.org/10.3390/ijms21051611
72. Liu G, Hou S, Tong P, Li J. Liposomes: Preparation, characteristics, and application strategies in analytical chemistry. Crit Rev Anal Chem [Internet]. 2022;52(2):392–412. Available from: http://dx.doi.org/10.1080/10408347.2020.1805293
73. Lombardo D, Kiselev MA. Methods of liposomes preparation: Formation and control factors of versatile nanocarriers for biomedical and nanomedicine application. Pharmaceutics [Internet]. 2022;14(3):543. Available from: http://dx.doi.org/10.3390/pharmaceutics14030543
74. Has C, Sunthar P. A comprehensive review on recent preparation techniques of liposomes. J Liposome Res [Internet]. 2020;30(4):336–65. Available from: http://dx.doi.org/10.1080/08982104.2019.1668010
75. Shah S, Dhawan V, Holm R, Nagarsenker MS, Perrie Y. Liposomes: Advancements and innovation in the manufacturing process. Adv Drug Deliv Rev [Internet]. 2020;154–155:102–22. Available from: http://dx.doi.org/10.1016/j.addr.2020.07.002
76. Bigazzi W, Penoy N, Evrard B, Piel G. Supercritical fluid methods: An alternative to conventional methods to prepare liposomes. Chem Eng J [Internet]. 2020;383(123106):123106. Available from: http://dx.doi.org/10.1016/j.cej.2019.123106
77. Trucillo P, Martino M, Reverchon E. Supercritical assisted production of lutein-loaded liposomes and modelling of drug release. Processes (Basel) [Internet]. 2021;9(7):1162.
78. Rebollo R, Oyoun F, Corvis Y, El-Hammadi MM, Saubamea B, Andrieux K, et al. Microfluidic manufacturing of liposomes: Development and optimization by design of experiment and machine learning. ACS Appl Mater Interfaces [Internet]. 2022;14(35):39736–45. Available from: http://dx.doi.org/10.1021/acsami.2c06627
79. Buttitta G, Bonacorsi S, Barbarito C, Moliterno M, Pompei S, Saito G, et al. Scalable microfluidic method for tunable liposomal production by a design of experiment approach. Int J Pharm [Internet]. 2024;662(124460):124460. Available from: http://dx.doi.org/10.1016/j.ijpharm.2024.124460
80. Zhang G, Sun J. Lipid in chips: A brief review of liposomes formation by microfluidics. Int J Nanomedicine [Internet]. 2021;16:7391–416. Available from: http://dx.doi.org/10.2147/IJN.S331639
81. Gouda A, Sakr OS, Nasr M, Sammour O. Ethanol injection technique for liposomes formulation: An insight into development, influencing factors, challenges and applications. J Drug Deliv Sci Technol [Internet]. 2021;61(102174):102174. Available from: http://dx.doi.org/10.1016/j.jddst.2020.102174
82. Bernal-Chávez SA, Romero-Montero A, Hernández-Parra H, Peña-Corona SI, Del Prado-Audelo ML, Alcalá-Alcalá S, et al. Enhancing chemical and physical stability of pharmaceuticals using freeze-thaw method: challenges and opportunities for process optimization through quality by design approach. J Biol Eng [Internet]. 2023;17(1):35. Available from: http://dx.doi.org/10.1186/s13036-023-00353-9

83. Šturm L, Poklar Ulrih N. Basic Methods for Preparation of Liposomes and Studying Their Interactions with Different Compounds, with the Emphasis on Polyphenols. Int J Mol Sci. 2021;22(12):6547. doi:10.3390/ijms22126547.
84. Bhattacharjee A, Das PJ, Dey S, Nayak AK, Roy PK, Chakrabarti S, et al. Development and optimization of besifloxacin hydrochloride loaded liposomal gel prepared by thin film hydration method using 32 full factorial design. Colloids Surf A Physicochem Eng Asp. 2019;124071.
85. Rane BR, Patil AK, Pingale PL, Jain AS, Morani DO, Kalamkar RV. Development and in-vitro characterization of liposomal gel of bifonazole for topical use. J Med Pharm Allied Sci. 2021 Oct-Nov;IC1(1):134-142.
86. Bhavya Shree T, Shravya K, Shreya D Shetty, Shreya J Poojari, Shriram H Patkar, Sindhura Pallavi. Formulation and evaluation of film forming gel of pumpkin leaves extract for antibacterial activity. Int J Modern Pharm Res. 2023;7(6):71-74.
87. Agrawal N, Sharma V, Maheshwari R. Formulation, development and evaluation of topical liposomal gel of fluconazole for the treatment of fungal infection. Panacea J Pharm Sci. 2017;6(1):43-89
88. Khot C, Kolekar K, Dabhole S, Mohite A, Nadaf S, Kumbhar PS, Disouza J. Optimized albendazole-loaded nanostructured lipid carrier gel: a redefined approach for localized skin cancer treatment. *RSC Pharm.* 2024;1(1042):1042–1054. doi:10.1039/d4pm00207e.
89. Vij NN, Saudagar RB. Formulation, development and evaluation of film-forming gel for prolonged dermal delivery of terbinafine hydrochloride. Int J Pharm Sci Res2014;5(9):537–554.
90. Li X, Zhang R, Liang R, et al. Preparation and characterization of sustained-release rotigotine filmforming gel. Int J Pharm 2014;460(1–2):273–279.
91. Kumar V, Sahoo SK. Lipid-based film-forming gels: An emerging approach in transdermal drug delivery systems. *J Pharm Sci*. 2019;108(6):1905-1918. doi:10.1016/j.xphs.2019.02.008.
92. Parhi, R.; Goli, V.V.N. Design and optimization of film-forming gel of etoricoxib using research surface methodology. *Drug Deliv. Transl. Res.* 2020, *10*, 498–514. [
93. Ong SGM, Chitneni M, Lee KS, Ming LC, Yuen KH. Evaluation of extrusion technique for nanosizing liposomes. Pharmaceutics [Internet]. 2016;8(4):36.
94. Han AS, Kim J, Park JW, Jin SG. Novel acyclovir-loaded film-forming gel with enhanced mechanical properties and skin permeability. J Drug Deliv Sci Technol [Internet]. 2022;70(103213):103213.
95. Chiong HS, Hakim MN, Sulaiman MR, Zakaria ZA, Zuraini A, Ong SGM, et al. Development and characterisation study of liposomes-encapsulated piroxicam. Int J Drug Deliv. 2011;3:64-73. doi:10.5138/ijdd.2010.0975.0215.03055.
96. Woo J, Wiggins RW, Mito S. Lipid-Based Niclosamide Delivery: Comparative Efficacy, Bioavailability, and Potential as a Cancer Drug. Lipidology. 2024;1(2):134–149. doi:10.3390/lipidology1020010
97. Kim DW, Kim KS, Seo YG, et al. Novel sodium fusidate-loaded film-forming hydrogel with easy application and excellent wound healing. Int J Pharm 2015;495(1):67–74.
98. Wasankar SR, Faizi SM, Deshmuk AD. Formulation and development of liposomal gel for topical drug delivery system. *Int J Pharm Sci Res.* 2012;3(11):4461-4474.
99. Shi J, Ma F, Wang X, Wang F, Liao H. Formulation of liposome gels of paeonol for transdermal drug delivery by Box-Behnken statistical design. *J Liposome Res.* 2012;22(4):270-278. doi:10.3109/08982104.2012.690159.
100. Tan C, Wang J, Sun B. Biopolymer-liposome hybrid systems for controlled delivery of bioactive compounds: Recent advances. *Biotechnol Adv.* 2021;48:107727.
101. Bornare, S.S.; Aher, S.S.; Saudagar, R.B. A Review: Film Forming Gel Novel Drug Delivery System. Int. J. Curr. Pharm. Res. 2018,10, 25–28.
102. Padula, C.; Nicoli, S.; Santi, P. Innovative formulations for the delivery of levothyroxine to the skin. Int. J. Pharm. 2009, 37, 12–16.