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Harnessing The Role of Polymer in Transferosomal Gel: Unlocking New Horizons in Novel Drug Delivery System

(Polymer-Driven Advancements in Transferosomal Gels)

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Abstract: Transferosomes represent a significant innovation in transdermal drug delivery, providing a highly adaptable and effective system for transporting therapeutic agents across the skin. Compared to traditional delivery methods, transferosomes offer enhanced skin permeability, excellent biocompatibility, improved stability, and fewer systemic side effects. Incorporating transferosomes into gel formulations further improves ease of application, patient adherence, and overall therapeutic efficacy. This review emphasizes the importance of key polymers and solvents in the formulation of transferosomes and examines their use in delivering various therapeutic agents, including antimicrobials, anti-inflammatory drugs, antihypertensives, peptides, antipsychotics, and treatments for hair loss. Ultimately, transferosomal gels present a promising and user-friendly approach for both topical and systemic drug delivery in contemporary pharmaceutical science.

Keywords*: Transferosomes, Transdermal Drug Delivery, Phospholipids, Skin Penetration, Controlled Release, Drug-Loaded Gels.*

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I. INTRODUCTION

Transferosomes are highly flexible vesicular carriers designed for targeted transdermal drug delivery. Composed of phosphatidylcholine and edge activators, they are capable of delivering large and small molecules to subcutaneous tissues with controlled release. The term "transferosome" combines Latin and Greek roots meaning “body that carries.” Their malleable membranes, formed from lipids and biocompatible softeners, allow them to deform and self-regulate, making them ideal for transdermal applications such as immunization and deep tissue targeting.[1-4] Transferosomes utilize an osmotic gradient from water evaporation to penetrate the stratum corneum via intracellular or transcellular pathways. Their non-toxicity, biodegradability, and ability to encapsulate both hydrophilic and lipophilic drugs make them highly effective. They can extend drug circulation, target specific tissues, reduce toxicity, and enhance bioavailability, making them superior to traditional formulations.[2] Because to their great deformability and combination of hydrophilic and hydrophobic qualities, transferosomes allow intact vesicles to penetrate more easily. Transfersomes are specialized vesicular carrier systems designed with an edge activator and at least one internal aqueous compartment enclosed by a lipid bilayer. These ultra-flexible vesicles possess self-optimizing and self-regulating characteristics due to their water-based core surrounded by a lipid membrane. Their inherent elasticity allows them to deform and pass through narrow pores or skin openings much smaller than their own size without any significant loss or damage to the vesicle.

It is obvious from a number of study publications that transferosomes may carry hydrophilic and lipophilic molecules, low and large molecular weight ($200 \leq MW \leq 106$) bioactive compounds, and both through the skin with a transport efficiency of more than 50%. Transfersomes have been reported in multiple published research studies to possess the ability to penetrate deep into the skin, form skin drug depots for long-term drug release, distribute therapeutic agents into deeper skin layers, and transport pharmaceuticals into the bloodstream.[5]

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➢ *Structure and Composition of Transferosomes:*

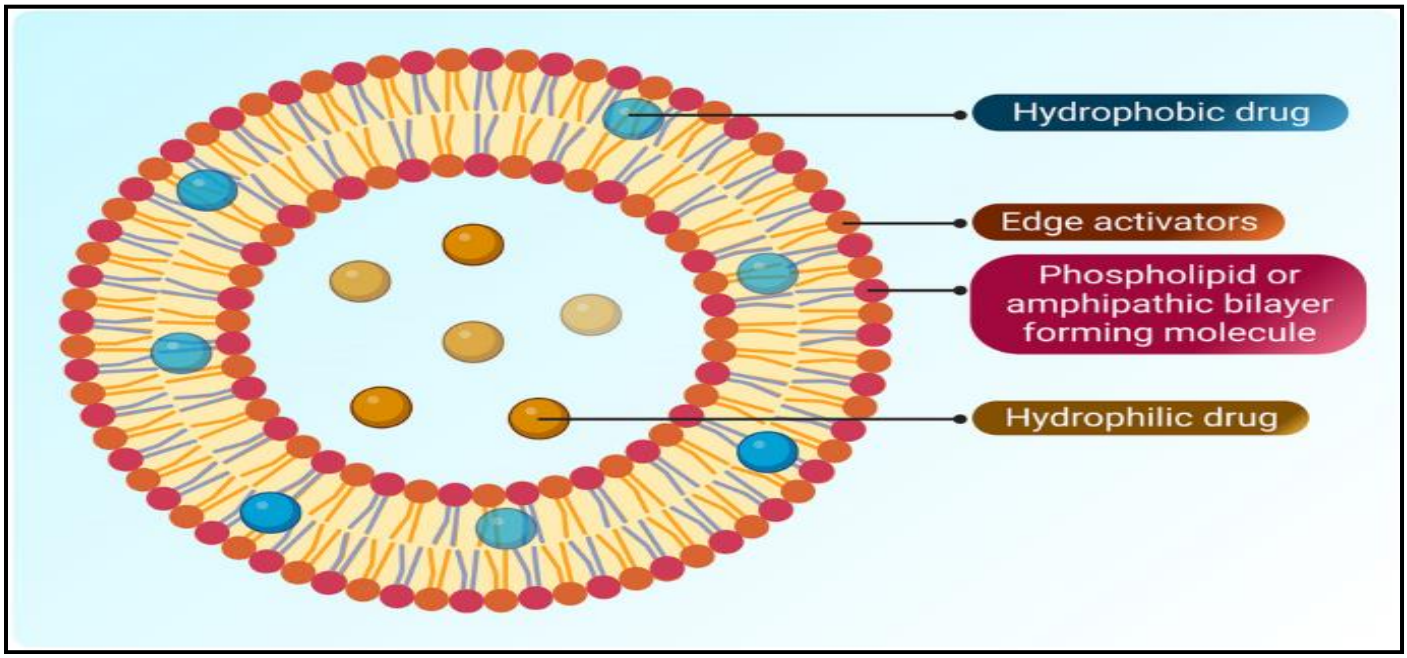

Fig 1 Structure of Transferosomes

Transferosomes are highly deformable vesicles capable of passing through narrow pores nearly as efficiently as water, despite being much larger. Vesicles sized 200–300 nm effectively penetrate the skin. Structurally, they combine features of liposomes and niosomes, containing phospholipids, cholesterol, and non-ionic surfactants (edge activators), making them the first generation of elastic liposomes.

- *Composition:*

The two primary aggregates that make up transferosomes are edge activators and phospholipids.The primary component is an amphipathic substance, such as soy or egg phosphatidylcholine, often consisting of a lipid mixture. These lipids serve as the vesicle-forming elements that construct the lipid bilayer.

- *Phospholipids:*

Vesicles are stabilized and their membrane is formed by phospholipids. Consequently, both the destabilizing agent and the membrane-forming agents, such as phospholipids. The most often utilized phospholipids are soy-based ones, such as hydrogenated soy phosphatidylcholine and soy phosphatidylcholine.

- *Edge Activators:*

Edge activators are non-ionic single-chain surfactants that enhance the fluidity and flexibility of the lipid bilayer in transferosomes. Common edge activators include sodium oleate, sodium cholate, sodium deoxycholate, DCP, KG, Spans (40–85), and Tweens (20, 60, 80). Their type and concentration influence vesicle size, entrapment efficiency, and zeta potential. Additionally, 3–10% alcohol (ethanol or methanol) is used as a solvent, with water or phosphate-buffered saline (pH 6.5–7) as the hydration medium. Materials commonly used for the preparation of transferosomes are summarized in [10]

Table 1 Materials commonly used for the preparation of transferosomes.

Ingredient	Examples	Functions
Phospholipid	Soya Phosphatidylcholine Egg Phosphatidylcholine Disteryl Phosphatidylcholine	Vesicle forming Component
Surfactant	Sodium Cholate Sodium deoxy Cholate Tween 80 Span 80	For Providing Flexibility
Alcohol	Ethanol, Methanol	As a Solvent
Dye	Rhodamine-123 Rhodamine-DHPE Flurescein-DHPE Nil red	For Confocal Scanning Laser Microscopy(CSLM) Study

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	6 Carboxy fluorescence	
Buffering Agent	Saline phosphate buffer (PH 6.5) 7% v/v ethanol Tris buffer (PH 6.5)	As a hydrating medium

- *Transferosomal Gel:*

Gel-based solutions containing transferosomes provide extra benefits in terms of application and adherence to the site of action. Transferosomes are incorporated into gels to preserve their structural integrity and to enable the controlled release of pharmaceuticals that are encapsulated, which improves therapeutic results. In particular, this delivery strategy is beneficial for medications that need sustained release patterns or have low bioavailability.

- *Advantages of Transferosomes:*

✓ *Protective Reservoir*:

Encapsulate drugs to protect them from metabolic degradation and allow gradual, sustained release.

✓ *Enzyme Protection:*

Shield sensitive drugs (e.g., proteins, peptides) from enzymatic breakdown.

✓ *Biocompatibility:*

Made from naturally derived, biodegradable phospholipids, ensuring safety and compatibility with the body.

✓ *Versatile Drug Delivery:*

Can deliver both low and high molecular weight drugs (e.g., albumin, insulin, corticosteroids).

✓ *Enhanced Skin Penetration:*

Highly deformable and elastic, allowing penetration through skin pores much smaller than their size.

✓ *High Stability:*

More stable than other lipid-based carriers, making them suitable for long-term storage and commercialization.

✓ *Low Irritation Risk:*

Composed of biocompatible components with low potential for irritation or allergic reactions, suitable for clinical use.

✓ *Targeted Delivery:*

Can be engineered for targeted delivery to specific skin layers or cells, enhancing therapeutic efficiency and reducing side effects.

- *Limitation:*

✓ Transferosome formulations tend to be expensive.
✓ They are susceptible to oxidative damage, which compromises their chemical stability.
✓ The high cost of lipid excipients and specialized manufacturing equipment makes transfersomal formulations relatively costly. Among the lipid components, phosphatidylcholine is most commonly used due to its lower cost.
✓ One major hurdle in using transfersomes for drug delivery is achieving high purity in natural phospholipids, which often leads to the use of synthetic alternatives.

➢ *Mechanism of Action of Transfersomes:*

Transfersomes are drug delivery systems capable of penetrating intact skin. While the exact mechanism by which they enhance the delivery of active compounds through the skin is not fully understood, two main theories have been proposed:

- Transferosomes act as intact carriers, maintaining their structure while transporting the drug through the skin.
- They disrupt the tightly packed intercellular lipids of the stratum corneum, functioning as penetration enhancers to facilitate the drug's entry and movement across this outermost skin layer.
- Across the intact horny layer,
- Through the hair follicles with the associated sebaceous glands, or
- Via the sweat glands

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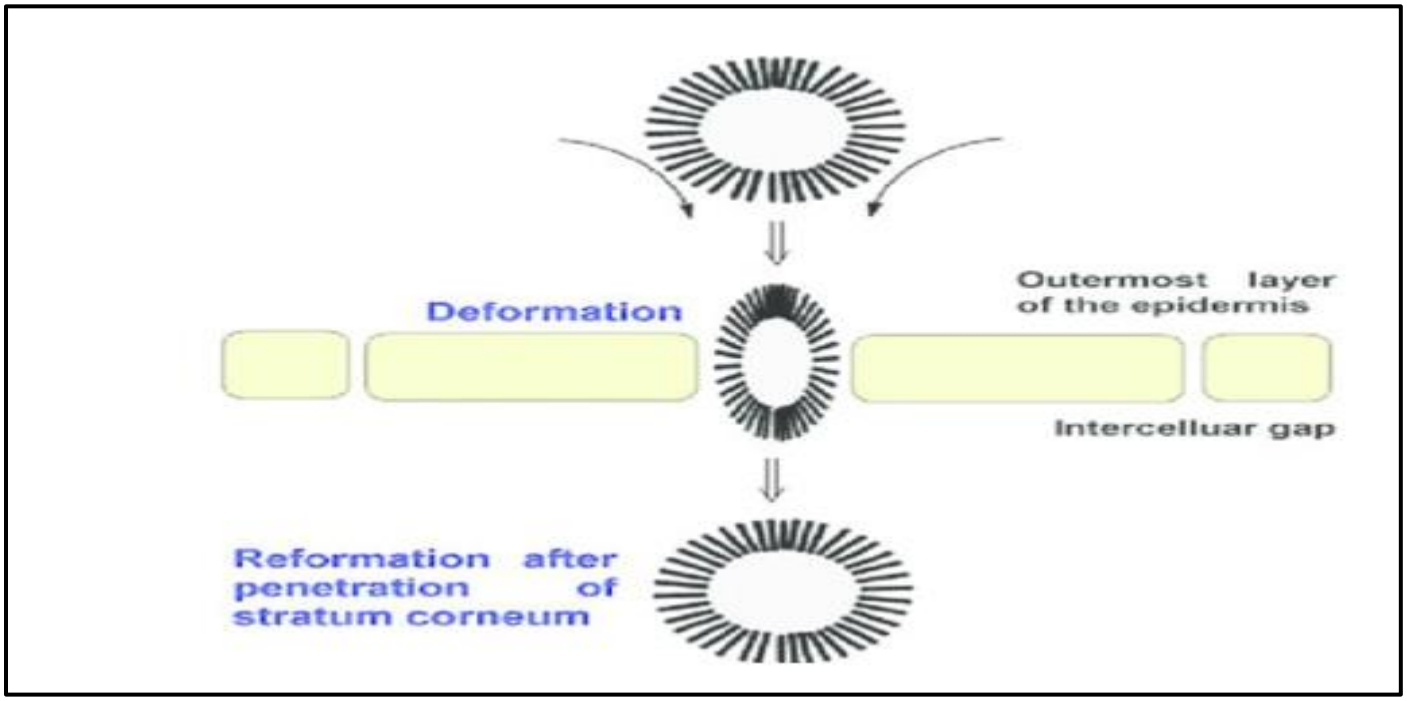

Fig 2 Represents the Potential Pathways for Substances to Traverse the Skin Barrier.

Transferosomes penetrate the skin through a complex mechanism involving hydration, osmotic pressure, and membrane dynamics. When lipids interact with water, vesicles move toward areas of higher water concentration, sometimes fusing with cell membranes to aid intracellular drug delivery. A transdermal osmotic gradient across the stratum corneum and epidermis drives vesicle movement, helping to form nanochannels and open intercellular spaces. Alcohols like ethanol, used in formulations, enhance skin penetration by modifying the lipid bilayer. Due to their flexible, self-regulating bilayer structure, transferosomes adapt to biological environments and overcome barriers with ease. Their high deformability and the osmotic gradient enable them to reach deep skin layers, including the dermis and blood vessels, by expanding intercellular pathways with minimal resistance.[20] The natural transdermal gradient creates a difference in water activity across the skin. This gradient leads to the formation of channels approximately 20–30 nm in width, allowing ultra-deformable, flexible transferosomes to move through the skin along the moisture gradient.[21] The evaporation of water from the skin's surface due to body heat generates an osmotic gradient. This gradient facilitates the flexible movement of transferosomes across the skin, enabling the delivery of therapeutic agents to targeted sites for either local or systemic treatment, while maintaining low systemic toxicity. The ability of transferosomes to penetrate the skin depends on the deformability of their membranes, which is determined by their composition.[2]

II. ROLE OF POLYMERS USED IN TRANSFEROSOMES

➢ *Phospholipid:*

Vesicular systems are primarily made of phospholipids, which are amphipathic molecules with a hydrophobic tail and a hydrophilic head.[23] Common synthetic phospholipids include dioleoyl- phosphatidyl- choline (DOPC), Dioleoyl-phosphatidylethanolamine (DOPE), Distearoylphosphatidyl-choline (DSPC), and Distearoylphosphatidyl- ethanolamine (DSPE). Among these, phosphatidylcholine phospholipids play a crucial role in drug delivery technologies due to their significant functional properties.[24]

The key advantage of phospholipid-based vesicular systems is their excellent compatibility with human membranes, including skin and internal membranes. For a drug to be absorbed, distributed, and eliminated, it must cross biological membranes—a process known as drug transport. Cellular membranes are composed of a bilayer of amphiphilic phospholipids, with hydrophobic tails facing inward and polar heads facing outward, creating a structure that interacts well with both lipophilic and aqueous environments.[25]

Phosphatidylcholine (PC) molecules are dispersible, not water-soluble, and naturally form bilayer sheets in aqueous environments to avoid contact between water and their hydrophobic tails. These sheets bend into sealed vesicles, minimizing free energy. The strong energy difference between hydrophilic and hydrophobic regions drives the formation of these stable, self-assembled bilayers. Unlike other amphiphilic agents (e.g., soaps, detergents), PC and its synthetic versions prefer bilayer structures over micelles, due to their unique structural characteristics.[26]

- *History:*

Phosphatidylcholine was initially isolated around 50 years ago in Odessa, Ukraine. Subsequent studies were conducted in Germany and Russia. For more than three decades, Sanofi-Aventis has marketed this compound, which is now registered in 53 countries. Currently, its primary uses include intravenous therapy for preventing fat embolisms in polytrauma patients, managing metabolic disorders, and serving as a hepatoprotective agent.[27]

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➢ *Polymers employed for the development of transferosomes:*

- *Lecithin:*

Lecithin is a yellow-brown fatty substance found in animal and plant tissues, composed of phospholipids, choline, fatty acids, glycerol, and other lipids. It is commonly sourced from soybeans, milk, marine organisms, and seeds, and is soluble in ethanol. As a key source of choline, it is fully metabolizable by the human body.

- *Applications:*

✓ Acting as a wetting, stabilizing, and dispersing agent
✓ Aiding in emulsification and encapsulation
✓ Enhancing catalytic activity and color intensity
✓ Providing strong stabilization and suspension
✓ Reducing foam in water-based paint systems

➢ *Soyaphosphatidyl Choline:*

Phosphatidylcholine is a key component of cell membranes and pulmonary surfactant, primarily located in the outer membrane layer. It is transported between membranes by phosphatidylcholine transfer protein. Structurally, it consists of a choline head, glycerophoric acid, and fatty acids. Supplementation may support cognitive function and memory with age but is not effective for dementia treatment.

- *Applications:*

Used in the management of inflammatory bowel disease.

➢ *Distearoyl Phosphatidyl Choline:*

This solid, stable compound should be stored at -20°C and kept away from strong oxidizing agents due to incompatibility. Vesicles formed by sonicating saturated-chain phosphatidylcholines in aqueous media are commonly used to model plasma membranes. Their size distribution changes over time below the phase transition temperature, but remains stable at or above it.

➢ *Dipalmitoyl Phosphatidylcholine:*

1,2-Dipalmitoyl-sn-glycero-3-phosphocholine (L-DPPC) is a zwitterionic phospholipid made of two palmitic acid chains, serving as the main component of pulmonary surfactant. It is primarily derived from phosphatidylcholine remodelling and is used in forming liposomal monolayers. L-DPPC-based proteoliposomes significantly enhance enzyme integration into erythrocyte membranes and show potential for active immunotherapy applications involving antigens.

➢ *Cholesterol:*

Cholesterol is a lipid and modified steroid produced by animal cells to maintain membrane structure and fluidity, allowing cellular flexibility. It is a precursor to vitamin D, steroid hormones, and bile acids, and the main sterol in the body. Most dietary cholesterol is poorly absorbed due to its esterified form. It regulates membrane fluidity, with its rigid ring reducing and flat side chain stabilizing the membrane. In neurons, it is essential for myelin sheath formation. Due to low water solubility, it is transported in blood via lipoproteins.

➢ *Deoxycholic Acid:*

Deoxycholic acid (DCA) is a secondary bile acid produced by intestinal microbiota from primary bile acids like cholic acid and chenodeoxycholic acid. It is alcohol- and acetic acid-soluble, appearing as a white crystalline powder, and acts as a detergent to isolate membrane proteins. In traditional Chinese medicine, it is a key component of Niuhuang, valued for its anti-inflammatory and immune-boosting effects. DCA also serves as an immunostimulant and is synthesized by the enzyme lyso-phosphatidylcholine acyltransferase.

- *Uses:*

✓ Employed in scientific studies involving liposomes, lipid bilayers, and biological membranes.
✓ Utilized in the synthesis of high-density lipoproteins (HDL).
✓ Aids in the treatment of localized inflammation.

- *Applications*:

✓ Facilitates fat emulsification to promote absorption in the intestines.
✓ Used to help prevent the formation of gallstones.
✓ When combined with phosphatidylcholine, sodium deoxycholate is applied in mesotherapy injections.
✓ Serves as an emulsifying agent in the food industry.
✓ Deoxycholic acid and its bile acid derivatives are used in nanotechnology applications.

➢ *TWEEN 80:*

Polysorbate 80 (Tween 80) is a non-ionic surfactant and emulsifier widely used in the food, cosmetic, and pharmaceutical industries. Made from polyethoxylated sorbitan and oleic acid, it appears as an amber, viscous, water-soluble liquid and is typically used above its critical micelle concentration (CMC). It stabilizes aqueous drug formulations (e.g., parenteral drugs, eye drops, and amiodarone) and dissolves well in ethanol and cottonseed oil. While generally safe, it may cause mild adverse effects but is non-carcinogenic. Cosmetic-grade forms have more impurities than food-grade ones.[29,30]

- *Uses:*

✓ Emulsifier in food production and ice cream stabilization
✓ Surfactant in cosmetics and soaps
✓ Solubilizing agent in mouthwashes
✓ Stabilizer in parenteral drug formulations
✓ Prevents milk protein-fat separation
✓ Tool for microbial strain identification

➢ *TWEEN 20:*

Tween 20 is a clear, yellow to yellow-green viscous liquid and a polyoxyethylene derivative of sorbitan monolaurate. It is a stable, low-toxicity surfactant commonly

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used as a detergent and emulsifier in pharmaceutical and scientific applications.

- *Applications:*

✓ Wetting agent in flavoured mouth drops and spreads
✓ Biotechnology applications
✓ Washing agent in immunoassays
✓ Blocking non-specific binding sites
✓ Protein stabilization in formulations
✓ Excipient in pharmaceutical emulsions and suspensions
✓ Used for safely detaching stamps from envelopes

➢ *SPAN 20:*

It is also referred to as sorbitan monolaurate. This substance is a blend of partial esters formed from sorbitol and its mono- and dianhydrides combined with edible lauric acid. It appears as an amber-colored, oily, and viscous liquid, or as light cream to tan-colored beads, flakes, or a hard, waxy solid with a mild odor. It is soluble in both hot and cold water.

➢ *SPAN 80:*

Span 80, also known as sorbitan oleate, is a non-ionic surfactant used above its critical micelle concentration (CMC), with optimal skin permeation at 10% concentration. It is mainly employed in forming cationic lipid vesicles and acts as a lipophilic linker in microemulsion formulations. Span 80 supports Lactobacillus viability and acid production in enriched media and significantly influences suspension stability at higher concentrations. It also serves as a coacervating agent in microsphere formation.

➢ *Ethanol:*

Ethanol (ethyl alcohol) is a volatile, colourless liquid with a mild odor, produced by fermenting sugars with yeast. It is phytoactive and known for causing alcohol intoxication. Due to its hydroxyl group, ethanol forms hydrogen bonds, making it more viscous and less volatile than similar compounds. First used as lamp fuel in the 1840s, it still plays a role in spirit lamps and affects multiple neurological systems.

- *Uses:*

✓ Solvent in perfumes and thermometers
✓ Ingredient in flavourings, colorants, and medicines
✓ Component in motor fuels, additives, and rocket propellants
✓ Used in beverages and cooking for dissolving hydrophobic flavour compounds

➢ *Methanol:*

Methanol (methyl alcohol or wood alcohol) is the simplest alcohol, appearing as a light, volatile, colourless, and flammable liquid. It is naturally produced by anaerobic bacteria and can be obtained from wood pyrolysis. As a polar solvent, methanol is used in antifreeze, fuel, ethanol denaturation, and industrial applications. However, in large amounts, it is toxic, as it metabolizes into formic acid and formate salts.

- *Toxicity:*

Methanol is highly toxic, with ingestion of just 10 mL potentially causing irreversible blindness or even death due to its CNS depressant effects.

- *Uses:*

✓ Solvent in UV spectroscopy, HPLC, and LC-MS
✓ Fuel in military rockets and camping/marine stoves
✓ Denaturant in polyacrylamide gel electrophoresis and ethanol (methylated spirits)
✓ Former antifreeze in early automobiles.

➢ *Chloroform:*

Chloroform is a colourless, dense liquid with a sweet odor, classified as a hazardous trihalomethane. It is soluble in water, organic solvents, and oils, and over 90% of its atmospheric presence comes from natural sources like seaweeds. Industrially, it is synthesized by heating chlorine with methane or chloromethane, and its deuterated form is widely used in NMR spectroscopy.

- *Uses:*

✓ Production of chlorofluoromethane, a refrigerant and intermediate for tetrafluoroethylene
✓ Laboratory solvent (chemically stable, non-flammable, volatile)
✓ Reagent in the Reimer–Tiemann reaction for forming dichlorocarbene
✓ Former anaesthetic due to CNS depressant effects
✓ Enhances K^+ ion flow through nerve channels

Table 2 Formulation Strategy for preparing Clindamycin and Benzyl Peroxide loaded Transferosomal Gel

Transferosomal Gel as 1%Clindamycin &2.5%Benzyl peroxide-based Therapy for Acne treatment	
Preparation of Transferosomes Suspension	Preparation of Transferosomal Gel
Method: Vortex-Sonication Method **Lipid**: Phospholipon 90H **Edge activators**: Tween 80/ Span 80	**Method**: Dispersion- **Gelling Agent**: Chitosan

- *Safety:*

Ingesting over 10 mL may cause respiratory or cardiac arrest, making it potentially lethal.

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III. POTENTIAL DRUG CARRIER FOR TRANSFEROSOMAL GEL

➢ *Delivery of Antimicrobial:*

Table 3 Formulation Strategy for preparing Cephalexin loaded Transferosomal Gel

Transferosomal Gel as Cephalexin-based Therapy for Skin Infections	
Preparation of Transferosomes	Preparation of Transferosomal Gel
Method: Thin film hydration Lipid: Phospholipon 90H Surfactant: Sodium deoxycholate	Method: Dispersion Gelling Agent: Carbopol 934
Skin Infections	
Caused by microbial invasion of skin and underlying tissues Ranges from mild to serious life-threatening infections Increased incidence due to aged population, critically ill, and immuno-compromised patients Emergence of multi-drug resistant pathogens	
Current Treatments	
Parenteral therapy: For patients with gastric problem Oral antibiotics: For patients with normal health conditions	
Challenges with Current Treatments	
Lack of permeation of antibiotic agents from topical formulations into deeper skin layers High doses of oral or parenteral dosage forms	

➢ *Delivery of Antibiotics:*

Current topical acne treatments, such as clindamycin, benzoyl peroxide, and retinoids, help reduce inflammation and bacterial growth. Clindamycin inhibits bacterial protein synthesis, while benzoyl peroxide reduces sebum and prevents bacterial proliferation. Their combination improves outcomes and lowers the risk of resistance. However, conventional formulations often suffer from poor skin penetration, irritation, and dryness, leading to low patient compliance. To overcome these challenges, advanced drug delivery systems are being developed to enhance absorption, minimize side effects, and improve effectiveness.

➢ *Delivery of Anti-Hypertensive Drugs:*

Table 4 Formulation Strategy for preparing Felodipine loaded Transferosomal Gel

Felodipine loaded transfersomal gel as therapy for angina pectoris	
Preparation of Transferosomes	Preparation of Transferosomal Gel
Method: Thin-film hydration technique Lipid: Cholesterol Edge activators: Sodium deoxycholate, Sodium cholate, Tween 80, Span 65, Span 60, and Span 20. Solvent : Chloroform: Methanol	Method: Dispersion Gelling agent: Hydroxypropyl methyl cellulose 4000 (HPMC 4000) containing 2% w/v mannitol

Felodipine, a dihydropyridine-type calcium channel blocker, is commonly prescribed for managing high blood pressure and angina pectoris. It is often favoured over non-dihydropyridine calcium channel blockers due to its greater selectivity as a vasodilator and its reduced impact on cardiac function.

➢ *Delivery of Peptide Hormones:*

Table 5 Formulation Strategy for preparing Insulin loaded Transferosomal Gel

Insulin loaded transfersomal gel as therapy for type -1diabetesmellitus	
Preparation of Transferosomes suspension	Preparation of Transferosomal Gel
-Method: Reverse Phase Evaporation Method -Lipids: Soya Lecithin and cholesterol -Surfactant: Tween80 -Edge activator: Sodium deoxycholate -Solvent: Diethyl ether and chloroform -Penetration enhancer: DMSO	-Method: Dispersion -Gelling agent: Methylcellulose gel

Parenteral insulin is widely used in clinical practice, but it can lead to several significant side effects, such as peripheral hyperinsulinemia, proliferation of smooth muscle cells, and diabetic micro- and macrovascular complications. Additionally, the need for daily injections presents challenges including physical discomfort, psychological stress, inconvenience, expense, and localized effects like hypertrophy and fat accumulation at the injection sites. To address these limitations, the transdermal route has emerged as a promising non-invasive alternative for insulin delivery in diabetic patients. Recently, transferosomes—vesicular drug delivery systems—have shown potential in improving the transdermal transport of medications when applied to the skin without occlusion.

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➢ *Delivery of Anti-Psychotic Drug:*

Table 6 Formulation Strategy for preparing Risperidone loaded Transferosomal Gel

Risperidone loaded transferosomal gel for schizophrenia and bipolar disorder management	
Preparation of Transferosomes suspension	Preparation of Transferosomal Gel
-Method: Reverse Phase Evaporation Method -Lipids: Soya Lecithin and cholesterol -Surfactant: Tween80 -Edge activator: Sodium deoxycholate -Solvent: Ether and chloroform	-Method: Dispersion -Gelling agent: Methylcellulose gel

Risperidone is available in oral and injectable forms, but these face challenges like low bioavailability, inconsistent plasma levels, poor patient adherence, and extrapyramidal side effects. To address these issues, researchers are exploring alternative delivery systems, with transferosomes—flexible vesicles for transdermal delivery—emerging as a promising option for sustained and improved risperidone therapy.

➢ *Delivery of Anti-Inflammatory Drug:*

Table 7 Formulation Strategy for preparing Piroxicam loaded Transferosomal Gel

Piroxicam loaded transferosomal gel for acute and chronic arthritic treatments	
Preparation of liposomes and Transferosomes dispersion	Preparation of Transferosomal Gel
Liposomes: -Method: Ethanol injection method -Constituents: Phosphatidylcholine, Cholesterol -Solvent: Ethanol **Transfersomal dispersion:** Method: Reverse Phase Evaporation Method -Lipids: Phospholipids -Surfactant: Tween80, Span80 -Solvent: Methanol and chloroform	-Method: Dispersion -Gelling agent: Carbopol 914 -Neutralizer: Triethanolamine

Piroxicam is a potent NSAID used to treat acute and chronic arthritis, but long-term use can cause side effects like gastric distress, nausea, and headaches, leading to poor patient compliance. A transdermal delivery system can help avoid first-pass metabolism and reduce these side effects. Studies have explored how different formulations affect piroxicam's skin penetration. Transferosomes show promise by forming a drug reservoir in the skin and enabling targeted delivery to deeper layers, which is beneficial for treating skin-related conditions.

➢ *Delivery of Potassium Channel Opener:*

Table 8 Formulation Strategy for preparing Minoxidil loaded Transferosomal Gel

Minoxidil loaded transfersomal gel for effective topical treatment of alopecia	
Preparation of Transferosomes suspension	Preparation of Transferosomal Gel
-Method: Thin Film Hydration Method -Lipids: Phospholipid and cholesterol -Surfactant: Tween80 -Solvent: Chloroform	-Method: Dispersion -Gelling agent: Commercial tincture gels and -Carbomer980

Minoxidil (MXD) is the most effective treatment for androgenetic alopecia (AGA), enhancing blood flow to hair follicles, prolonging the growth phase, and shortening the resting phase of the hair cycle. AGA, a common genetic and androgen-dependent condition, causes hair follicle miniaturization and affects both men and women. While traditional ethanol-based MXD formulations have limited skin penetration, newer delivery systems improve localization and controlled release but often fail to reach deeper skin layers. Transferosomes, flexible liposomes with edge activators, overcome this by penetrating deep into the skin, making them a promising transdermal system for delivering MXD effectively to the dermis and hair follicles in alopecia treatment.

IV. CONCLUSION

Transferosomes are an innovative and effective transdermal drug delivery system known for their high deformability and ability to penetrate the skin barrier. Incorporating phospholipids, cholesterol, and surfactants enhances their stability, flexibility, and drug-loading capacity. When formulated into gels, they offer improved controlled release, patient compliance, and applicability. Transferosomal gels have shown success in delivering various drugs, including antimicrobials, anti-inflammatories, antihypertensives, peptides, and treatments for skin and hair conditions. Compared to conventional methods, they provide better drug penetration, fewer systemic side effects, and enhanced therapeutic outcomes. With ongoing research and optimization, transferosomal gels have the potential to

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become a widely used platform for both topical and systemic drug delivery, offering a versatile, safe, and efficient solution in modern pharmaceuticals.

- *Conflict of Interest*:
  The author declares that there is no conflict of interest.

- *Funding Source:* None

- *Ethical Statements:* None

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