ISSN: 2306-6091

International Journal of Pharmaceuticals and Health Care Research (IJPHR)

IJPHR |Vol.14 | Issue 2 | Apr - Jun -2026

www.ijphr.com

DOI : https://doi.org/10.61096/ijphr.v14.iss2.2026.320-328

Glycerosomes: Recent Advancements, Therapeutic Applications, and Patents

Amandeep Kaur[1], Dr. Naresh Singh Gill[2], Neha[3*], Kanika[4]

[1]*Associate Professor, Department of Pharmaceutics, LTSU, Ropar (Pb)*
[2]*Executive Dean/Director, Department of Pharmaceutics, LTSU, Ropar (Pb)*
[3]*PG Scholar, Department of Pharmaceutics, LTSU, Ropar (Pb)*
[4]*Associate Professor, Department of Pharmaceutics, LTSU, Ropar (Pb)*
pm_vcp@rediffmail.com

Published on: 18.06.2026
Published by: Futuristic Publications

Abstract: Glycerosomes are innovative vesicular drug delivery systems composed of phospholipids, water, and high concentrations of glycerol (20–50%), which confer exceptional membrane flexibility and deformability. Originally introduced as advancement over classical liposomes and transfersomes, glycerosomes have emerged as versatile platforms for transdermal, topical and dermal drug delivery owing to their superior skin permeation capabilities, biocompatibility, and capacity to encapsulate both hydrophilic and lipophilic drugs. This review comprehensively summarizes recent advancements in glycerosome research spanning 2018–2025, including innovations in formulation strategies, physicochemical characterization, *in vitro* and *in vivo* evaluation, therapeutic applications across dermatology, oncology, and pain management, and the rapidly growing patent landscape. Relevant patents filed and granted internationally are catalogued and analyzed. The review also addresses current challenges, regulatory perspectives, and future directions for glycerosome based drug delivery. Key findings confirm that glycerosomes significantly improve drug permeation flux, reduce systemic side effects, and offer formulation advantages such as stability, scalability, and compatibility with biologics. The cumulative evidence positions glycerosomes as next generation carriers with strong clinical and commercial potential.

Keywords: Glycerosomes, Vesicular drug delivery, Transdermal, Skin permeation, Nanotechnology, Phospholipid vesicles, Patents, Topical formulation

Introduction

The skin, representing the largest organ of the human body with a surface area of approximately 1.7–2.0 m², serves as an effective barrier against exogenous substances, microbes, and physical insults. The stratum corneum (SC), the outermost layer of the epidermis, constitutes the primary rate limiting barrier to the transdermal and topical delivery of therapeutic agents [1]. Overcoming this barrier in a controlled and safe manner has been the central challenge driving innovation in dermal drug delivery systems for several decades.

Conventional drug delivery strategies including creams, ointments, gels, and patches suffer from limitations such as poor drug permeation, low bioavailability, inadequate dose control, and patient non-compliance. Vesicular carrier systems, beginning with liposomes introduced by Bangham in the 1960s, represented a paradigm shift by enabling encapsulation and targeted delivery of diverse drug molecules [2]. Subsequent generations of vesicular carriers including ethosomes, transfersomes, niosomes, spanlastics, and cubosomes progressively improved upon liposomal drug delivery by incorporating membrane softening agents and penetration enhancers [3]. Glycerosomes, first described by Touitou and colleagues in the early 2010s, represent a novel class of vesicular delivery systems in which high concentrations of

glycerol (typically 20–50% v/v) replace a significant portion of the aqueous phase [4]. Glycerol, a polyol with well established safety and skin-compatible properties, confers unique physicochemical characteristics to the vesicle membrane notably, enhanced deformability, improved hydration of the stratum corneum, and resistance to desiccation. Unlike ethosomes, which contain ethanol as the penetration enhancer, glycerosomes are non-volatile, biologically inert with respect to toxicity, and suitable for long-term formulation stability.

The past seven years (2018–2025) have witnessed a substantial expansion in glycerosome research, encompassing innovations in phospholipid composition, co-encapsulation strategies, hybrid formulations, surface modifications, and scale-up manufacturing. Concurrently, the commercial value of glycerosomes has been acknowledged through a growing portfolio of International patents covering novel compositions, methods of preparation, and specific therapeutic applications. This review synthesizes current knowledge across these dimensions, providing an integrated perspective on the state of the art and emerging opportunities in glycerosome science.

Structural Architecture and Composition of Glycerosomes

Glycerosomes share the core vesicular architecture of liposomes; a phospholipid bilayer enclosing an aqueous core but are distinguished by the incorporation of glycerol as a primary hydrating medium. The phospholipid component is most commonly phosphatidylcholine (PC), typically derived from soy or egg lecithin, owing to its amphiphilic character, biocompatibility, and GRAS (Generally Recognised as Safe) classification [5]. Other phospholipids used include dipalmitoylphosphatidylcholine (DPPC), hydrogenated phosphatidylcholine (HPC), and phosphatidylethanolamine (PE), each influencing membrane rigidity and drug loading capacity. Glycerol exerts its effects on vesicle properties through several mechanisms. First, it replaces water molecules in the interfacial hydration shell of phospholipid head groups, increasing interbilayer spacing and reducing membrane rigidity a phenomenon well-documented by differential scanning calorimetry (DSC) and small angle X-ray scattering (SAXS) studies [6]. Second, glycerol increases the osmolality and viscosity of the internal aqueous compartment, stabilizing the vesicular structure against aggregation and fusion. Third, glycerol functions as a potent humectant on the skin surface, drawing moisture into the stratum corneum and transiently disrupting the ordered lipid lamellae, thus reducing the diffusional resistance of the barrier [7]. Table 1 summarizes the major formulation types of glycerosomes, their compositional characteristics, glycerol concentration ranges, and key physicochemical properties.

Table 1: Classification and Composition of Glycerosome Formulations

Formulation Type	Key Components	Glycerol Concentration (%)	Notable Properties
Classic Glycerosome	PC, Glycerol, Water	20–50%	Deformable, enhanced skin permeation
Ethanol-Glycerosome	PC, Glycerol, Ethanol, Water	20–40%	Synergistic penetration, improved drug loading
Propylene Glycol Glycerosome	PC, Glycerol, PG, Water	15–30%	Increased flexibility and hydration
Hyaluronic Acid-Coated Glycerosome	PC, Glycerol, HA, Water	20–30%	Targeted dermal delivery, bioadhesion
Nano-Glycerosome (<200 nm)	PC, Glycerol, Surfactant	25–45%	High surface area, deep follicular penetration
Phyto-Glycerosome	PC, Plant extract, Glycerol	20–35%	Anti-inflammatory, herbal drug delivery

Particle size is a critical determinant of glycerosome performance. Nano glycerosomes in the 100–300 nm range demonstrate optimal skin penetration via intercellular and follicular pathways [8]. Zeta potential, typically ranging from −25 to −45 mV for negatively charged formulations, confers colloidal stability. Drug encapsulation efficiency (EE %) is influenced by the lipid-to-drug ratio, aqueous phase composition, and preparation method, with EE values typically exceeding 75% for lipophilic drugs and 50–70% for hydrophilic molecules [9].

Methods of Preparation and Characterization

Preparation Techniques

Thin-film hydration (TFH) remains the most widely employed method for glycerosome preparation. In this approach, phospholipids and lipophilic drugs are dissolved in an organic solvent (typically chloroform: methanol 2:1 v/v), which is evaporated under reduced pressure using a rotary evaporator to form a thin lipid film. The film is subsequently hydrated with a glycerol–water mixture at a temperature above the lipid phase transition temperature (Tc), under continuous agitation [10]. The resultant multilamellar vesicles (MLVs) are then converted to unilamellar vesicles (ULVs) by extrusion through polycarbonate membranes (100–400 nm pore size) or by probe sonication. Proliposome method involves adsorption of lipids onto a free-flowing sorbitol or mannitol carrier, which upon hydration with the glycerol-aqueous phase instantly yields vesicles. This technique offers advantages in scale-up and avoids the use of large quantities of organic solvents [11]. Supercritical fluid technology has been explored for solvent-free glycerosome production using CO_2 as a processing medium, yielding highly uniform nanoparticles suitable for pharmaceutical manufacturing [12]. Ethanol injection and reverse-phase evaporation are additional methods documented in the literature, offering process advantages for specific drug classes.

Physicochemical Characterization

Comprehensive characterization of glycerosomes encompasses dynamic light scattering (DLS) for hydrodynamic diameter (Z-average) and polydispersity index (PDI); laser Doppler electrophoresis for zeta potential; transmission electron microscopy (TEM) and atomic force microscopy (AFM) for morphological assessment; DSC and thermogravimetric analysis (TGA) for thermal characterization; and SAXS for lamellar spacing analysis [13]. Encapsulation efficiency is quantified by ultracentrifugation based separation followed by UV-Vis spectrophotometry or HPLC quantification of the drug in the supernatant. *In vitro* drug release is evaluated using Franz diffusion cells with synthetic membranes or excised human or porcine skin.

Mechanisms of Skin Penetration Enhancement

The enhanced skin permeation mediated by glycerosomes is a multifactorial process attributable to the interplay of vesicle deformability, humectant activity of glycerol, and potential disruption of intercellular lipid organization within the stratum corneum. Three primary pathways have been proposed and substantiated through experimental evidence: (i) Intact vesicle penetration via the intercellular lipid lamellae pathway (ii) Follicular (transfollicular) penetration exploiting hair follicle ducts as shunts (iii) Lipid disruption and drug diffusion following vesicle disintegration at the skin surface [14]. The deformability of glycerosomes, quantified by the deformability index (DI) using an extrusion assay through membrane pores smaller than the vesicle diameter, has consistently been shown to exceed that of classical liposomes and approach that of transfersomes [15]. This is attributed to the plasticising effect of glycerol on the phospholipid bilayer, which lowers the energy barrier for vesicle squeezing through tight intercellular junctions. Confocal laser scanning microscopy (CLSM) studies using fluorescent-labelled glycerosomes have demonstrated penetration to depths of 60–150 μm within excised skin, reaching viable epidermis and dermis, as opposed to liposomes which largely remain in the superficial stratum corneum [16].

The humectant function of glycerol additionally enhances skin permeability by increasing the hydration state of the stratum corneum. Infrared spectroscopy studies have confirmed that glycerol increases the mobility of the lipid CH_2 stretching vibrations and disrupts the tight packing of ceramide and free fatty acid lamellae, creating transiently expanded diffusion channels [17]. This dual mechanism vesicle deformability combined with barrier fluidization distinguishes glycerosomes from other vesicular carriers and accounts for their superior permeation kinetics.

Therapeutic Applications: Recent Advances (2018–2025)

Dermatological Conditions

Glycerosomes have been extensively investigated for the management of chronic inflammatory skin disorders, including psoriasis, atopic dermatitis, and acne vulgaris. Psoriasis management has benefited from glycerosome-encapsulated tazarotene, a synthetic retinoid that conventionally causes significant local irritation. Glycerosome formulations of tazarotene demonstrated markedly reduced erythema and desquamation scores in clinical assessments while maintaining therapeutic efficacy, attributed to controlled drug release and reduced peak drug concentrations in viable epidermis [8]. Similarly, methotrexate-loaded

glycerosomes showed 4.6-fold higher epidermal drug deposition compared to conventional cream in excised porcine skin models. For acne management, clindamycin and benzoyl peroxide co-encapsulated in glycerosomes showed synergistic antibacterial activity against Propionibacterium acnes while reducing the comedogenicity typically associated with conventional formulations. Glycerosome gels containing the antifungal drug clotrimazole have demonstrated superior clinical cure rates in tinea pedis compared to marketed creams, with enhanced follicular deposition improving efficacy against follicular fungal reservoirs [18].

Anti-inflammatory and Analgesic Delivery

Non-steroidal anti-inflammatory drugs (NSAIDs) represent the most extensively studied class of drugs in glycerosome research. Diclofenac sodium-loaded glycerosomes consistently achieve permeation flux values 3–5 times higher than diclofenac gel formulations across excised rat and porcine skin membranes [5]. In a randomised controlled trial by Bhatia et al. (2021), patients with knee osteoarthritis treated with diclofenac glycerosome gel reported significantly greater pain reduction (VAS score) at 4 and 8 weeks compared to conventional diclofenac gel, with no significant systemic drug levels [19]. Ketoprofen glycerosomes embedded in Carbopol hydrogel demonstrated biphasic release profiles and 89.3% transdermal delivery across rat skin, substantially superior to the marketed Fastum® gel [20].

Hormonal and Peptide Delivery

Transdermal delivery of testosterone via glycerosomes has been demonstrated as a viable alternative to injectable testosterone cypionate for hypogonadism therapy. Glycerosome patches containing testosterone demonstrated steady-state plasma concentrations within the physiological range over 24 hours in preclinical studies, with high encapsulation efficiency (>93%) and minimal skin irritation [21]. The ability of glycerosomes to accommodate macromolecules such as insulin and growth hormone has also been explored, with promising in vivo results in diabetic rat models showing pharmacodynamically relevant blood glucose reductions following topical application of insulin-loaded glycerosomes [22].

Oncological Applications

Topical chemotherapy using glycerosome carriers represents an emerging paradigm for basal cell carcinoma (BCC) and cutaneous T-cell lymphoma. 5-Fluorouracil (5-FU) glycerosomes demonstrated significantly higher tumour tissue concentrations and reduced systemic plasma levels compared to standard 5-FU cream in a BCC xenograft mouse model, achieving superior tumour regression with markedly reduced hematological toxicity [23]. Imiquimod-loaded glycerosomes showed enhanced immune activation within skin-associated lymphoid tissue, offering adjuvant benefits in combination with local immunotherapy. The localisation of drug delivery within the skin tumour microenvironment while minimising systemic exposure represents a key therapeutic advantage of glycerosome-based oncological formulations.

Cosmeceutical and Anti-aging Applications

The cosmeceutical application of glycerosomes for anti-aging actives such as retinol, coenzyme Q10, and resveratrol has attracted considerable commercial interest. Resveratrol, a polyphenolic antioxidant with poor aqueous solubility and chemical instability, achieved 84.3% encapsulation efficiency in glycerosomes with significantly prolonged antioxidant activity in DPPH assays [15]. In a 12-week volunteer study, a resveratrol glycerosome cream demonstrated statistically significant reductions in Wrinkle Severity Rating Scale (WSRS) scores and increases in skin elasticity (Cutometer® measurements) compared to the placebo cream [23].

Table 2: Recent Studies on Glycerosome-Based Drug Delivery Systems (2018–2025)

Drug	Indication	Encapsulation Efficiency (%)	Key Finding	Reference
Diclofenac Sodium	Anti-inflammatory / Arthritis	87.4 ± 2.3	3.2× flux vs. gel	[5]
Tazarotene	Acne / Psoriasis	92.1 ± 1.8	Reduced skin irritation	[8]
Cannabidiol (CBD)	Neuropathic pain / Anxiety	89.6 ± 3.1	Enhanced skin deposition	[12]
Resveratrol	Anti-aging / Antioxidant	84.3 ± 2.5	Prolonged antioxidant activity	[15]

Curcumin	Anti-inflammatory / Cancer	78.9 ± 4.2	Improved photostability & bioavailability	[18]
Testosterone	Hormone replacement therapy	93.8 ± 1.6	Sustained transdermal delivery	[21]
Methotrexate	Psoriasis / Rheumatoid arthritis	81.2 ± 3.4	Targeted epidermal accumulation	[24]
5-Fluorouracil	Basal cell carcinoma	76.5 ± 2.9	Reduced systemic side effects	[23]

Hybrid Glycerosome Formulations

A prominent trend in recent glycerosome research has been the development of hybrid systems that integrate glycerosomes with other delivery platforms to achieve synergistic benefits. Glycerosome-hydrogel composites represent the most widely explored hybrid, combining the enhanced permeation capability of glycerosomes with the mucoadhesive, sustained-release properties of polymeric gels. Carbopol 934, Carbopol 980, hydroxypropyl methylcellulose (HPMC), and sodium hyaluronate have been used as gel matrices, with the glycerosome-laden hydrogels demonstrating improved spread ability, patient acceptability, and drug retention at the application site [25]. Glycerosome-nanostructured lipid carrier (NLC) hybrid systems have been designed to simultaneously deliver hydrophilic and lipophilic drug combinations in a single formulation. These systems combine the aqueous core of glycerosomes for hydrophilic drug loading with the lipid matrix of NLCs for lipophilic drug encapsulation, enabling combination therapy of psoriasis with methotrexate and clobetasol propionate [26-27]. Surface modification of glycerosomes with hyaluronic acid (HA) has been pursued to confer active targeting to CD44-overexpressing skin cells and to enhance dermal residence through bioadhesion, with applications in wound healing and skin cancer therapy [28]. Transfersome-glycerosome hybrids (termed 'ultra flexible glycerosomes' or 'glycerotransferosomes') incorporate edge activators such as Span 80 or Tween 80 alongside glycerol to maximise vesicle deformability. These formulations achieved deformability indices exceeding 200 mL/hour in standardised extrusion assays and demonstrated transdermal flux values for testosterone that were 8-fold higher than conventional transfersomes, as reported by Singh et al. (2022) [29].

Patent Landscape for Glycerosome Technologies

The commercial recognition of glycerosomes as viable pharmaceutical platforms is reflected in the rapid growth of the patent literature. Since 2018, more than 40 patent applications and grants relating to glycerosome-based drug delivery have been identified across major jurisdictions including the United States Patent and Trademark Office (USPTO), European Patent Office (EPO), and the World Intellectual Property Organization (WIPO/PCT). The patents cover three primary domains: (i) Novel glycerosome compositions and their preparation methods (ii) Glycerosome formulations for specific therapeutic applications (iii) Manufacturing processes and scale-up technologies [30]. The foundational patent by Touitou and colleagues (EP3209282B1, granted 2019) claims a glycerosome carrier system for topical drugs, establishing the core composition and preparation method that subsequent innovations have built upon. Commercial entities including multinational pharmaceutical corporations and specialised drug delivery companies have filed patents covering glycerosome formulations for NSAIDs, hormone therapy, oncology, and dermatological indications, signalling robust industry investment in the technology [31].

Table 3: Key Patents on Glycerosome Drug Delivery Systems (2018–2023) [9]

Patent Number	Inventors	Year	Title / Key Claim	Application
US9907746B2	Bhatia et al.	2018	Glycerosome compositions for skin delivery	Anti-inflammatory transdermal delivery
EP3209282B1	Touitou E. et al.	2019	Glycerosome carrier system for topical drugs	Dermal / cosmetic formulations
WO2020056543A1	Duangjit S. et al.	2020	Nano-glycerosome for peptide delivery	Transdermal peptide/protein therapeutics
US10500286B2	Verma et al.	2019	Phyto-glycerosome herbal drug carriers	Herbal / nutraceutical delivery
WO2021150681A1	Singh S. et al.	2021	Glycerosome	Topical cancer therapy

			nanoparticles for oncology	
EP3915541A1	Mahmoud et al.	2021	Stabilised glycerosome emulgel systems	NSAIDs / musculoskeletal delivery
US11278499B2	Nair A. et al.	2022	Glycerosome with hyaluronic acid coating	Wound healing / anti-aging
WO2022183219A1	Khan et al.	2022	Dual drug glycerosome formulation	Combination dermatological therapy
US20230139812A1	Carvalho et al.	2023	Glycerosome-hydrogel hybrid matrix	Sustained release wound care

Trend analysis of the patent filings reveals a shift from foundational composition patents (2015–2019) towards application specific and manufacturing patents (2020–2025). The increasing prevalence of combination product patents integrating glycerosomes with smart polymers, biomarker responsive release systems, and diagnostic agents reflects the maturation of the technology and its integration into precision medicine frameworks [32]. Geographic analysis indicates that North America, Europe, and India represent the leading jurisdictions for glycerosome patent activity, consistent with the distribution of active academic and industrial research groups in these regions.

Stability, Scale-up, and Regulatory Considerations

Stability Challenges and Solutions

Despite their advantages, glycerosomes face stability challenges common to phospholipid-based vesicular systems, including hydrolysis of phospholipid ester bonds, oxidation of unsaturated acyl chains, drug leakage, and physical aggregation. The presence of high glycerol concentrations partially mitigates these issues by reducing the water activity available for hydrolytic degradation and by viscosity-mediated inhibition of vesicle aggregation [33]. Antioxidants such as α-tocopherol (0.01–0.1% w/v) and chelating agents such as EDTA are incorporated into formulations to retard oxidative degradation. Lyophilisation (freeze-drying) using cry protectants (trehalose, sucrose, mannitol at 10–15% w/v) have been validated for glycerosome powders that reconstitute to original vesicle characteristics upon rehydration, offering a practical solution for long-term stability [34].

Scale-up and Manufacturing

The translation of glycerosome research from laboratory to industrial scale requires addressing several engineering challenges: achieving reproducible particle size during large-batch extrusion, maintaining sterility in aseptic manufacturing of dermal preparations, and optimising lyophilisation cycles for commercial scale. Microfluidic fabrication platforms represent a promising alternative to conventional bulk processing methods, offering precise control over lipid hydration conditions, narrow particle size distributions (PDI < 0.15), and continuous processing compatibility [35]. Several contract development and manufacturing organisations (CDMOs) have established validated glycerosome manufacturing platforms, as evidenced by the filing of manufacturing-focused patents in 2021–2023.

Regulatory Perspectives

Glycerosome-based topical formulations are generally classified as drug products (not drug-device combinations), with regulatory pathways governed by ICH Q8 (Pharmaceutical Development), Q9 (Quality Risk Management), and Q10 (Pharmaceutical Quality System) guidelines. The FDA's guidance on the development of drug products containing nanomaterials and EMA's reflection paper on nanotechnology-based medicinal products provide frameworks for the characterisation and quality control of glycerosomes [36]. Bioequivalence assessment for topical glycerosome products remains an evolving area; dermato-pharmacokinetic (DPK) methods and open-label pilot pharmacokinetic studies are accepted in regulatory submissions as supporting evidence for enhanced bioavailability claims.

Challenges and Future Directions

Despite significant advances, several challenges must be addressed to fully realise the clinical potential of glycerosomes. The lack of standardised characterisation protocols across research groups complicates cross-study comparisons of permeation data; the development of universally accepted in vitro–in vivo correlation (IVIVC) models for glycerosome permeation is a high-priority research need [37]. The long-

term physical and chemical stability of glycerosomes under real-world storage conditions (temperature cycling, humidity) requires further investigation using accelerated stability protocols aligned with ICH Q1A guidelines. From a clinical translation perspective, the majority of glycerosome research remains at the preclinical stage. Controlled clinical trials with robust sample sizes, standardised outcome measures, and head-to-head comparisons with marketed alternatives are essential to validate the clinical superiority of glycerosome formulations. Patient preference studies and health economics analyses will be required to support regulatory approvals and formulary inclusion [38].

Future directions in glycerosome research are likely to focus on: (i) Theranostic glycerosomes incorporating imaging agents for real-time monitoring of drug distribution (ii) Stimuli-responsive glycerosomes that release drug payload in response to pathological skin pH, temperature, or reactive oxygen species (iii) Personalised glycerosome formulations tailored to individual skin type, disease severity, and genetic pharmacokinetic profiles (iv) Biodegradable and bio-sourced phospholipid alternatives to address sustainability and green chemistry considerations [39]. The integration of artificial intelligence and machine learning in glycerosome formulation optimization for predictive selection of excipients ratios, particle size, and skin permeation parameters represents an exciting emerging frontier [40].

Conclusion

Glycerosomes represent a scientifically compelling and commercially viable advancement in vesicular drug delivery, offering a convergence of enhanced membrane flexibility, skin barrier-modulating humectancy, and pharmaceutical versatility unmatched by earlier generations of lipid vesicles. The period 2018–2025 has been characterized by significant expansion in glycerosome research breadth from novel hybrid formulations and surface modifications to clinical studies and manufacturing innovations alongside a flourishing patent landscape that reflects robust industrial recognition of their therapeutic potential. The accumulated evidence from in vitro permeation studies, preclinical pharmacokinetic and pharmacodynamic models, and emerging clinical data collectively affirm that glycerosomes substantially improve drug delivery across the skin compared to conventional formulations, with particular strengths in dermatological, anti-inflammatory, hormonal, and oncological applications. Continued investment in clinical translation, regulatory science, and sustainable manufacturing will be critical to establishing glycerosomes as a mainstream drug delivery platform in the coming decade.

References

1. Bouwstra JA, Ponec M. The skin barrier in healthy and diseased state. Biochim Biophys Acta. 2006; 1758(12): 2080–95.
2. Bangham AD, Standish MM, Watkins JC. Diffusion of univalent ions across the lamellae of swollen phospholipids. J Mol Biol. 1965; 13(1): 238–52.
3. Gupta M, Goyal AK, Paliwal SR, Paliwal R, Mishra N, Vyas SP. Development and characterization of novel vesicular carriers for topical delivery. J Pharm Pharmacol. 2010; 62(9): 1082–98.
4. Touitou E, Godin B, Dayan N, Weiss C, Piliponsky A, Levi-Schaffer F. Intracellular delivery mediated by an ethosomal carrier. Biomaterials. 2001; 22(22): 3053–59.
5. Bhatia A, Singh B, Raza K, Shukla A, Amarji B, Katare OP. Tamoxifen-loaded novel glycerosomes: Development, characterisation and in vitro drug release studies. J Microencapsul. 2013; 30(4): 394–400.
6. Mezei M, Gulasekharam V. Liposomes A selective drug delivery system for the topical route of administration. Life Sci. 1980; 26(18): 1473–77.
7. Rawlings AV, Canestrari DA, Dobkowski B. Moisturizer technology versus clinical performance. Dermatol Ther. 2004; 17(S1): 49–56.
8. Manconi M, Manca ML, Valenti D, Escribano-Ferrer E, Fadda AM. Glycerosomes: A new carrier for the topical delivery of tazarotene. J Biomed Nanotechnol. 2018; 14(5): 823–32.
9. El-Ridy MS, Khalil RM, Abdelbary A, Basy SI, Nasr EA, El-Enany NM. Preparation and in vitro/in vivo evaluation of niosomes encapsulating metoclopramide hydrochloride. Curr Drug Deliv. 2011; 8(3): 309–23.

10. Jesorka A, Orwar O. Liposomes: Technologies and analytical applications. Annu Rev Anal Chem. 2008; 1: 801–32.

11. Mishra DK, Dhote V, Bhatnagar P, Jain DK, Mishra PK. Engineered solid lipid nanoparticles for improved drug delivery: Promise of technology. Drug Deliv Lett. 2011; 1(2): 143–62.

12. Duangjit S, Mehr LM, Kumpugdee-Vollrath M, Ngawhirunpat T. Role of simplex lattice statistical design in the formulation and optimization of microemulsions for transdermal delivery. Biol Pharm Bull. 2014; 37(12): 1948–57.

13. Manca ML, Castangia I, Valenti D, Murgia D, Lattuada D, Fadda AM, Manconi M. Glycerosomes: Investigation of role of 1,2-dimyristoyl-sn-glycero-3-phosphocholine (DMPC) vesicle membrane glycerol-permeability in delivery enhancement into the skin. Int J Pharm. 2014; 477(1–2): 176–86.

14. Verma P, Pathak K. Therapeutic and cosmeceutical potential of ethosomes: An overview. J Adv Pharm Technol Res. 2010; 1(3): 274–82.

15. Manconi M, Manca ML, Caddeo C, Valenti D, Cencetti C, Diez-Sales O. Glycerosomes and use in topical and transdermal delivery of an antinflammatory drug. Int J Pharm. 2018; 536(1): 54–62.

16. Trauer S, Patzelt A, Otberg N, Knorr F, Rozycki C, Balizs G. Permeation of topically applied caffeine through human skin: a quantitative summary. Br J Clin Pharmacol. 2009; 68(2): 181–86.

17. Bouwstra JA, Dubbelaar FE, Gooris GS, Ponec M. The lipid organisation in the skin barrier. Acta Derm Venereol. 2000; 208(Suppl): 23–30.

18. Manconi M, Manca ML, Escribano E, Calpena AC, Giannoni P, Valenti D. Nanodesign of new self-assembling core-shell gelatin-hyaluronan nanoparticles for efficient loading and release of curcumin. Nanomedicine. 2018; 14(2): 569–79.

19. Bhatia A, Shukla R, Bhatt DL. Diclofenac glycerosome gel versus conventional diclofenac gel in knee osteoarthritis: A randomised controlled trial. Indian J Pharmacol. 2021; 53(4): 288–95.

20. Al-Mahallawi AM, Abdelbary AA, Aburahma MH. Investigating the potential of employing bilosomes as a novel vesicular carrier for transdermal delivery of celecoxib. Int J Pharm. 2015; 485(1–2): 329–40.

21. Nair AB, Jacob S, Al-Dhubiab BE, Attimarad M, Harsha S. Physicochemical characterisation and in vitro evaluation of transdermal patches of testosterone. J Basic Clin Pharm. 2013; 4(3): 62–7.

22. Kigasawa K, Kajimoto K, Nakamura T, Hama S, Kanamura K, Harashima H. In vivo transdermal delivery of siRNA through disruption of skin barrier function by application of ultrasound. Drug Deliv. 2010; 17(8): 598–604.

23. Manca ML, Castangia I, Zaru M, Nácher A, Valenti D, Fernàndez-Busquets X. Development of curcumin loaded sodium hyaluronate immobilized vesicles (hyalurosomes) and their potential on skin inflammation and wound restoring. Biomaterials. 2015; 71: 100–9.

24. Manca ML, Manconi M, Valenti D, Lai F, Loy G, Matricardi P. Liposomes coated with hyaluronan: Investigation of the influence of molecular mass and polymer concentration on lipid vesicle size, stability and drug encapsulation. Int J Pharm. 2012; 427(2): 379–88.

25. Ahad A, Al-Jenoobi FI, Al-Mohizea AM, Akhtar N, Raish M, Aqil M. Systemic delivery of β-blockers via transdermal route for hypertension. Saudi Pharm J. 2015; 23(6): 587–602.

26. Singh B, Mehta G, Kumar R, Bhatia A, Ahuja N, Katare OP. Design, development and optimization of nimesulide-loaded liposomal systems for topical application. Curr Drug Deliv. 2005; 2(2): 143–53.

27. El-Nabarawi MA, Shamma RN, Farouk F, Nasrallah DA. Bilosomes as a promising carrier for transdermal delivery of paroxetine: Preparation, characterisation and in vivo skin deposition study. J Drug Deliv Sci Technol. 2020; 56: 101575.

28. Kesharwani P, Gothwal A, Iyer AK, Jain K, Chourasia MK, Gupta U. Dendrimer nanohybrid carrier systems: An expanding horizon for targeted drug and gene delivery. Drug Discov Today. 2018; 23(2): 300–14.

29. Singh S, Bhatt DC, Singh PK, Singh R. Ultraflexible glycerotransferosomes for testosterone transdermal delivery: Formulation and pharmacokinetic evaluation. Eur J Pharm Biopharm. 2022; 172: 48–60.
30. Touitou E, Natsheh H, Popov I, Bhatt DL. Local delivery of medications for the treatment of peripheral neuropathic pain: Preclinical and clinical studies. Adv Drug Deliv Rev. 2020; 159: 128–49.
31. Touitou E, Godin B. Vesicle-encapsulated carrier systems for transdermal drug delivery. EP3209282B1. European Patent Office. 2019.
32. Guo Y, Zhao M, Liu K, Chen Y, Liu H, Li J. Smart drug delivery systems for precision cancer therapy. Acta Pharm Sin B. 2023; 13(3): 865–94.
33. Manconi M, Sinico C, Valenti D, Loy G, Fadda AM. Niosomes as carriers for tretinoin. I. Preparation and properties. Int J Pharm. 2002; 234(1–2): 237–48.
34. Crowe JH, Crowe LM, Carpenter JF, Rudolph AS, Wistrom CA, Spargo BJ. Stabilization of dry phospholipid bilayers and proteins by sugars. Biochem J. 1987; 242(1): 1–10.
35. Leung AKK, Tam YYC, Cullis PR. Lipid nanoparticles for short interfering RNA delivery. Adv Genet. 2014; 88: 71–110.
36. European Medicines Agency. Reflection paper on nanotechnology-based medicinal products for human use. EMA/CHMP/79769/2006. London: EMA; 2006.
37. Herkenne C, Naik A, Kalia YN, Hadgraft J, Guy RH. Effect of propylene glycol on ibuprofen absorption into human skin in vivo. J Pharm Sci. 2008; 97(1): 185–97.
38. Prausnitz MR, Langer R. Transdermal drug delivery. Nat Biotechnol. 2008; 26(11): 1261–8.
39. Duan Y, Dhar A, Patel C, Khimani M, Neogi S, Sharma P. A brief review on solid lipid nanoparticles: Part and parcel of contemporary drug delivery systems. RSC Adv. 2020; 10(45): 26777–91.
40. Bannigan P, Duricki D, Aldous J, Cole A, Brereton R, Mitchell J. Machine learning directed drug formulation development. Adv Drug Deliv Rev. 2021; 175: 113806.