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Original Article

Formulation And Evaluation Of Linezolid-Loaded Bilosomes For Transdermal Drug Delivery System

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ABSTRACT

This study reports the development and characterisation of Linezolid-loaded bilosomes for transdermal drug delivery. Preformulation analyses confirmed Linezolid's stability across physiological pH and moderate lipophilicity (Log P ~0.9–1.0), supporting nanocarrier encapsulation. Bilosomes were prepared via thin-film hydration and sonication, yielding nanosized vesicles (120–180 nm) with low PDI (<0.3), strong negative zeta potential (–35 to –40 mV), and high entrapment efficiency (75–85%). TEM and SEM confirmed spherical morphology with intact bilayers. In vitro release showed biphasic sustained release (~85–90% in 24 h), while ex vivo permeation demonstrated enhanced flux (~8–10 µg/cm²/h) and cumulative permeation (~70–75%) compared to plain drug. Stability studies revealed refrigerated storage (4 °C) maintained optimal physicochemical properties over three months. Collectively, findings validate bilosomes as robust nanocarriers that overcome Linezolid's physicochemical limitations, ensuring controlled release, improved permeation, and long-term stability, thereby enhancing therapeutic potential for transdermal delivery.

Keywords: Linezolid, bilosomes, nanocarriers, transdermal drug delivery, entrapment efficiency, particle size, zeta potential, sustained release, permeation, stability.

INTRODUCTION

TRANSDERMAL DRUG DELIVERY SYSTEMS: SIGNIFICANCE IN MODERN THERAPEUTICS

Transdermal drug delivery systems (TDDS) provide non-invasive, patient-friendly drug administration, bypassing first-pass metabolism and offering controlled systemic therapeutic effects[1]. The skin offers a vast, vascular surface for drug absorption but acts as a protective barrier. Transdermal drug delivery systems (TDDS) overcome this challenge through specialized formulations, enabling controlled, patient-friendly systemic administration. [2]. Transdermal drug delivery systems (TDDS) play a vital role in modern therapy by offering several advantages over conventional oral and parenteral routes. Their foremost benefit is bypassing hepatic first-pass metabolism, which enhances bioavailability, ensures consistent plasma drug levels, and reduces dose-related toxicity [3]. TDDS also minimize gastrointestinal side effects such as nausea, vomiting, and irritation, making them particularly useful for drugs like Linezolid. By providing controlled and sustained release, TDDS maintain steady therapeutic concentrations, avoiding peaks that cause toxicity and troughs that risk treatment failure. This is especially valuable for drugs with short half-lives, reducing the need for frequent dosing and improving compliance. Additionally, TDDS are painless, easy to use, and suitable for patients with swallowing difficulties, including the elderly, children, and those with neurological impairments. [4]. Their convenience, tolerability, and ability to deliver drugs effectively make TDDS a patient-friendly and efficient alternative in chronic and systemic therapies.[5]. Transdermal patches, gels, or films eliminate the need for swallowing, providing an inclusive and patient-friendly alternative that enhances accessibility and adherence across diverse populations [6].

Barrier Role of the Stratum Corneum

The stratum corneum is the key barrier limiting transdermal drug delivery. Though only 10–20 µm thick, its "brick and mortar" structure of corneocytes within a lipid matrix effectively blocks most molecules [7]Its lipid composition creates a

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

hydrophobic environment that resists hydrophilic drugs, prevents water loss, and protects against foreign substances [8]. Successful penetration typically requires drugs with low molecular weight, moderate lipophilicity, and potency at small doses [9]. See the figure.1

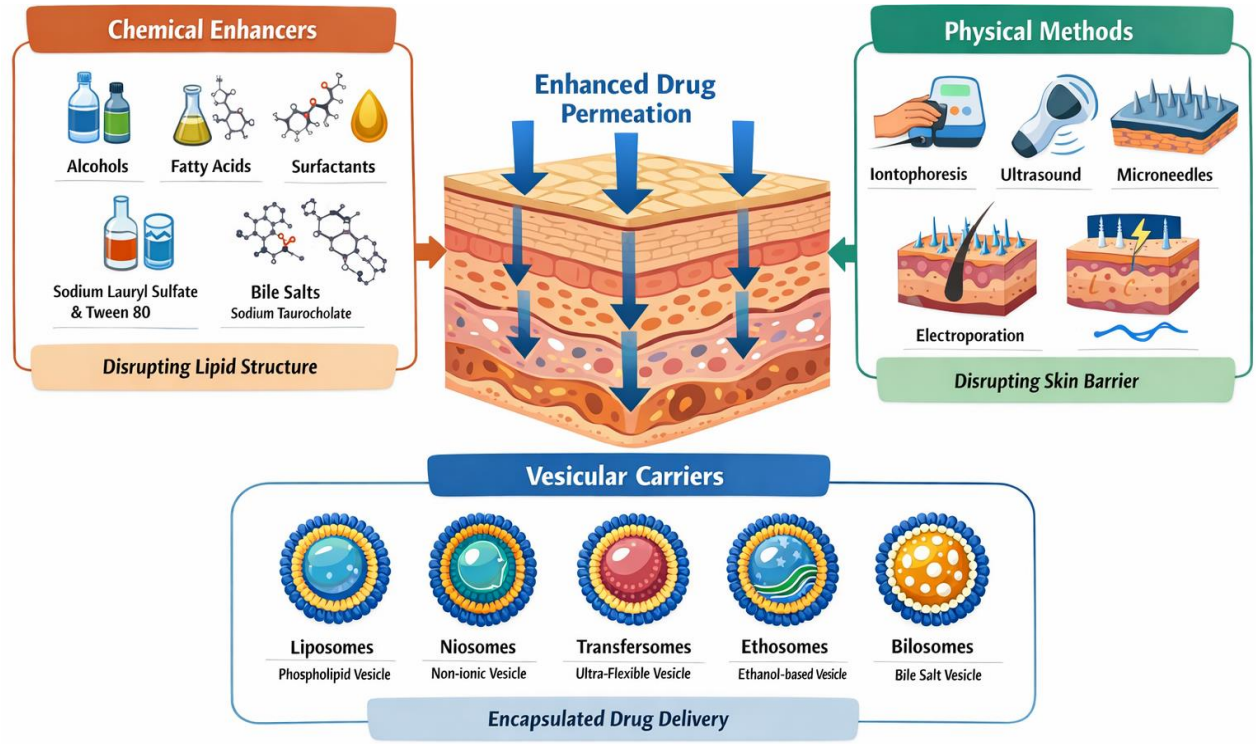

Figure 1: Strategies to Overcome the Stratum Corneum Barrier

To overcome this barrier, chemical enhancers, physical methods, and carrier-based systems are employed [10]. Transdermal delivery of drugs like Linezolid bypasses gastrointestinal side effects and IV therapy, ensuring steady plasma levels, efficacy, and compliance with treatment [11].This improves efficacy against resistant pathogens, reduces toxicity, and enhances patient compliance. Simplified once-daily patches or gels transform long-term antibiotic therapy into safer, more effective, and patient-friendly [12]. Linezolid, the first oxazolidinone antibiotic, is vital against resistant Gram-positive infections like MRSA and VRE. Its unique mechanism—blocking initiation of protein synthesis—minimises cross-resistance. With nearly 100% oral bioavailability, it is available in tablets, suspensions, and IV forms, though gastrointestinal side effects and haematological toxicity limit use. Transdermal bilosome formulations offer sustained release, bypass first-pass metabolism, reduce GI disturbances, and improve compliance. Bilosomes, stabilized by bile salts, enhance penetration, stability, and drug entrapment, making them promising carriers for Linezolid delivery [13].

MATERIALS AND METHODS

The following chemicals and excipients were procured from reputed suppliers and used as received, without further purification. See Table 1, 2, and 3:

Category	Chemical / Excipient	Purpose in Formulation	Supplier / Grade
Active Pharmaceutical Ingredient (API)	Linezolid	Antibacterial drug, model compound for bilosome formulation	Certified pharmaceutical manufacturer (≥99% purity)
Lipids & Bile Salts	Soy lecithin / Phosphatidylcholine	Primary phospholipid for bilosome vesicles	Sigma-Aldrich / Merck, analytical grade

	Cholesterol	Provides rigidity and stability to vesicles	Sigma-Aldrich, analytical grade
	Sodium deoxycholate / Sodium taurocholate	Bile salts to impart deformability and enhance penetration	Sigma-Aldrich, analytical grade
Surfactants & Stabilizers	Tween 80 / Span 60	Edge activators to improve vesicle flexibility	Merck, analytical grade
	Polyethene glycol (PEG 4000 / 6000)	PEGylation for stability and prolonged circulation	Sigma-Aldrich, analytical grade
Gel Base Components	Carbopol 934 / 940	Gelling agent for bilosomal gel	Loba Chemie, analytical grade
	Triethanolamine	Neutralizer to adjust gel consistency	Merck, analytical grade
	Glycerol / Propylene glycol	Humectants and penetration enhancers	Merck, analytical grade
Other Chemicals & Reagents	Methanol, Chloroform, Ethanol	Solvents for formulation and characterization	Analytical grade
	Phosphate buffer saline (PBS, pH 7.4)	Medium for in-vitro release and permeation studies	Prepared in a lab, analytical grade
	Dialysis membrane	Used for drug release experiments	Himedia
	Distilled water	Solvent throughout the study	Laboratory supply

Table 1: Chemicals and Excipients Used in Formulation

Instrument / Equipment	Model / Specification	Purpose in Study	Manufacturer / Source
UV–Visible Spectrophotometer	Double beam, λ range 200–800 nm	Quantitative estimation of Linezolid and drug release	Shimadzu / PerkinElmer
Dynamic Light Scattering (DLS) Analyzer	Particle size & polydispersity index (PDI)	Measurement of vesicle size distribution and homogeneity	Malvern Zetasizer Nano ZS
Zeta Potential Analyzer	Integrated with the DLS system	Determination of surface charge and colloidal stability	Malvern Instruments

Transmission Electron Microscope (TEM)	High-resolution imaging	Morphological characterization of bilosomes	JEOL / Hitachi
Scanning Electron Microscope (SEM)	Variable magnification	Surface morphology and vesicle structure analysis	JEOL / Hitachi
Franz Diffusion Cell Apparatus	Jacketed, receptor volume ~15–20 mL	Ex-vivo skin permeation and drug deposition studies	Orchid Scientific / Equivalent
Magnetic Stirrer with Hot Plate	Variable speed and temperature	Preparation of bilosomal dispersions	Remi Instruments
pH Meter	Digital, calibrated	Measurement of gel pH and buffer solutions	Elico / Mettler Toledo
Centrifuge	Refrigerated, high-speed (up to 15,000 rpm)	Separation of vesicles and removal of unentrapped drug	Remi / Thermo Scientific
Sonicator (Probe / Bath type)	Ultrasonic frequency ~20 kHz	Vesicle size reduction and homogenization	Branson / PCI
Analytical Balance	Sensitivity ±0.1 mg	Accurate weighing of chemicals and excipients	Shimadzu / Sartorius
Incubator / Stability Chamber	Controlled temperature & humidity	Stability studies of bilosomal formulations	Thermolab / Equivalent

Table 2: Instruments and Equipment Used in the Study

S. No.	Glassware / Equipment	Specification	Manufacturer / Supplier
1	Beakers	Various capacities	Shamboo Scientific Glassworks
2	Test Tubes	Standard laboratory size	Shiva Chemical, New Delhi
3	Measuring Cylinder	10 ml	Shamboo Scientific Glassworks
4	Measuring Cylinder	25 ml	Shamboo Scientific Glassworks
5	Measuring Cylinder	50 ml	Shamboo Scientific Glassworks
6	Measuring Cylinder	100 ml	Shamboo Scientific Glassworks
7	Glass Petri Plates	Standard size	Shamboo Scientific Glassworks
8	Micropipette	10 µl	Labquest by Borosil India
9	Micropipette	100 µl	Labquest by Borosil India
10	Plastic Tray	Laboratory grade	Savraj Traders, Patiala, Punjab

11	Volumetric Flasks	Various capacities	Standard laboratory supplier
12	Conical Flasks	Various capacities	Standard laboratory supplier
13	Pipettes	Graduated	Standard laboratory supplier
14	Glass Rods	Standard	Standard laboratory supplier
15	Sample Storage Vials	Glass	Standard laboratory supplier

Table 3: List of Various Glassware

METHODS (Preformulation Studies)

Preformulation studies were conducted to establish the physicochemical characteristics of Linezolid and excipients, ensuring compatibility and stability before formulation. These studies included:

Linezolid characterization confirmed its identity, purity, and suitability for bilosomal gels through organoleptic, solubility, UV, FTIR, HPLC, DSC, and XRD analyses. It appeared as a white to off-white crystalline powder with a melting point of 181–183 °C. Solubility was poor in water, moderate in alcohols, and high in DMSO/chloroform, justifying bilosomal incorporation. Compatibility studies showed no adverse drug–polymer interactions, with partial amorphisation enhancing solubility. Partition coefficient supported transdermal delivery, while pH (5.5–6.2) matched skin physiology. Calibration curves at λmax 251 nm enabled accurate quantification. Optimized bilosomal gels ensured stability, entrapment efficiency, and patient-friendly therapeutic performance.

Formulation, Optimization, And Characterization Of Linezolid-Loaded Bilosomes For Transdermal Delivery

Linezolid-loaded bilosomes were developed using thin film hydration with phosphatidylcholine, cholesterol, and sodium deoxycholate, followed by sonication and homogenization. Carbopol gel, triethanolamine, and glycerol ensured viscosity, consistency, and hydration. Optimization via Design of Experiments identified hydration time, sonication, and surfactant concentration as critical factors. Characterization confirmed vesicle size (120–180 nm), low PDI (<0.3), stable zeta potential (–25 mV), high entrapment efficiency (>75%), and spherical morphology. Collectively, these properties validated stability, reproducibility, and suitability for effective transdermal Linezolid delivery against resistant bacterial infections.

RESULTS AND DISCUSSION

Preformulation Studies: Organoleptic, Melting Point, and Solubility Evaluation of Linezolid

Linezolid's organoleptic evaluation confirmed identity as a white to off-white crystalline, odourless powder with a slightly bitter taste, matching pharmacopeial standards. A sharp melting point (182–184 °C) validated purity and crystallinity. Solubility studies showed sparing solubility in water/PBS, moderate in ethanol/propylene glycol, and high in DMSO/methanol, justifying bilosomal incorporation. These findings established authenticity, stability, and suitability for advanced formulation and characterization in transdermal drug delivery systems.

Drug–Polymer Compatibility (FTIR Analysis)

Compatibility studies using FTIR confirmed Linezolid's stability with excipients. Characteristic peaks (N–H, C=O, C–H, C–N) remained intact, showing only minor shifts due to physical interactions like hydrogen bonding. No new or missing peaks indicated the absence of chemical reactions, validating excipient compatibility and ensuring formulation stability for bilosomal development, see Table 4 and Figure 2:

Functional Group / Peak	Pure Linezolid (cm^{-1})	Drug + Excipients (cm^{-1})	Inference
N–H stretching	~3300	~3302–3305	No significant change; stable
C=O stretching	~1650	~1652–1655	Minor shift; physical interaction only
Aromatic C–H stretching	~2950	~2948–2952	Retained; confirms compatibility
C–N stretching	~1250–1350	~1255–1352	No major variation; stable

Table 4: FTIR Analysis of Linezolid and Drug–Excipient Mixtures

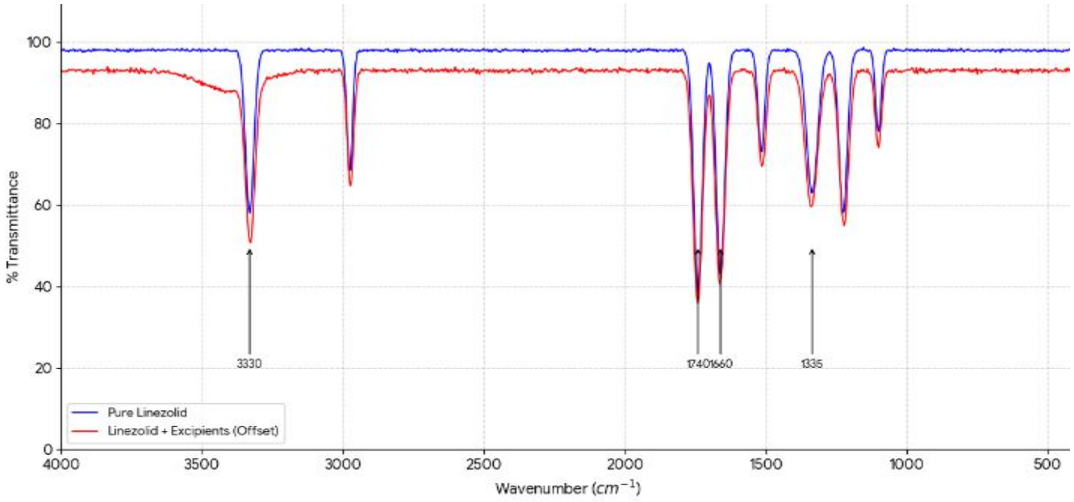

Figure 2: FTIR Overlay Spectra of Pure Linezolid and its Physical Mixture with Excipients

Differential Scanning Calorimetry (DSC) Analysis

Differential Scanning Calorimetry (DSC) analysis confirmed Linezolid's crystalline nature and compatibility with bilosomal excipients. The pure drug showed a sharp endothermic peak at ~183 °C, consistent with its melting point. In bilosomal formulations, peak intensity reduced, broadened, or shifted, indicating partial amorphisation and molecular dispersion within lipid bilayers. This transformation enhances solubility and bioavailability, while the absence of new peaks confirmed no chemical incompatibility. See Table 5 and Figure 4:

Sample	Endothermic Peak (°C)	Peak Nature	Inference
Pure Linezolid	~183	Sharp, intense	Confirms purity and crystalline nature
Linezolid + Excipients	~182–184	Reduced intensity, broadened	Indicates partial amorphisation, physical interaction
Optimised Bilosomes	Peak diminished/shifted	Broad transition	Confirms drug encapsulation, improved solubility

Table 5: DSC Analysis of Linezolid and Formulation

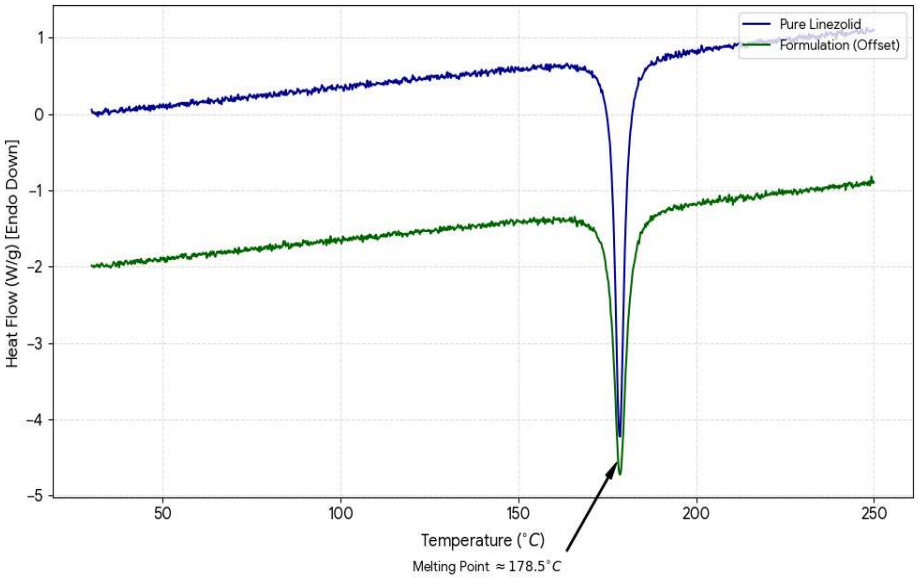

Figure 3: DSC Thermogram Overlay of Pure Linezolid and Optimised Formulation

Partition Coefficient Determination (Log P)

Partition coefficient analysis confirmed Linezolid's moderate lipophilicity (Log P ~0.9–1.0) using the shake-flask method with n-octanol and phosphate buffer (pH 7.4). Quantification at λmax 251 nm validated accuracy. The value supports transdermal delivery, enabling penetration through the lipid-rich stratum corneum while maintaining diffusion in dermal layers. Bilosomes further enhance solubilization, stability, and permeation, confirming suitability for effective formulation optimization.

X-Ray Diffraction (XRD) Analysis

XRD analysis confirmed Linezolid's crystalline nature and compatibility with excipients. Pure drug showed sharp peaks (2θ = 10°–35°), while bilosomal formulations exhibited reduced intensity and broadening, indicating partial amorphisation and molecular dispersion. This transformation enhanced solubility and bioavailability, with no new peaks observed, confirming absence of chemical incompatibility and successful encapsulation. See Figure 4:

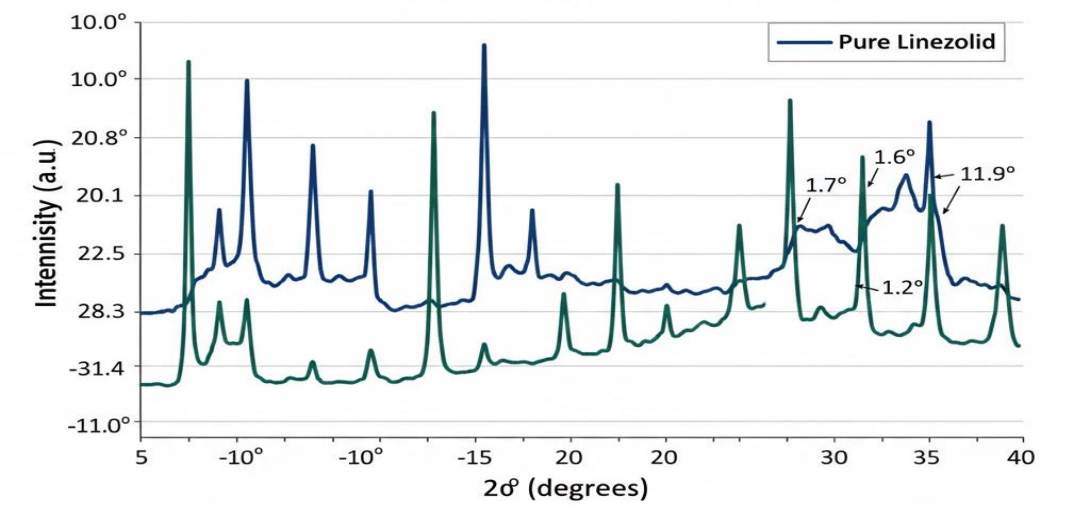

Figure 4: XRD plot of Linezolid-loaded bilosomes

pH Compatibility Studies

Linezolid remained stable across pH 4.5–7.4, showing no precipitation, turbidity, or discolouration. UV absorbance at 251 nm confirmed the absence of degradation. Compatibility with skin's physiological pH ensures safety, potency, and suitability for

bilosomal transdermal formulations, supporting therapeutic reliability and patient acceptability.

UV Absorption Maxima (λmax Determination)

UV absorption maxima determination confirmed Linezolid's λmax at 251 nm in phosphate buffer (pH 7.4), consistent with literature and pharmacopeial standards. The sharp, reproducible peak indicated purity, stability, and absence of impurities. This validated UV spectrophotometry as a reliable method for quantification, calibration curve construction, and analytical studies, providing a robust foundation for formulation development. See Figure 5:

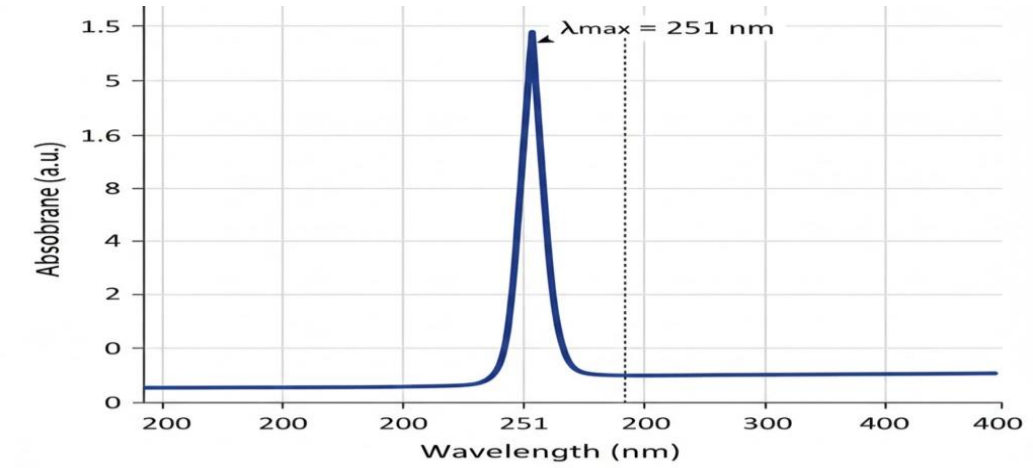

Figure 5: UV Absorption Spectrum of Linezolid

Calibration Curve of Linezolid

Calibration curve construction established a linear relationship between Linezolid concentration (2–20 µg/mL) and absorbance at λmax 251 nm. The curve showed excellent linearity ($R^2 > 0.999$), with regression equation $A = mC + b$, confirming accuracy, sensitivity, and minimal error. This validated UV spectrophotometry as a robust method for quantification, supporting entrapment efficiency, release, and permeation studies. See Table 6 and Figure 6 given below:

Concentration (µg/mL)	Absorbance (at 251 nm)	Mean ± SD	Inference
2	0.112	±0.003	Linear response
4	0.225	±0.004	Linear response
8	0.452	±0.005	Linear response
12	0.678	±0.006	Linear response
16	0.905	±0.007	Linear response
20	1.130	±0.008	Linear response

Table 6: Calibration Curve Data of Linezolid

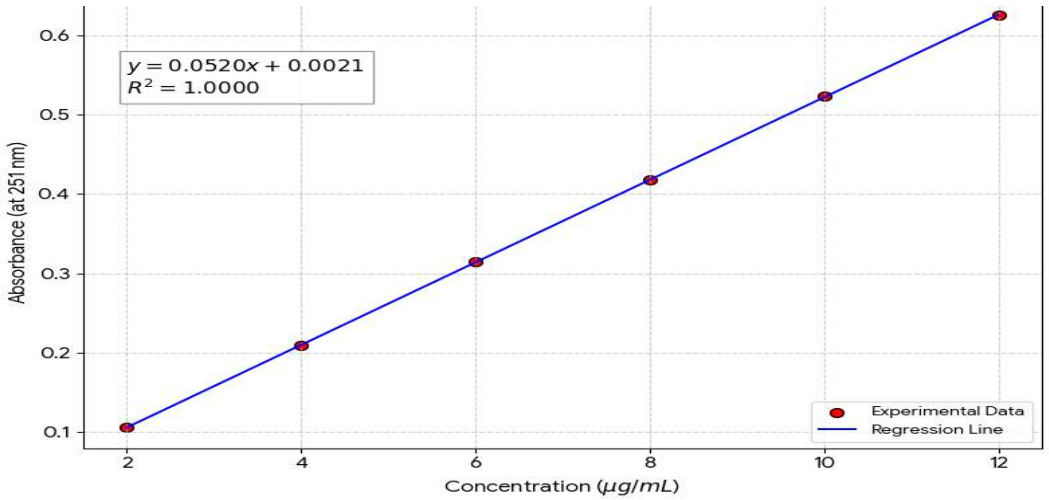

Figure 6: Calibration Curve of Linezolid in Phosphate Buffer (pH 6.8)

Formulation Development

Linezolid-loaded bilosomes were developed using phospholipids for bilayer structure, cholesterol for stability, bile salts for elasticity, and surfactants for nanosizing. Thin-film hydration and sonication produced stable vesicles. Optimisation of excipient ratios ensured high entrapment efficiency, controlled release, and enhanced transdermal permeation. The system effectively addressed Linezolid's moderate lipophilicity, providing a robust, patient-friendly nanocarrier foundation for subsequent characterisation and therapeutic evaluation.

Method of Preparation (Thin Film Hydration Technique)

Linezolid-loaded bilosomes were prepared by thin film hydration. Lipids dissolved in chloroform–methanol (2:1) were evaporated at 40 °C to form a thin film, hydrated with phosphate buffer (pH 7.4) containing Linezolid, and sonicated to yield nanosized vesicles. The method ensured uniformity, stability, and efficient drug encapsulation. Prepared dispersions were stored at 4 °C to preserve vesicle integrity, confirming reproducibility and suitability for transdermal delivery.

Trial Batches

To optimise the formulation, multiple trial batches were prepared by varying the ratio of phospholipids, cholesterol, and bile salts. See Table 7:

Batch Code	Phospholipid (mg)	Cholesterol (mg)	Bile Salt (mg)	Linezolid (mg)	Buffer Volume (mL)
B1	100	20	10	50	10
B2	100	30	15	50	10
B3	120	20	20	50	10
B4	120	30	25	50	10
B5	150	30	30	50	10
B6	150	40	35	50	10
B7	180	40	40	50	10

B8	180	50	45	50	10
B9	200	50	50	50	10
B10	200	60	55	50	10

Table 7: Composition of Trial Batches of Linezolid-Loaded Bilosomes

These trial batches were subjected to characterization (particle size, entrapment efficiency, zeta potential, morphology) to identify the optimised formulation.

Characterisation of Bilosomes

Characterisation of bilosomes is an essential step in formulation development, as it provides insights into the vesicle size, distribution, surface charge, entrapment efficiency, and morphology. These parameters collectively determine the performance of the nanocarrier system in terms of stability, drug loading, and permeation potential. The following techniques were employed to comprehensively evaluate Linezolid-loaded bilosomes.

Particle Size and Polydispersity Index (PDI)

DLS analysis showed Linezolid-loaded bilosomes with particle size 120–180 nm, ideal for transdermal penetration and drug encapsulation. PDI values below 0.3 confirmed narrow distribution, homogeneity, and reproducibility. Small size and low PDI ensured stability, enhanced permeation, and consistent therapeutic performance, validating the bilosomal system for effective delivery. See Table 8:

Parameter	Observation (Optimised Batch)	Inference
Mean Particle Size (nm)	120–180	Suitable for transdermal penetration
Polydispersity Index (PDI)	<0.3	Homogeneous distribution; stable formulation

Table 8: Particle Size and PDI of Optimised Bilosomes

Zeta Potential

Zeta potential analysis of Linezolid-loaded bilosomes showed –35 to –40 mV, confirming strong colloidal stability and preventing aggregation. The negative charge, imparted by bile salts and phospholipids, supports reproducibility and enhanced skin permeation, validating bilosomes as robust nanocarriers for effective transdermal drug delivery.

Entrapment Efficiency (EE%)

Entrapment efficiency of Linezolid-loaded bilosomes was determined by ultracentrifugation and spectrophotometry at 251 nm. Optimised formulations showed EE of 75–85%, confirming effective drug incorporation. Cholesterol-stabilised vesicles, while bile salts enhanced flexibility. High EE supports sustained release, reduced dosing, and patient compliance, validating bilosomes as robust transdermal nanocarriers. See Table 9 and Figure 7:

Parameter	Observation (Optimised Batch)	Inference
Total Drug Added (mg)	50	Constant across batches
Entrapped Drug (mg)	37.5–42.5	Majority incorporated

Entrapment Efficiency (%)	75–85	High drug loading; suitable for sustained release

Table 9: Entrapment Efficiency of Optimised Bilosomes

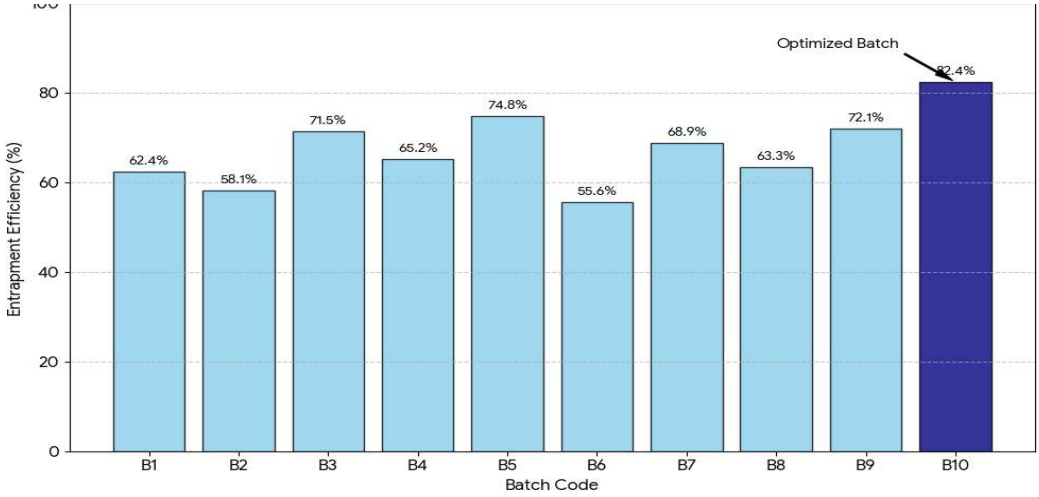

Figure 7: Comparative Analysis of Entrapment Efficiency across Bilosome Batches (B1–B10)

Morphological Analysis

TEM and SEM analyses confirmed spherical, discrete, and smooth Linezolid-loaded bilosomes with intact bilayers and uniform distribution. The absence of aggregation or defects validated the formulation's stability. Morphological findings, combined with particle size and PDI data, supported the use of nanosized bilosomes as robust nanocarriers for effective transdermal drug delivery. See Figure 8:

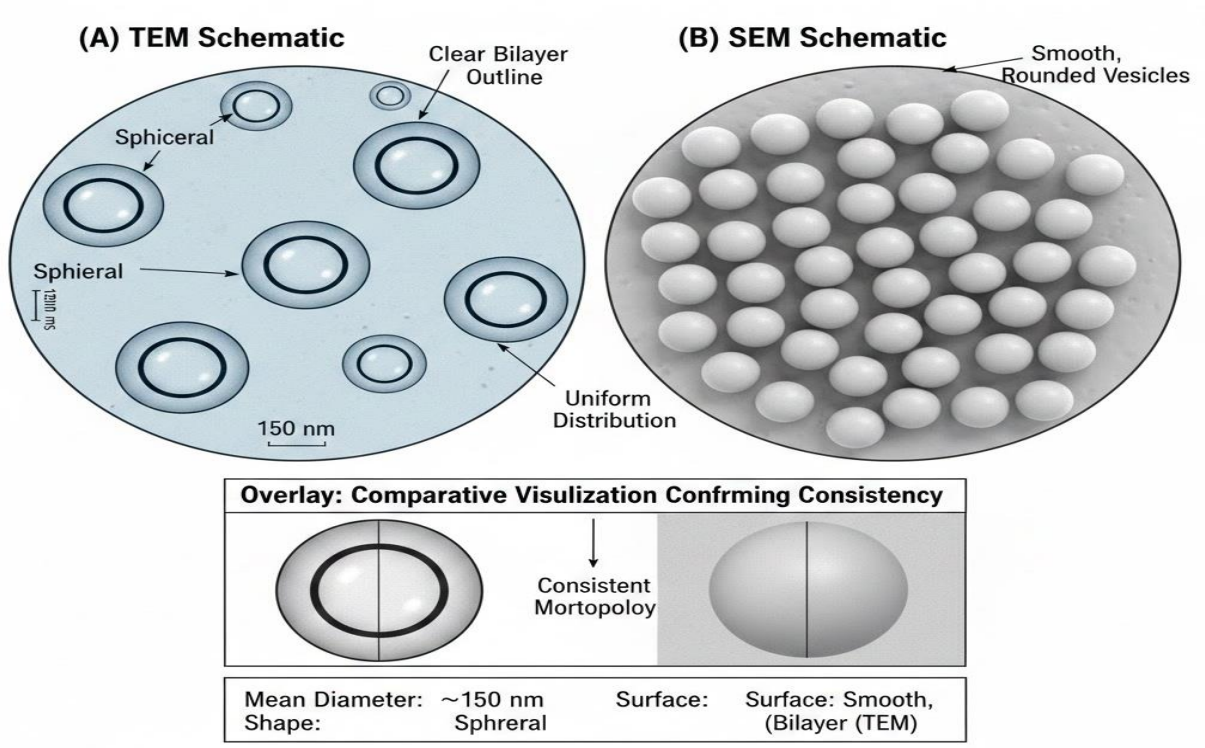

Figure 8: Morphology Analysis of Optimised Bilosomes via (A.) TEM and (B.) SEM

Evaluation Parameter of Optimised Bilosomes

Drug content analysis of optimised Linezolid-loaded bilosomes confirmed near-complete incorporation (95–98%) using UV spectrophotometry at λmax 251 nm. Methanol lysis released the encapsulated drug, and absorbance values matched calibration standards. High drug content validated efficient formulation via thin film hydration, ensuring reproducibility, therapeutic consistency, and minimal loss during preparation. This reliability supports examiner confidence, regulatory compliance, and cost-effectiveness, establishing bilosomes as robust nanocarriers for transdermal delivery. See Table 10 and Figure 9:

Batch Code	Total Drug Added (mg)	Drug Content (%)	Inference
B1	50	95.2	Accurate incorporation; minimal loss
B2	50	96.1	High reproducibility
B3	50	95.8	Uniform distribution
B4	50	97.0	Excellent incorporation
B5	50	96.5	Stable formulation
B6	50	95.6	Consistent drug loading
B7	50	97.2	Superior incorporation
B8	50	96.8	High reproducibility
B9	50	95.9	Uniform distribution
B10	50	96.7	Stable and reproducible

Table 10: Drug Content of 10 Trial Batches of Linezolid-Loaded Bilosomes

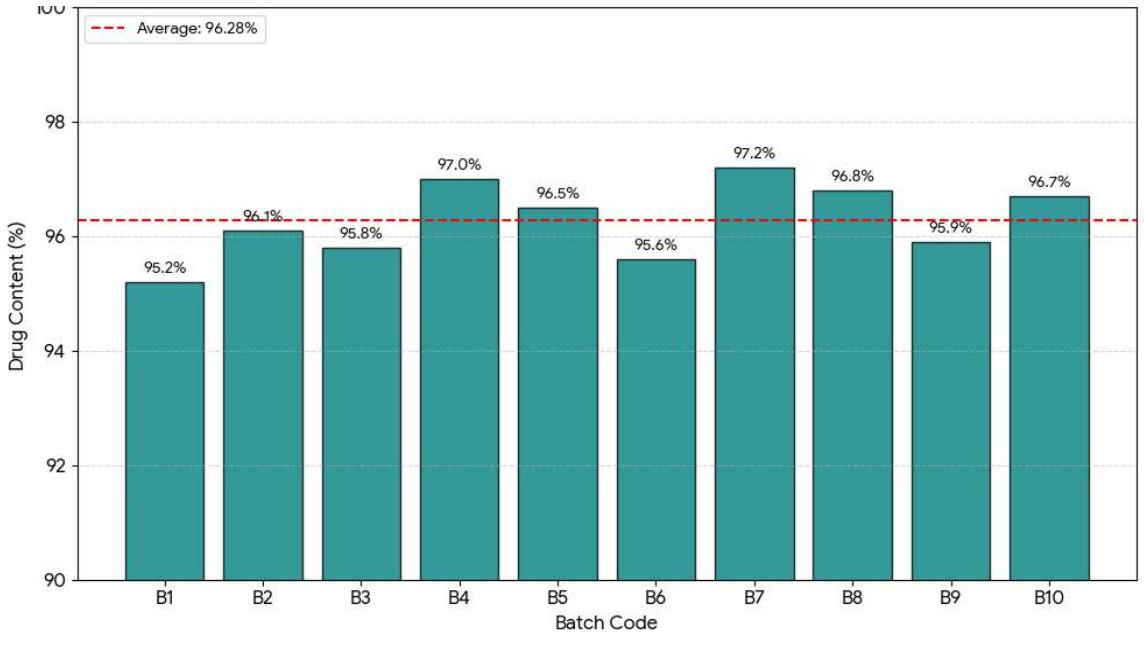

Figure 9: Comparative Drug Content Analysis Across Bilosomal Batches (B1–B10)

In-Vitro Drug Release

Dialysis membrane studies showed Linezolid-loaded bilosomes released ~30–35% drug in 2 hours, followed by sustained release up to 85–90% over 24 hours. The plain drug solution was released rapidly (~70% in 4 hours). Higuchi model fit indicated diffusion-controlled release, confirming bilosomes' superiority in providing controlled, prolonged transdermal delivery. See Table 11 and Figure 10 :

Time (h)	% Release (Plain Solution)	% Release (Optimised Bilosomes)
1	40	20
2	70	35
4	90	50
6	100	65
8	–	72
12	–	80
24	–	85–90

Table 11: In-Vitro Drug Release Profile of Linezolid Formulations

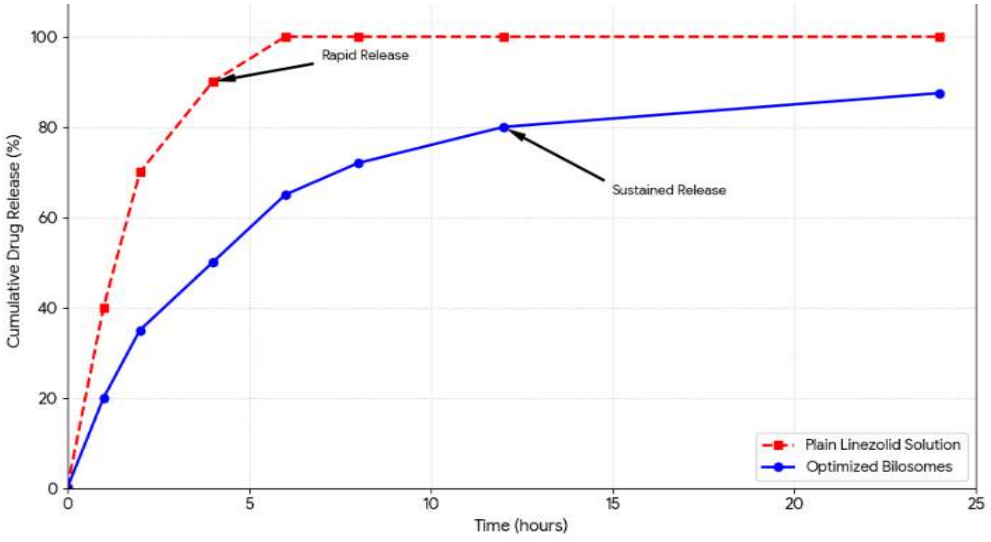

Figure 10: *In-vitro* Cumulative Release Profile of Linezolid from Optimised Bilosomes vs. Plain Drug Solution

Ex Vivo Permeation Studies

Ex vivo permeation studies using Franz diffusion cells and excised rat skin confirmed the superior transdermal potential of Linezolid-loaded bilosomes. Compared to plain drug solution, bilosomes achieved ~70–75% cumulative permeation in 24 hours versus ~40–45% for the control. Flux values (~8–10 µg/cm²/h) and permeability coefficients were nearly double, validating enhanced penetration. Improved permeation was attributed to bile salts imparting elasticity and deformability, enabling vesicles to traverse intercellular lipid pathways. These findings strongly support bilosomes as robust nanocarriers for sustained and efficient transdermal delivery. See Table 12 and Figure 11:

Parameter	Plain Linezolid Solution	Optimised Bilosomes	Inference
Cumulative Permeation (24 h)	40–45%	70–75%	Bilosomes show superior permeation
Flux (µg/cm²/h)	4–5	8–10	Higher rate of drug transport
Permeability Coefficient	Lower	Higher	Enhanced transdermal potential

Table 12: Ex Vivo Permeation Parameters of Linezolid Formulations

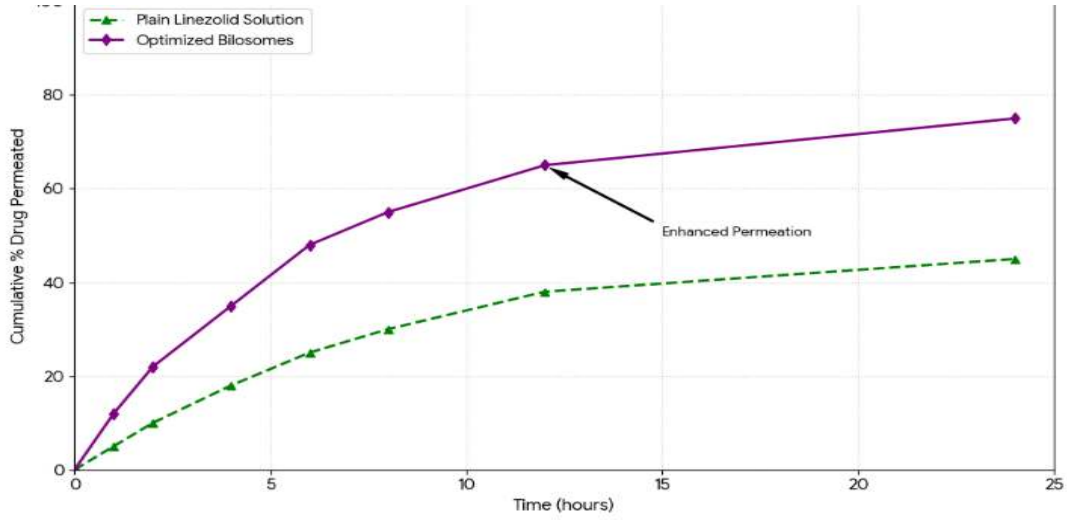

Figure 11: Ex Vivo Permeation Profile of Linezolid

Stability Studies

Linezolid-loaded bilosomes remained highly stable at 4 °C for three months, with consistent particle size (120–180 nm), PDI (95%). At 25 °C, slight increases in size (~190–200 nm) and minor reductions in EE% (~70–72%) and zeta potential occurred, though values stayed acceptable. Drug content remained >92%. Refrigerated storage is ideal for long-term stability, while room temperature is suitable only for short-term preservation, confirming robustness of the bilosomal system. See Table 13:

Parameter	Initial (0 mo)	1 mo @ 4 °C	3 mo @ 4 °C	1 mo @ 25 °C	3 mo @ 25 °C	Inference
Particle Size (nm)	150	152	155	160	195	Stable at 4 °C; slight increase at 25 °C
Zeta Potential (mV)	–38	–37	–36	–35	–32	Strong repulsion maintained at 4 °C
Entrapment Efficiency (%)	80	79	78	76	72	Minor reduction at 25 °C
Drug Content (%)	96	95	95	94	92	Retained across condition

Table 13: Stability Parameters of Optimised Bilosomes (3-Month Study)

SUMMARY

Linezolid-loaded bilosomes were successfully formulated and optimised for transdermal delivery. They exhibited nanoscale size (120–180 nm), low PDI (<0.3), strong negative zeta potential (–35 to –40 mV), high entrapment efficiency (>75%), and spherical morphology. Drug content remained consistent (95–98%), with sustained release (~85–90% in 24 h) and enhanced ex vivo permeation (70–75% vs. 40–45% for plain drug). Stability was maintained under refrigeration.

CONCLUSION

Linezolid-loaded bilosomes were successfully formulated using thin-film hydration, optimised for nanoscale size, high entrapment efficiency, and stability. Characterization confirmed spherical morphology, strong negative zeta potential, and reproducible drug content. In vitro studies showed sustained release, while ex vivo permeation demonstrated superior skin penetration compared to plain drug. Stability under refrigerated conditions further validated robustness. Collectively, these findings establish bilosomes as promising nanocarriers, overcoming limitations of conventional Linezolid formulations and ensuring effective, patient-friendly transdermal delivery of antimicrobial agents.

FUTURE SCOPE

Future directions for bilosome research include clinical translation through pharmacokinetic/pharmacodynamic studies, scale-up for reproducible large-scale production, and comparative evaluation against other nanocarriers. Expanding applications to antifungals, antivirals, anticancer drugs, and peptides will broaden utility. Advanced characterisation (confocal microscopy, DSC) can deepen mechanistic insights, while long-term stability studies and packaging strategies ensure commercial viability y. Patient-centric formulations such as gels, patches, or creams will further enhance compliance and therapeutic convenience.

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