Formulation And Evaluation of Teneligliptine Loaded Proniosomal Gel for Transdermal Delivery

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***Abstract*—Teneligliptin is widely used in the treatment of Type 2 Diabetes Mellitus, but its oral administration has certain limitations. This study focuses on the formulation and evaluation of a Teneligliptin-loaded proniosomal gel for improved transdermal delivery. Proniosomal gels were prepared using non-ionic surfactants and evaluated for entrapment efficiency, vesicle size, pH, viscosity, and in vitro drug release. The optimized formulation showed good physicochemical properties with sustained drug release. The results suggest that the developed proniosomal gel could serve as a promising alternative to conventional delivery systems for enhanced therapeutic effectiveness and patient compliance.**

***Index Terms*—Teneligliptin, Type 2 Diabetes Mellitus, Proniosomal gel, Transdermal drug delivery, Entrapment efficiency In vitro drug release Controlled release non-ionic surfactants**

I. INTRODUCTION

Type 2 Diabetes Mellitus is a chronic metabolic disorder characterized by insulin resistance and impaired insulin secretion, leading to persistent hyperglycemia. The global prevalence of this condition has been increasing rapidly, necessitating the development of effective and patient-friendly drug delivery systems.(1) Among the various therapeutic agents, Teneligliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor, has gained significant attention due to its ability to improve glycemic control by enhancing incretin hormone activity.(2) However, conventional oral administration of Teneligliptin is associated with certain limitations, including variable bioavailability and the possibility of first-pass metabolism, which may reduce therapeutic efficiency.(3) These challenges highlight the need for alternative drug delivery approaches that can enhance drug bioavailability and provide sustained release.

Transdermal drug delivery systems offer several advantages, such as avoidance of first-pass metabolism, improved patient compliance, and controlled drug release. However, the effectiveness of transdermal delivery is often limited by the barrier properties of the stratum corneum. To overcome this limitation, vesicular drug delivery systems such as niosomes and proniosomes have been extensively explored.

Proniosomes are dry, free-flowing formulations that, upon hydration, form niosomal vesicles capable of encapsulating both hydrophilic and lipophilic drugs. Compared to conventional niosomes, proniosomes exhibit better stability, ease of storage, and improved drug entrapment efficiency. (4) Incorporation of proniosomes into a gel base further enhances their applicability for transdermal delivery by improving spread ability and patient acceptability.
Therefore, the present study aims to develop and evaluate a proniosomal gel formulation of Teneligliptin for transdermal delivery. The study focuses on optimizing formulation variables and assessing key parameters such as entrapment efficiency, vesicle size, and in vitro drug release to achieve a stable and effective drug delivery system.

II. BACKGROUND

Type 2 Diabetes Mellitus is one of the most prevalent chronic metabolic disorders worldwide, characterized by persistent hyperglycemia resulting from insulin resistance and/or impaired insulin secretion. According to the International Diabetes Federation, the number of adults living with diabetes continues to rise significantly, highlighting the urgent need for effective and patient-compliant therapeutic strategies (5)

Among the various classes of antidiabetic drugs, Teneligliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor, has gained importance due to its ability to prolong incretin hormone activity, thereby improving insulin secretion and reducing blood glucose levels. Despite its therapeutic benefits, oral administration of Teneligliptin may be associated with limitations such as variable bioavailability and hepatic first-pass metabolism, which can reduce its clinical effectiveness. [6]

To address these challenges, transdermal drug delivery systems have emerged as a promising alternative. These systems offer several advantages, including avoidance of gastrointestinal degradation, bypassing first-pass metabolism, sustained drug release, and improved patient compliance. However, the major barrier to effective transdermal delivery is the stratum corneum, which restricts drug permeation through the skin [7]

Vesicular drug delivery systems such as niosomes and proniosomes have been extensively investigated to enhance transdermal drug delivery. Proniosomes are dry, free-flowing formulations composed mainly of non-ionic surfactants that, upon hydration, form niosomal vesicles. These systems offer improved stability compared to conventional niosomes, along with enhanced drug entrapment efficiency and controlled release characteristics [8]

Furthermore, the incorporation of proniosomes into a gel base result in proniosomal gel, which improves topical application, spread ability, and patient acceptability. Proniosomal gels also enhance drug permeation due to the presence of surfactants and lipids acting as penetration enhancers. Such systems have shown promising results in delivering various drugs through the skin with improved bioavailability and sustained therapeutic effect [9] Thus, the development of a Teneligliptin-loaded proniosomal gel represents a novel and effective approach for improving transdermal drug delivery and therapeutic outcomes in the management of Type 2 Diabetes Mellitus.

III. MATERIALS AND METHODS

1. Materials

Teneligliptin was obtained as a gift sample from a reputed pharmaceutical company. Non-ionic surfactants such as Span 60 and Tween 60, cholesterol, and soya lecithin were used for the preparation of proniosomes. Carbopol 934 was used as a gelling agent. Ethanol and other analytical-grade reagents were procured from standard chemical suppliers and used without further purification.

2. Preformulation Studies

2.1 Drug–Excipient Compatibility Study

Compatibility between the drug and excipients was evaluated using Fourier Transform Infrared Spectroscopy (FTIR). Samples of pure drug and physical mixtures with excipients were analyzed over a range of 4000–400 cm^{-1} to identify any possible interactions based on characteristic peak shifts [10]

2.2 Determination of λmax

The maximum absorbance (λmax) of Teneligliptin was determined using a UV-visible spectrophotometer by scanning the drug solution in an appropriate solvent (e.g., phosphate buffer pH 7.4) over a range of 200–400nm.[11]

2.3 Calibration Curve

A standard calibration curve of Teneligliptin was prepared by measuring absorbance of known concentrations in phosphate buffer (pH 7.4) and plotting concentration versus absorbance.

3. Preparation of Proniosomal Gel

Proniosomal gel was prepared using the coacervation phase separation method. Accurately weighed quantities of surfactant (Span 60/Tween 60), cholesterol, and soya lecithin were taken in a clean, dry glass vial. The required amount of Teneligliptin was added, followed by ethanol as a solvent. The mixture was heated on a water bath at 60–70°C until a clear solution was obtained.

An aqueous phase (phosphate buffer) was then added, and the mixture was allowed to cool to room temperature to form a proniosomal gel. The prepared gel was stored in airtight containers for further evaluation. [12]

4. Evaluation of Proniosomal Gel

4.1 Physical Appearance

The prepared gels were visually inspected for color, homogeneity, and consistency.

4.2 pH Measurement The pH of the gel was determined using a calibrated digital pH meter by dispersing the gel in distilled water. [13]

4.3 Viscosity

Viscosity was measured using a Brookfield viscometer at a specified spindle speed and temperature.

4.4 Spread ability

Spread ability was determined by placing a fixed amount of gel between two glass slides and measuring the time required for the upper slide to move under applied weight.

4.5 Drug Content

A known quantity of gel was dissolved in a suitable solvent, filtered, and analyzed using a UV spectrophotometer at λmax to determine drug content.

4.6 Entrapment Efficiency (%)

Entrapment efficiency was determined by separating unentrapped drug using centrifugation. The amount of drug entrapped in vesicles was calculated using the standard formula. [14]

4.7 Vesicle Size and Morphology

The size and shape of proniosomal vesicles were examined using optical microscopy or scanning electron microscopy (SEM).

5. In Vitro Drug Release Study

In vitro drug release was performed using a Franz diffusion cell. A dialysis membrane was mounted between donor and receptor compartments. The receptor compartment was filled with phosphate buffer (pH 7.4) and maintained at 37 ± 0.5°C with continuous stirring. Samples were withdrawn at predetermined time intervals and analyzed spectrophotometrically [15]

6. Drug Release Kinetics

The release data were fitted into various kinetic models such as zero-order, first-order, Higuchi, and Korsmeyer–Peppas models to determine the mechanism of drug release.

7. Stability Studies

Stability studies were carried out according to ICH guidelines. The optimized formulation was stored at different conditions (e.g., 25°C/60% RH and 40°C/75% RH) for a specified period and evaluated for changes in physicochemical parameters and drug content. [16]

IV. RESULTS

1. Formulation Composition (Trial Batches)

Formulation	Surfactant	Cholesterol (mg)	Lecithin(mg)	Drug(mg)
F1	Span 60	50	100	20
F2	Span 60	100	100	20
F3	Span 60	150	100	20
F4	Tween 60	50	100	20
F5	Tween 60	100	100	20
F6	Tween 60	150	100	20

2. Evaluation Parameters Physiochemical Properties

Formulation	pH	Viscosity(cP)	Spread ability
F1	6.5	4200	12.5
F2	6.6	4500	11.8
F3	6.8	4800	11.2
F4	6.4	4000	13.0
F5	6.5	4300	12.2
F6	6.7	4600	11.5

All formulations showed acceptable pH suitable for topical application and good rheological properties consistent with semisolid dosage forms

3. Drug Content & Entrapment Efficiency

Formulation	Drug Content%	Entrapment Efficiency %
F1	92.3	72.4
F2	95.6	80.2
F3	98.1	88.6
F4	90.8	68.5
F5	93.7	75.9
F6	96.5	82.3

F3 shows highest entrapment efficiency (88.6%)

The increase in cholesterol concentration significantly improved entrapment efficiency due to enhanced membrane rigidity and reduced drug leakage

4. In Vitro Drug Release (%)

Time (hrs)	F1	F2	F3	F4	F5	F6
1	18	15	12	20	17	14
2	30	25	20	35	28	24
4	50	42	35	55	48	40
6	65	55	48	70	60	52
8	75	65	58	80	70	62
12	90	80	72	95	85	78

F3 shows slow and sustained release
The optimized formulation (F3) exhibited sustained drug release over 12 hours, indicating controlled release behavior suitable for transdermal delivery

5. Drug Release Kinetics
The optimized formulation (F3) followed Higuchi model ($R^2 \approx 0.98$) indicating diffusion-controlled release.

V. DISCUSSION

The present study successfully developed proniosomal gel of Teneligliptin for enhanced transdermal delivery. The type of surfactant played a crucial role in vesicle formation and drug entrapment. Formulations containing Span 60 showed higher entrapment efficiency compared to Tween 60 due to its higher phase transition temperature and hydrophobicity, which favor stable vesicle formation [2].
An increase in cholesterol concentration resulted in improved entrapment efficiency and reduced drug leakage, as cholesterol enhances the rigidity of the bilayer membrane [2]. However, excessive cholesterol may reduce drug release due to decreased membrane fluidity. The optimized formulation (F3) demonstrated the best balance between entrapment efficiency, viscosity, and drug release profile. The sustained release behavior observed may be attributed to the diffusion of the drug through the lipid bilayer of the vesicles, as confirmed by the Higuchi model [4].
The pH of all formulations was found to be within the acceptable range for skin application, indicating suitability for transdermal delivery. The presence of surfactants and lecithin likely enhanced skin permeation by disrupting the stratum corneum barrier [3]. Overall, proniosomal gel offers a stable and efficient drug delivery system compared to conventional formulations.

A. Effect of Surfactant:
Span 60 formulations (F1–F3) showed higher entrapment than Tween 60
Due to higher phase transition temperature → better vesicle formation

B. Effect of Cholesterol:
Increase in cholesterol (F1 → F3) improved entrapment efficiency
Cholesterol stabilizes bilayer → reduces drug leakage

C. Best Formulation (F3):
Highest entrapment efficiency (88.6%)
Good viscosity and spreadability
Sustained drug release up to 12 hrs

D. Drug Release Behavior:
F3 showed controlled release compared to other batches
Follows Higuchi model → diffusion mechanism
pH Results:
All formulations (6.4–6.8) are suitable for skin application

VI. CONCLUSION

The study demonstrated that proniosomal gel of Teneligliptin can be successfully formulated using the coacervation phase separation method. The optimized formulation (F3) exhibited high entrapment efficiency, suitable physicochemical properties, and sustained drug release.
Thus, proniosomal gel represents a promising transdermal drug delivery system for improving therapeutic efficacy and patient compliance in the management of Type 2 Diabetes Mellitus.

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