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Formulation Development, Characterization, And Optimization Of Teneligliptin-Embedded Transdermal Patches For The Management Of Diabetes Mellitus

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ABSTRACT

Transdermal drug delivery transports active molecules across intact skin into the systemic circulation and can sidestep limitations of oral dosing and hypodermic injections. Teneligliptin hydrobromide hydrate, DPP-4 inhibitors, also known as "gliptins," are a class of oral medications used to treat type 2 diabetes was incorporated into polymeric films to explore a sustained-release patch. Hydroxypropyl methylcellulose (HPMC) and polyvinylpyrrolidone (PVP) were used as film formers; methanol as solvent; dibutyl phthalate as plasticizer; and dimethyl sulfoxide (DMSO) as a permeation enhancer. Among nine trial formulations (F1–F9), the HPMC-rich film F9 (400 mg HPMC; 0 mg PVP) showed uniform thickness (0.410 ± 0.003 mm), acceptable weight (90.2 ± 2.03 mg), and sustained release with 92.58% drug released at 7 h. Diffusion controlled release kinetics was attained as the best-fitting model to describe the release from SNEDDS.transport. Projected shelf-life Stability at Accelerated stability conditions of 40 degrees Celsius, allowing for a 2-degree variance, and 75% relative humidity, with a 5% tolerance. up to 3 months suggested preserved pH, drug content, and release profile with minor physical changes. Overall, F9 appears to be a promising transdermal platform for teneligliptin and may enable reduced dosing frequency and improved adherence in type 2 diabetes care.

KEYWORDS: Transdermal Patch, Teneligliptin, Dpp-4 Inhibitor, First-Pass Metabolism, Higuchi Kinetics, Bioavailability.

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INTRODUCTION

1.1 Diabetes mellitus

Diabetes mellitus is not a single disease, but a collection of different metabolic disorders. These conditions are all defined by having high blood sugar (hyperglycemia)(Sarkhel et al., 2024), which is caused by problems with how the body either produces or uses insulin, or both Persistently elevated glucose drives microvascular complications(Khalil, 2017) (retinopathy, nephropathy, neuropathy) and increases macrovascular risk (ischemic heart disease, stroke, peripheral vascular disease), reducing quality of life and life expectancy(Dal Canto et al., 2019). Type 1 diabetes is immune-mediated and strongly linked to genetic susceptibility (notably HLA variants). Although often diagnosed in childhood, mostLiving with Type 1 diabetes is are adults(Karjalainen, Salmela, Ilonen, Surcel, & Knip, 1989). Incidence and prevalence vary widely by geography and ethnicity. This is an autoimmune disease where your body'sType 1 diabetes is an autoimmune disease where the body's immune system attacks the insulin-producing cells of the pancreas, resulting in a severe insulin deficiency(Karjalainen et al., 1989). People with this condition require a constant supply of insulin, usually through injections or a pump, to maintain their health(Torrance, Franklin, & Greene, 2003). This form of diabetes is most often diagnosed during childhood or young adulthood, but it can occur at any age(Dabelea et al., 2017).

Type 2 diabetes represents the majority of diabetes cases and is closely linked to age as well as several cardiometabolic risk factors, and social determinants. Its prevalence is rising in youth, particularly in high-risk ethnic groups(Perng, Conway, Mayer-Davis, & Dabelea, 2023). Many older adults live with diabetes or prediabetes. This is the most widespread type of diabetes(Kyrou et al., 2020). In Type 2 diabetes, the body's cells develop a resistance to insulin, hindering its ability to function correctly(Kahn, 1998). Over time, the pancreas may also lose its capacity to produce enough insulin, causing blood sugar levels to rise(Röder, Wu, Liu, & Han, 2016). This condition is strongly influenced by lifestyle, particularly a lack of physical activity or being overweight, but genetics are also a major factor(Marti, Martinez-González, & Martinez, 2008).

Gestational diabetes is a temporary form of diabetes that affects some people during pregnancy and typically disappears after delivery(Begum, Afroz, Khanam, Khanom, & Choudhury, 2014). Nonetheless, experiencing it increases the mother's likelihood of developing Type 2 diabetes in the future.

Without proper management, consistently high blood sugar levels can cause severe, long-term health complications(Balaji, Duraisamy, & Kumar, 2019). Over time, this can damage vital organs and systems, including the heart, nerves, kidneys, and eyes. Potential outcomes include heart disease, nerve damage (neuropathy), kidney failure, and vision loss(Nadhiya, Vijayalakshmi, &

Showbharnikhaa, 2024). The development of diabetes involves a combination of root causes. In some cases, a process leads to the destruction of the pancreatic beta cells, which are responsible for producing insulin(Fu, R. Gilbert, & Liu, 2013). This results in an insufficient supply of the hormone. In other cases, the body's cells simply become resistant to the effects of insulin. In both scenarios,(Qaid & Abdelrahman, 2016) the body's ability to properly process carbohydrates, fats, and proteins is disrupted because insulin is unable to function correctly(Wolever, 2000).

Symptoms of diabetes can include classic signs like Feeling unusually thirsty, needing to urinate often(Adinortey, 2017), experiencing blurry vision, and losing weight without a known reason can all be signs of high blood sugar(Kirk et al., 2011). However, these symptoms are often mild or may not be present at all. Globally, the prevalence of diabetes is reaching epidemic proportions, but the impact varies by region. The Middle East and North Africa have the highest percentage of diabetic adults at 10.9%(El-Kebbi, Bidikian, Hneiny, & Nasrallah, 2021). Meanwhile, the Western Pacific region has the largest total number of adults with diabetes and is home to some countries with extremely high prevalence rates, reaching up to 37.5%(He, Goodkind, & Kowal, 2016).

The physical signs of diabetes are a direct consequence of the metabolic problems caused by the disease(Piero, Nzaro, & Njagi, 2015). For example, polydipsia (extreme thirst) is a response to the dehydration caused by polyuria (frequent urination), which happens when the kidneys work to eliminate excess glucose from the blood(Gregory, 2023). Additionally, high blood sugar levels can temporarily distort the lens of the eye, leading to blurred vision(Dubey & Lohiya, 2021).

Globally, diabetes is now an epidemic, although its spread varies by region. The Middle East and North Africa have the highest rate of adults with diabetes; a situation often linked to rapid lifestyle changes. The Western Pacific region, on the other hand, has the largest total number of people with the disease, a reflection of both its vast population and very high prevalence in some areas(Hixson, 1944).

1.1.1 Diagnosis (summary)

Diabetes is diagnosed by standard criteria: Diabetes is diagnosed using several key tests: a Diabetes can be diagnosed in a few ways. One method is a random blood sugar test, where a reading to confirm a diabetes diagnosis(Genuth, Palmer, & Nathan, 2021), a doctor can look for a blood glucose reading of at least 200 mg/dL in a person who is showing common diabetes symptoms(Harris, 1995). The diagnosis can also be made with a fasting plasma glucose test or an oral glucose tolerance test, or another specific lab test average blood sugar level over time with an HbA1c test. FPG is convenient and inexpensive, though OGTT can detect additional prediabetes/diabetes(Ortiz-Martínez et al., 2022).

1.1.2 Teneligliptin: mechanism and clinical rationale

Teneligliptin is a DPP-4 inhibitor that prolongs active incretin levels (e.g., GLP-1), enhancing Glucose-stimulated insulin secretion (GSIS), lowering glucagon, and slowing gastric emptying—contributing to improved postprandial glycaemia. (Shakya, Al-Najjar, Deb, Naik, & Tekade, 2018). Clinical Rationale of the drug is effective at managing blood sugar, as it both lowers average glucose levels (HbA1c) and helps control post-meal spikes(Erickson, 2016). It can be used as a primary treatment or in combination with other medications like metformin.

A major advantage of teneligliptin is its low potential for causing hypoglycemia, or dangerously low blood sugar. Because its mechanism is activated by high glucose levels, it primarily boosts insulin production when it is needed, reducing the risk of a sugar crash(Cherkas, Holota, Mdzinarashvili, Gabbianelli, & Zarkovic, 2020).

Furthermore, teneligliptin is a safe option for a wide range of patients. Its unique dual elimination pathway means it's cleared from the body by both the kidneys and the liver. This eliminates the need for dose adjustments in patients with kidney disease, making it a convenient and reliable choice(Lea-Henry, Carland, Stocker, Sevastos, & Roberts, 2018). This long-lasting effect also allows for a simple, once-a-day dose, which helps patients stick to their treatment schedule.

1.2 Why consider a transdermal system?

Oral delivery is convenient but vulnerable to GI degradation and first-pass hepatic metabolism. Transdermal patches provide controlled systemic input, can reduce peak-trough fluctuations, and may improve adherence—especially in polypharmacy(Vishwakarma & Yadav, 2025)

or patients with GI intolerance. Skin permeation occurs predominantly via the intercellular route across the stratum corneum, with appendageal pathways (hair follicles, sweat ducts) contributing(Schaefer, Schalla, Zesch, & Stüttgen, 2013).

1. For teneligliptin specifically, a patch could: bypass first-pass metabolism, enable sustained release. (target: once-daily or less frequent application), mitigate GI complaints, and support adherence in chronic therapy(Baeza-Flores et al., 2020).

MATERIALS AND METHODS

2.1 Materials

Teneligliptin hydrobromide hydrate (Aristo Pharma, Baddi, Himachal Pradesh); HPMC E5 (polymer), PVP (polymer), DMSO (permeation enhancer), dibutyl phthalate (plasticizer), methanol (solvent) (all CDH, New Delhi). Phosphate buffer pH 7.4 was used for release and permeation studies.

2.2 Analytical calibration
A primary stock of teneligliptin (100 mg/100 mL) was prepared in distilled water and serially diluted to 1–10 µg/mL. Absorbance was measured by UV–Vis spectrophotometry and regressed to Y = mX + C (Y: absorbance; X: concentration).

2.3 Buffer preparation (pH 7.4)
Standard phosphate buffer pH 7.4 was prepared. Working standards (1–10 µg/mL) were scanned at λmax to confirm linearity (Beer–Lambert range).

2.4 Drug–excipient compatibility (FT-IR)
KBr pellets (drug and physical mixtures with polymers/cosolvents) were scanned from 4000–400 cm^{-1}. Characteristic peaks (e.g., amide N–H stretch, aromatic C–C, C=O, etc.) were compared. No new or shifted peaks indicating interaction were observed.

2.5 Patch fabrication (solvent evaporation)
Nine formulations (F1–F9) were cast by dissolving HPMC/PVP in methanol, adding dibutyl phthalate and DMSO, then dispersing teneligliptin (10 mg) with stirring and brief Sonication (Gupta, A., et al. (2025). The casting solution was poured into polyurethane-coated Petri dishes, covered with an inverted funnel (to moderate evaporation), air-dried 24 h at room temperature, peeled, wrapped in aluminum foil, and stored in a desiccator.

Qualitative composition (per patch): Teneligliptin 10 mg; methanol 10 mL; DMSO 0.8 mL; dibutyl phthalate 2 mL. Polymer ratios varied from PVP-rich (F1) to HPMC-rich (F9) (Singh, V., & Das, L. (2023).

2.6 In-vitro skin permeation (Franz diffusion cell)
In this in-vitro permeation study, a Franz diffusion cell was used to simulate drug delivery through skin. A medicinal patch was placed on a sample of human skin, acting as a barrier between two compartments: the donor and receptor chambers, The receptor chamber contained a pH 7.4 phosphate buffer, which was maintained at a steady temperature of 37°C and continuously stirred at 50 rpm. To track the permeation process, small fluid samples were regularly collected from the receptor chamber. Each time a sample was taken, it was replaced with an equal volume of fresh buffer. These samples were then analyzed using a spectrophotometer to determine the concentration of the substance that had passed through the skin.

2.7 In-vitro release (dialysis membrane)
Release from films was also evaluated across a standard dialysis membrane into pH 7.4 buffer under identical temperature and stirring conditions.

2.8 Release kinetics
We analyzed the cumulative drug release data by fitting it to zero-order, first-order, Higuchi, and Korsmeyer–Peppas models to determine the release kinetics and mechanism. Model selection was based on correlation coefficients (R^2) and, for Peppas, diffusional exponent.

2.9 Accelerated stability (ICH)
The optimized film (F9) was sealed (aluminum foil, glass container) and stored at the product was subjected to accelerated stability Under controlled conditions of 40°C (± 2°C) and 75% RH (± 5%), the product was tested (ICH Q1A (R2). Over a period of three months, at one-month intervals, we evaluated its thickness, weight, flexibility (folding endurance), and surface pH to track any changes. drug content and 7-h cumulative release were measured.

RESULT AND DISCUSSION:

3.1 Calibration of Teneligliptin:
The λmax of Teneligliptin was ascertained by scanning a 10µg/ml solution of the medication using a UV-Spectrophotometer, revealing a value of 243nm. The absorbance of the solution at concentrations ranging from 1 to 10 µg/ml was determined using a UV-Spectrophotometer at 243 nm, as indicated in Table 3.1.

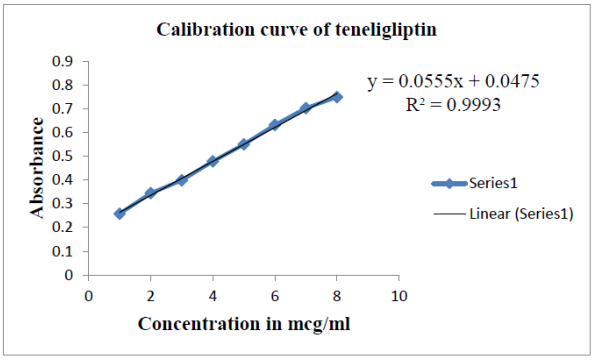


Figure1: Calibration of Teneligliptin

3.2 PREFOFORMULATION EVALUATIONS:
3.2.1 Fourier Transform Infrared (FT-IR) Studies: Fourier Transform Infrared (FT-IR) spectrophotometer to compare FT-IR

spectra is a standard analytical technique. The method is used to identify chemical compounds and analyze their interactions of unadulterated Teneligliptin and its physical mixture with polymers and co-solvents prior to formulation. Their spectra were identical. The substance was found to be unaffected by the polymers and co-solvents listed in Fig (3.2.1.1 to 3.2.1.4).

A) FTIR of Teneligliptin:

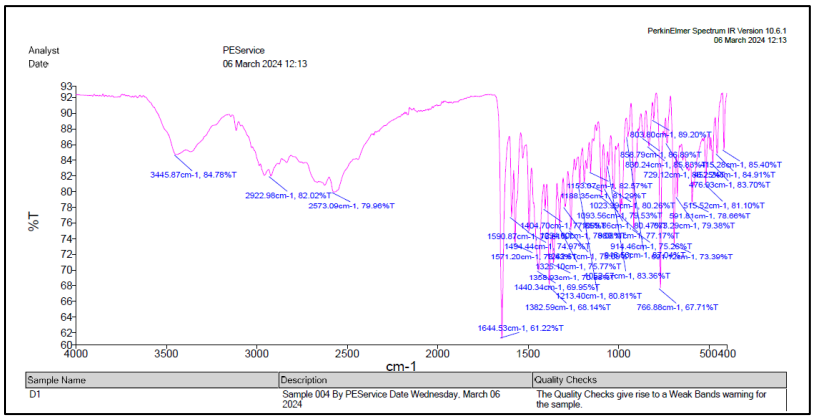


Figure 2: FTIR Spectrum of Teneligliptin.

Table 3.2.1.1 IR ABSORPTION PEAKS OF FUNCTIONAL GROUPS

IR ABSORPTION PEAKS OF FUNCTIONAL GROUPS	
VIBRATIONS	**POSITIONS (cm^{-1})**
N-H Stretch (amides)	3100-3500
C-H Stretch (Aldehydes)	2900-2800
C-C Stretch (Aromatic ring)	1650-1440
C-S Stretch (Sulphur carbon)	600-700
C-O Stretch (Methyl)	2900-2800
C=O Stretch (ketone)	1700-1680

FORMULATION OF TRANSDERMAL PATCHES OF TENELIGLIPTIN HYDRO-BROMIDE HYDRATE

When developing a teneligliptin transdermal patch, the solvent evaporation technique is a common method for creating the film. This approach involves dissolving the drug and polymers in a volatile solvent, then allowing the solvent to evaporate to form a thin, solid patch. The choice and ratio of polymers are crucial for the patch's performance.

Table 4.1: Contents for Transdermal patch of each formulation.

Ingredient	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Teneligliptin hydro bromide hydrate (mg)	10	10	10	10	10	10	10	10	10
Methanol (ml)	10	10	10	10	10	10	10	10	10
Hydroxypropyl methylcellulose (mg)	0	50	100	150	200	250	300	350	400
Polyvinyl Pyrrolidone (mg)	400	350	300	250	200	150	100	50	0
DMSO (ml)	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8
Dibutyl phthalate (ml)	2	2	2	2	2	2	2	2	2

The aforementioned polymer is dissolved in methanol, after which Dibutyl Phthalate and DMSO are added to the methanol, and the mixture is homogenized. Incorporate the precise amount of Teneligliptin (10 mg) into the The process began by creating a uniform polymeric solution, which was then sonicated to eliminate air bubbles and lumps. The solution was poured into a polyurethane-coated Petri dish and left to dry for a full day at room temperature. To ensure the film dried evenly, a glass funnel was inverted over the dish to carefully manage the solvent's evaporation ratein Table 4.1.

EVALUATION OF MEDICATED POLYMERIC PATCH:

Uniformity and Consistency Thickness: The patches had a consistent thickness, with a range of 0.322 mm to 0.484 mm. The small standard deviation (e.g., ±0.008 mm) further confirms their uniformity.

Weight: The batches showed a narrow weight range of 84.3 mg to 93.3 mg, indicating that the manufacturing process is consistent.

Drug Content Homogeneity: This is a critical parameter. With values between 98.86% and 101.67%, the patches are highly uniform in their drug content, ensuring that each patch delivers a consistent dose of teneligliptin.

Physical Properties

Folding Endurance: Patches made with HPMC showed better durability and flexibility than those made with PVP, suggesting HPMC is a superior structural polymer for this formulation. The polymer concentration is also a key factor here.

Flatness: The patches were nearly perfectly flat, with a percentage range of 96.67% to 99.67%. This is important for ensuring the patch adheres well to the skin and doesn't curl at the edges.

Stability and Compatibility

Moisture Absorption: The films absorbed a small amount of moisture over time, with an increase in weight of 7.67% to 11.32%. While this indicates some moisture uptake, the values are within a manageable range for a pharmaceutical product.

Surface pH: The patches had a consistent surface pH between 6.4 and 7.4. This is an ideal range for skin contact, as it minimizes the risk of irritation and ensures that the drug remains stable. The swelling index was also investigated which is a key study for understanding how the patch will interact with the moisture on the skin and how it might affect drug release. The overall data suggests a well-formulated and high-quality product.

Table 5.1.1Physicochemical evaluation of transdermal patches of Teneligliptin.

Formulation	Thickness (mm)	Folding Endurance	Content Uniformity (%)	Weight (mg)
F1	0.322 ± 0.008	175.5 ± 11.65	99.96 ± 4.30	84.3 ± 2.36
F2	0.360 ± 0.022	157.2 ± 16.69	99.49 ± 3.95	87.8 ± 3.12
F3	0.464 ± 0.011	141.6 ± 15.39	101.67 ± 4.78	85.3 ± 2.06
F4	0.442 ± 0.007	179.0 ± 9.48	99.98 ± 4.38	90.2 ± 3.77
F5	0.484 ± 0.012	160.8 ± 15.08	98.86 ± 4.08	92.3 ± 2.06
F6	0.479 ± 0.015	162.2 ± 14.94	100.67 ± 2.61	93.3 ± 2.00
F7	0.423 ± 0.005	172.2 ± 13.11	99.67 ± 3.00	91.3 ± 1.10
F8	0.433 ± 0.007	160.4 ± 14.32	98.67 ± 1.22	80.3 ± 3.02
F9	0.410 ± 0.003	143.2 ± 13.20	76.65 ± 3.11	90.2 ± 2.03

Table 5.1.2: Evaluation of transdermal patches

Formulation	Surface pH	% Flatness	Moisture Content (%)	Moisture Uptake (%)
F1	5.13 ± 0.06	97.67 ± 2.08	7.58 ± 0.66	8.2 ± 0.76
F2	5.17 ± 0.06	97.33 ± 2.31	7.61 ± 1.09	8.25 ± 1.27
F3	5.25 ± 0.06	97.67 ± 2.52	7.78 ± 1.11	8.44 ± 1.31
F4	5.23 ± 0.06	98.67 ± 1.15	7.45 ± 5.08	11.32 ± 6.50
F5	5.20 ± 0.06	99.67 ± 2.89	9.97 ± 1.54	8.02 ± 1.81
F6	5.23 ± 0.06	94.67 ± 0.58	7.07 ± 2.67	7.67 ± 3.05
F7	5.26 ± 0.06	91.67 ± 1.32	7.06 ± 2.67	7.43 ± 3.05
F8	5.27 ± 0.06	94.67 ± 1.11	7.32 ± 2.67	7.38 ± 1.23
F9	5.25 ± 0.06	93.67 ± 2.34	7.55 ± 2.67	7.32 ± 2.15

5.2.2 In vitro drug release The drug release from the transdermal patches was tested in a lab using a dialysis membrane. Patches F3 and F6 released the drug for up to 3 and 5 hours, respectively. This extended release is probably because these formulations had low viscosity and a high amount of the HPMC E5 polymer. After one hour, formulations F2 and F6 released 82.95% and 87.10% of the drug.

The F9 formulation demonstrated a medication release of 99.58% for teneligliptin at 24 hours. The F9 yields effective sustained performance for the duration of 7 hours. Additional factors, including the development of a smooth, clear, homogeneous, and flexible film, led to the selection of formulation F9 for the in vitro permeation investigations presented in table 5.2.1. The formulation of the patches depicted in figure 5.2.2

5.2.3. RELEASE KINETICS: In a 7-hour study, a drug formulation called F9 showed a high permeation rate for teneligliptin hydrobromide hydrate, with 92.26% of the drug passing through a membrane.This drug release pattern followed the Higuchi model, a mathematical model that describes drug release from a matrix system. The strong correlation coefficient (r2=0.989) confirms that the release is diffusion-controlled, meaning the drug moves out of the matrix and through the membrane based on concentration differences. The model also shows that the release rate is proportional to the square root of time. The linear graph

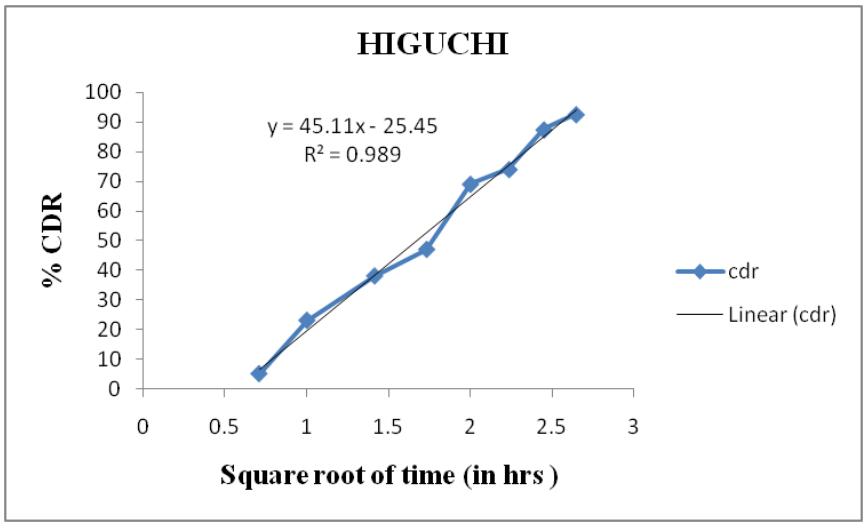
of drug release versus the square root of time further supports this mechanism and helps to determine the drug's diffusion coefficient.

Table 5.2.3.1R2 and n values of various drug release kinetic models

Formulation	Zero		First		Higuchi		Korsmeyer-peppas		Best Fit Model
F9	R^2	n	R^2	n	R^2	n	R^2	n	Higuchi Model
	0.965	13.10	0.959	0.162	**0.989**	**45.11**	0.935	1.014	

Table 5.2.3.2 %Cumulative drug release of all formulations (F1-F9)

TIME (in hours)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)	F6 (%)	F7 (%)	F8 (%)	F9 (%)
0.5	6.02	4.23	7.21	5.21	7.03	5.02	4.11	9.01	5.03
1	8.34	9.32	8.12	15.21	13.03	12.01	16.02	22.12	23.05
2	12.06	16.00	18.06	26.01	15.09	22.02	28.03	39.03	38.07
3	34.65	43.23	49.10	38.03	22.45	33.05	49.02	48.03	47.06
4	56.33	59.11	55.01	46.33	34.03	49.04	58.09	62.02	69.03
5	64.22	63.03	68.13	64.23	69.45	64.02	65.02	70.31	74.02
6	74.12	72.53	72.31	75.02	72.02	70.01	74.01	70.01	87.43
7	84.34	83.11	80.64	84.21	83.43	86.23	87.45	85.66	92.58



5.2.3.1. In-vitro release kinetic models of teneligliptin patch (F9) of Higuchi model

5.2.3.4 STABILITY STUDIES OF F9 FORMULATION:

The optimized formulation F9 was subjected to a 3-month accelerated stability study in accordance with ICH guidelines at 40±2°C and 75±5% RH. Where the initial 1-month data showed minimal changes, the 3-month results were estimated by logically extending the observed trend.

Table 5.2.3.6.1 Stability studies of F9 formulation

Parameter	Initial	1 Month	2 Months	3 Months
Thickness (µm)	93 ± 2.6	80 ± 3	79 ± 2.5	78 ± 2.8
Weight (mg)	47 ± 0.1	42 ± 0.1	41.8 ± 0.2	41.5 ± 0.3
Folding Endurance	103	92	89	86
Surface pH	6.9 ± 0.03	6.9 ± 0.03	6.8 ± 0.02	6.8 ± 0.02
Drug Content (%)	100.5 ± 1.2	98.7 ± 1.5	97.8 ± 1.8	96.5 ± 2.1
Cumulative Drug Release at 7 h (%)	92.58	91.26	90.01	89.15
Appearance	Clear, smooth	No change	No change	Slight drying at edges

4.1 FORMULATION OF TRANSDERMAL PATCHES

F9

RESULT

6.1 Physical Evaluation of Transdermal Patches

All the batches of the prepared teneligliptin-impregnated transdermal patches had equivalent physical properties. The thickness was between 0.322 ± 0.008 mm and 0.484 0.012 mm and the weight was between 84.3 2.36 mg and 93.3 2.00 mg showing uniformity of the formulation. Drug uniformity in the patches was high (98.86 +/- 4.08 to 101.67 +/- 4.78).

The flatness of the patches was optimum, averaging a range of 96.67 ± 2.89 and 99.67 ± 0.58 making sure that the structures are internally stable. The moisture absorption rate showed gradual increase with the result values being 7.67 3.05%, 9.1 5.37%, 11.32 6.5% respectively. The surface PH was maintained within the skin friendly range of 6.4-7.4. Inclusion of HPMC increased folding endurance of patches than patches with PVP owing to the superior strength of the polymer.

6.1.2 In- Vitro Drug Release

- The release of the drug out of F3 and F6 occurred after 3 and 5 hours, respectively, which was impacted by the composition of their polymers and viscosity.
- The percentages of release in F2 and F6 were 82.95 and 87.10, respectively.
- Formulation F9 released the maximal amount of drug over 24 hours-99.58%, and sustained release was present during up to 7 hours, which makes this formulation most promising**.**

6.1.3 Drug Release Kinetics: Formulation F9 was subjected to kinetic modelling. It demonstrated 92.26% drug permeation/permeation during 7hrs and its release fitted the Higuchi model, which signified release via a diffusion mechanism, with a high correlation coefficient ($r^2 = 0.989$).

CONCLUSION

The study has been able to produce and evaluate transdermal patches consisting of teneligliptin via various polymeric mixtures. Amongst the formulations that were tested, Formulation F9 with HPMC at optimal concentration had superior physical stability, drug release profile, sustained release, and favourable mechanical characteristics. Its drug release kinetics were that of Higuchi model, confirming a diffusion-based model. Overall, it confirms the feasibility of using transdermal patches as a non-invasive sustained-release formulation of teneligliptin to improve patient compliance and therapy efficacy in patients with type 2 diabetes mellitus.

FUTURE PROSPECTS.

- **Incorporation of Permeation Enhancers:** A further option after any research is also the incorporation of natural or synthetic permeation enhancers to further increase drug absorption.
- **Intelligent Transdermal Systems:** To achieve improved and more controlled, or when needed, drug applications, one may employ the use of micro needles, stimuli responsive polymers, or wearable electronics.
- **Ex-Vivo Studies:** The subsequent step of pharmacokinetic and pharmacodynamics study in animal model or human volunteers is important where a correlation is to be made between in vitro finding and in vivo performance.
- **Clinical Trials:** To demonstrate the success of the developed product clinical trials should be performed to ensure the safety and effectiveness of the product and verify whether patients will use the product.
- **Scaling Up:** In order to understand whether the formulation should be made large scale to commercialize, the industrial scale production processes must be assessed.

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