RESEARCH PAPER

Development and Optimization of an Herbal Polymeric Matrix Transdermal Patch for Potential Anti-diabetic Drug Delivery

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ABSTRACT

Background: Diabetes mellitus has a large worldwide health burden, rendering transdermal medication administration a compelling alternative to oral medication due to first-pass metabolism and superior systemic bioavailability. The present research intended to create and investigate a matrix-shaped antidiabetic herbal transdermal patch including Gymnema sylvestre and Tinospora cordifolia extracts from Box-Behnken design refinement. Methods: Hydroalcoholic extracts of G. sylvestre, and T. cordifolia were medicinally evaluated by phytochemical screening, fluorescence analysis, and TLC. Drug-excipient compatibility was assessed before a formulation employing FTIR and DSC. A three-factor, three-level Box-Behnken design was applied, with PVA amount (%), ethanol concentration (%), and drying time (h) as the independent variables. Fifteen formulations were developed by solvent casting using PVA, HPMC, and chitosan as polymers and PEG 400. Glycerol, DMSO, and Tween 80 are utilised as excipients. Patches were tested for thickness, folding endurance, tensile strength, moisture uptake, water vapour distribution, surface pH, drug content, in-vitro drug release, and release kinetics. Stability assessments lasted 60 days at 25°C/60% RH and 40°C/75% RH. Phytochemical analysis showed alkaloids, glycosides, flavonoids, saponins, steroids, and tannins in both extracts. FTIR and DSC verified drug-excipient compatibility. The improved formulation (Run 14: PVA 70%, ethanol 35%, drying 36 h) possessed a thickness of 0.38±0.01 mm, folding endurance over 140, tensile strength of 3.80±0.16 kg/cm², drug content at 99.1±0.7%, and cumulative drug release of 96.2±1.5% over a 24 hour period. Drug release follows zero-order kinetics (R^2=0.981) with Korsmeyer-Peppas exponent n=0.62, indicating non-Fickian transport.

The patch remained stable in both storage conditions, with no noticeable changes to the drug content or release profile. Conclusion: The tailored herbal transdermal patch showed superior physicochemical qualities, long-term drug release, and stability, indicating its potential for transdermal antidiabetic therapy.....

Keywords: Gymnema Sylvestre, Tinospora Cordifolia, transdermal patch, Box-Behnken design, drug release kinetics, herbal antidiabetic, solvent casting..

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INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder marked by chronic hyperglycemia due to reduced insulin production, insulin action, or both [1]. The International Diabetes Federation reported that 537 million people worldwide had diabetes in 2021, with forecasts of 783 million by 2045 [1]. India alone has regarding 101 million diabetic patients, ranking second globally in diabetes prevalence [2]. Type 2 diabetes mellitus (T2DM) accounts for 90-95% of all cases and has been linked to serious microvascular and macrovascular complications including neuropathy, nephropathy, retinopathy, and cardiovascular disease.[3]

Despite their high application, conventional oral antidiabetic medications face complications like hepatic first-pass metabolism, gastrointestinal complications, frequent dosing, and insufficient patient compliance. [4]. Transdermal drug delivery systems (TDDS) present an appealing alternative by delivering sustained and controlled drug release across the skin, circumventing first-pass metabolism, preserving steady plasma drug levels, and enhancing patient compliance [5]. Various polymer-based transdermal patch formulations have demonstrated the versatility of this delivery route for diverse therapeutic agents [33, 36, 48]. Matrix-type transdermal patches are especially beneficial owing to their manufacturing simplicity, cost-effectiveness, and capacity for uniform drug release [6].

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Gymnema sylvestre R.Br. (Asclepiadaceae), often referred to as "Gudmar" or "Madhunashini," is a widely used antidiabetic herb that is rich in gymnemic acids, gurmarin, and flavonoids. These compounds can induce insulin secretion, repopulate pancreatic beta cells, and suppress the absorption of glucose to generate hypoglycemic effects [7]. Berberine, palmatine, and tinocordiside occur in Tinospora cordifolia (Willd.) Miers (Menispermaceae), also referred to as "Guduchi" or "Amrita." These substances possess antidiabetic properties through insulin-mimetic action, enhanced sensitivity to insulin, and antioxidant protection [8]. It's cytotoxic and immunomodulatory effects of this plant have been further examined [45]. Both species are one of the many Asian medicinal herbs whose application in curing metabolic syndrome is extensively documented [51]. When taken together, these two herbs give a synergistic approach to managing diabetes focusing on numerous pathophysiological cellular pathways and polyherbal formulations have shown a promising anti-hyper glycemic activity [43].

Box-Behnken design (BBD) is a response surface methodology that efficiently optimises formulation variables with a limited number of experimental runs while differentiating among main effects, interaction effects, and quadratic effects [9]. It is particularly useful for medication formulation improvement as it excludes extreme factor combinations and needs fewer runs than complete factorial designs [10]. This design approach has been productively implemented in a range of therapeutic and biotechnological optimising cases [39, 40].

The objective of this study was to create and evaluate a matrix-type antidiabetic herbal transdermal patch integrating *G. sylvestre and T. cordifolia* extracts using a Box-Behnken design refinement. The study involved pharmacognostic evaluation of the herbal extracts, Preformulation compatibility tests, formulation optimisation, a thorough physicochemical evaluation, in-vitro drug release trials, plus release kinetics simulation. Release kinetics modeling, comparative evaluation of optimized versus non-optimized formulations, and stability assessment.

2. MATERIALS AND METHODS

2.1 Plant Material and Extraction

Dried stems of *Tinospora cordifolia* (Willd.) Miers and *Gymnema sylvestre* R.Br. were authenticated and acquired from a trustworthy herbal supplier. The plant materials were reduced in size and recovered with a hydroalcoholic solvent (ethanol: water, 50:50 v/v) using the Soxhlet extraction method. The extracts were concentrated under reduced pressure and preserved in sealed vessels at 4°C until use.

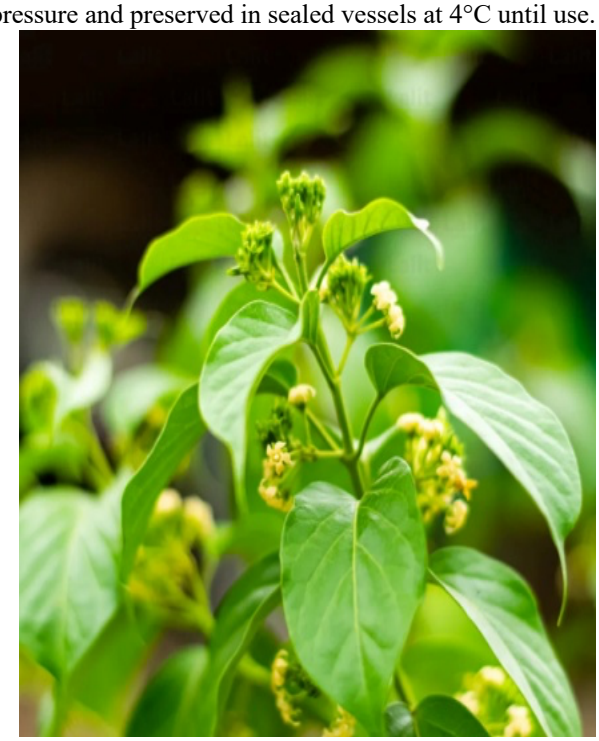

Figure 1: Leaf Morphology of Gymnema sylvestre.

2.2 Pharmacognostic Evaluation:

2.2.1 Phytochemical Screening:

The hydroalcoholic extracts for *G. sylvestre and T. cordifolia*. were tested to qualitative phytochemical analysis for the presence of carbohydrates, decreasing sugars, alkaloids, glycosides, flavonoids, saponins, steroids/terpenoids, tannins, proteins, and resins using standard chemical tests including Molisch's test, Fehling's test, Mayer's test, Dragendorff's test, Keller-Killiani test, Legal's test, Shinoda's test, a lead acetate test, foam test, Salkowski test, ferric chloride test, Biuret's test, Millon's test, and resin test [11].

2.2.2 Fluorescence Analysis:

Fluorescence investigation of the powdered drug was performed by treating it with various reagents including hydrochloric acid, sulphuric acid, and sodium hydroxide in methanol, ferric chloride, acetic acid, ammonium hydroxide, and picric acid. The treated samples were analyzed under visible light and UV light (366 nm) for a unique fluorescence. [12]

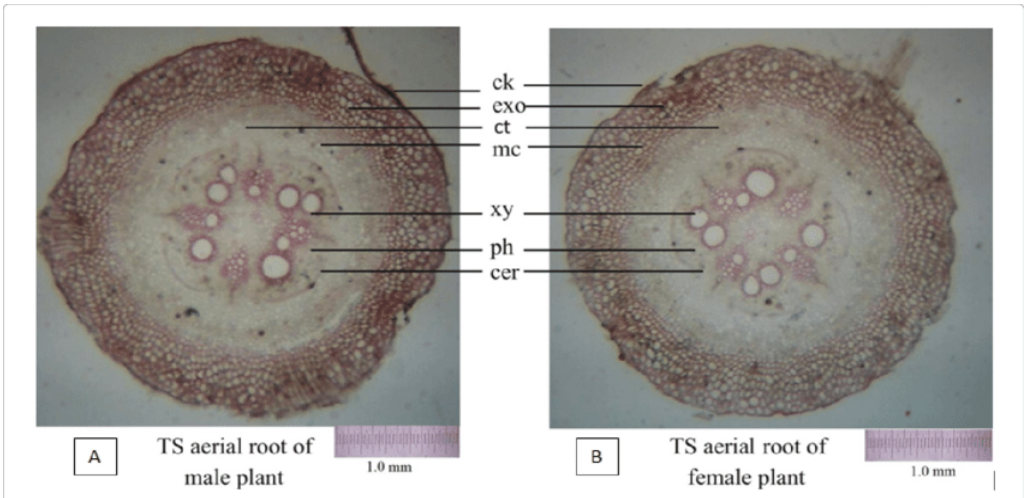

Figure 2: Microscopic T.S. of Gymnema sylvestre Leaf.

Figure 3: Stem Morphology of Tinospora cordifolia.

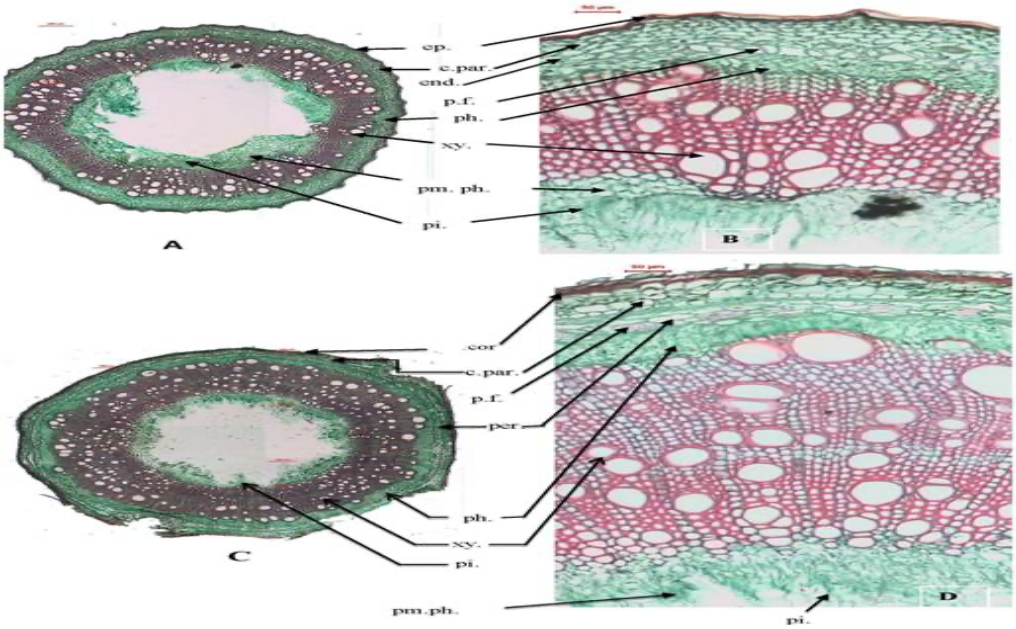

Figure 4: Microscopic T.S. of Tinospora cordifolia Stem

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.**2.3 Preformulation Studies:**
Preformulation experiments were conducted undertaken to assess the compatibility of the herbal extracts and formulation excipients. Fourier transform infrared spectroscopy (FTIR) was employed with the KBr pellet method to identify unique functional groups and identify potential drug-excipient interactions [13]. Differential scanning calorimetry (DSC) was utilized to measure the thermal attributes of the pharmaceuticals, excipients, and physical combinations [14]. Both thermoanalytical and spectroscopic techniques are frequently utilized for drug-excipient compatibility evaluations [35, 41]. Moisture content, total ash, acid-insoluble ash, sulphated ash, alcohol-soluble extractive, and water-soluble extractive were all determined according to standard Pharmacopeial methods. [15]

2.4 Formulation Development by Box-Behnken Design:
A three-factor, three-level Box-Behnken experimental design was employed to maximise the formulation variables. The independent variables looked at were: X_1 = PVA material (30-70%), X_2 = ethanol concentration (20-50%), and X_3 = drying frequency (12-36 hr). The dependent responses examined comprised tensile strength (kg/cm²), moisture uptake (%), thickness (mm), water vapour transmission (g/m²/24 h), surface pH, and folding endurance. A total of 15 experimental runs were generated, including three center of gravity replicates. [9] Design of tests has become usual in pharmaceutical formulation optimization. [37, 38, 42]
The solvent casting method was employed to fabricate the matrix-type transdermal patches. HPMC (5%), chitosan (2%), G. sylvestre extract (1%), T. cordifolia extract (1%), PEG 400 (2%), glycerol (3%), DMSO (2%), and Tween 80 (2%) comprised the consistent formulation composition. PVA concentration, ethanol concentration (as a percentage of the solvent system), and drying duration were the variables. Chitosan dissolved in dilute acetic acid was added to the polymer solution after PVA and HPMC were dispersed in the hydroalcoholic solvent system. With constant stirring, the drug extracts, polymers, and permeation enhancers were added to the polymer solution. According to the experimental design, the uniform solution was cast on a glass plate and dried under closely observed conditions. [16] Similar solvent casting approaches have been described for herbal transdermal patch development [44, 46].

2.5 Evaluation of Transdermal Patches:
2.5.1 Thickness: A digital micron was implemented to measure patch thickness at five different places, and the average was determined. [17]
2.5.2 Folding Endurance: The patch creased repeatedly at the same place until it broke or showed obvious cracks. Folding endurance was described as the number of folds sustained [18].
2.5.3 Tensile Strength: A universal tensile testing apparatus was implemented for determining tensile strength. Two clamps were set up for holding three-by-one-centimeter patch strips, and force was applied until the strip broke. The force at break was divided by the cross-sectional area to find the tensile strength. [17].
2.5.4 Moisture Uptake: Patches were weighed and placed in a desiccator filled with a saturated potassium chloride solution (75% RH) for eighteen hours. The weight difference was utilized to calculate a percentage of hydration uptake [19].
2.5.5 Water Vapour Transmission Rate (WVTR) was calculated using a modified ASTM cup method. The patch was sealed over a cup of distilled water, and weight loss was monitored over 24 hours [20].
2.5.6 Surface pH: To determine the surface pH, place the patch in contact with 0.5 mL distilled water for 1 hour and use a pH meter [18].
2.5.7 Drug Content: To determine the drug content, the patch was immersed in a suitable solvent and measured spectrophotometrically at a suitable λmax. [21].
2.5.8 In-vitro drug release was studied using a Franz diffusion cell with a cellulose acetate membrane. The receptor compartment contained phosphate buffer pH 7.4 at 37±0.5°C. Samples were collected at specified intervals and considered spectrophotometrically [22].
2.5.9 Release Kinetics: To determine the drug release mechanism, in-vitro drug release data were fitted using several kinetic models such as zero-order, first-order, Higuchi, Korsmeyer-Peppas, and Hixson-Crowell [23]. Multidimensional approaches that combine release kinetics and morphological analysis have been suggested for comprehensive assessment of sustained-release systems. [47]

2.6 Stability Studies:
Stability evaluations were carried out on the revised formulation in line to the ICH Q1A (R2) specifications [24]. The patches were stored at 25°C/60% RH and 40°C/75% RH for 60 days. To investigate any physical or chemical changes during storage, samples were examined for drug content and cumulative drug release on days 0, 30, and 60. [25]

3. RESULTS:

3.1 Phytochemical Screening:
The phytochemical examination of *G. sylvestre and T. cordifolia* hydroalcoholic extracts revealed the presence of a variety of bioactive components. The results are presented in Tables 1 and 2 G. sylvestre extract was identified as positive for carbohydrate (Molisch's test), reducing sugars (Fehling's test), alkaloids (Mayer's and Dragendorff's tests), glycosides (Keller-Killiani test), flavonoids (Shinoda's test), saponins (foam test), steroids/terpenoids (Salkowski test), and tannins (ferric chloride test), yet not for proteins (Biuret's test). T. cordifolia extract was tested positive for alkaloids (Dragendorff and Mayer's tests), glycosides (Legal's test), flavonoids (lead acetate test), steroids (Salkowski test), carbohydrates (Anthrone test), saponins (foam test), tannins (ferric chloride test), proteins (Millon's test), and resins (resin test).

Table 1: Phytochemical Screening of Gymnema sylvestre Hydroalcoholic Extract:

S. No.	Chemical Group	Test	Inference
1	Carbohydrates	Molisch's Test	Positive
2	Reducing sugars	Fehling's Test	Positive
3	Alkaloids	Mayer's Test	Positive
4	Alkaloids	Dragendorff's Test	Positive
5	Glycosides	Keller-Killiani	Positive
6	Flavonoids	Shinoda's Test	Positive
7	Saponins	Foam Test	Positive
8	Steroids/Terpenoids	Salkowski Test	Positive
9	Tannins	FeCl3 Test	Positive
10	Proteins	Biuret's Test	Negative

Figure 5: Preliminary Phytochemical Screening of Tinospora cordifolia Ethanolic Extract.

Table 2: Phytochemical Screening of Tinospora cordifolia Hydroalcoholic Extract:

S. No.	Chemical Group	Test	Inference
1	Alkaloids	Dragendorff's Test	Positive
2	Alkaloids	Mayer's Test	Positive
3	Glycosides	Legal's Test	Positive
4	Flavonoids	Lead acetate test	Positive
5	Steroids	Salkowski Reaction	Positive
6	Carbohydrates	Anthrone Test	Positive
7	Saponins	Foam Test	Positive
8	Tannins	FeCl3 Test	Positive
9	Proteins	Millon's Test	Positive
10	Resins	Resin test	Positive

3.2 Fluorescence Analysis:

The fluorescence investigation of powdered drugs treated with various reagents indicated substantial colour changes in either visible and UV light (366 nm). These results are summarised in Table.3.

Table 3: Fluorescence Analysis of Powdered Drug:

S. No.	Treatment	Visible Light	UV Light (366 nm)
1	Drug as such	Brown	Light grey
2	Drug + HCl conc.	Brown	Black
3	Drug + H2SO4 conc.	Black	Light grey
4	Drug + 1N NaOH in MeOH	Light brown	Violet
5	Drug + FeCl3	Greenish brown	Black
6	Drug + Acetic acid glacial	Reddish brown	Grey
7	Drug + NH4OH	Blackish brown	Brown
8	Drug + Picric acid	Dark brown	Brown

3.3 Identity, Purity and Strength Parameters:

The characterisation, purity, and strength parameters of the herbal extracts were determined utilising standard Pharmacopeial procedures. The results are presented in Table.4.

Table 4: Identity, Purity and Strength Parameter:

Parameter	Value
Moisture	3.5%
Total Ash	8.6%
Acid-insoluble Ash	2.35%
Sulphated Ash	9.3%
Alcohol-soluble Extractive	6.6%
Water-soluble Extractive	16.5%

3.4 Preformulation Studies:

Preformulation analysis confirmed that the specified excipients were appropriate for the formulation. An FTIR examination found peaks at 3380 cm^{-1} (O-H stretching, G. sylvestre), 1735 cm^{-1} (C=O stretching, G. sylvestre), 1610 cm^{-1} (C=N stretching, T. cordifolia), 3300 cm^{-1} (O-H hydrogen bonded, PVA), and 3450 cm^{-1} (O-H stretching, HPMC). The drug-excipient physical mixture combinations did not demonstrate significant modifications or suppression of particular peaks, confirming compatibility [13]. DSC thermograms demonstrated no additional thermal events or significant variations in melting endotherms in the physical matrix compared to individual components, suggesting the absence of drug-excipient interactions [14]. The results are displayed in Table 5.

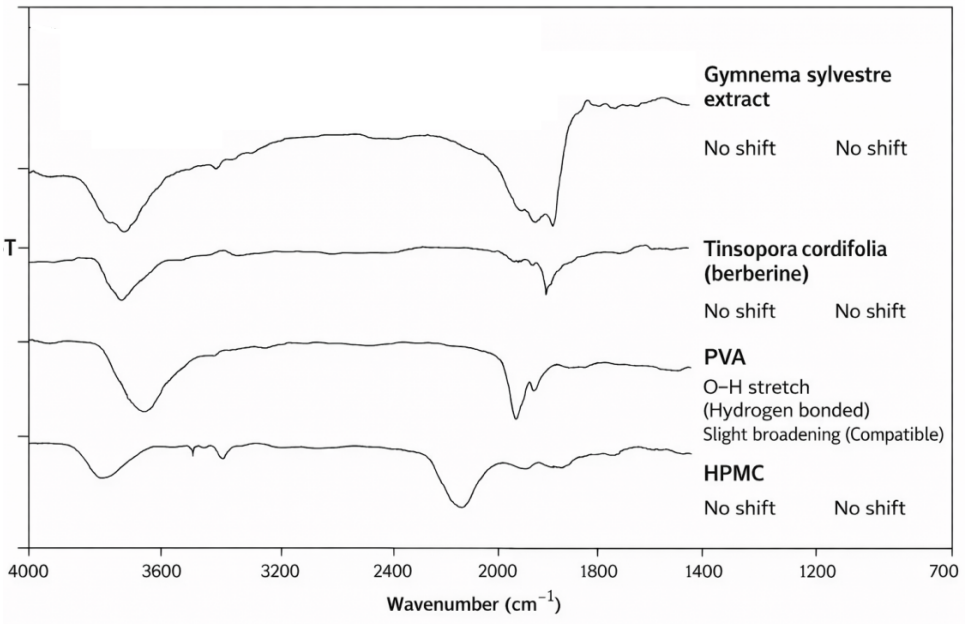

Figure 6: FT-IR Spectral Analysis of Drug and Excipients.

Table 5: FTIR Peak Analysis of Drug and Excipients:

Component	Peak (cm^{-1})	Functional Group	Change
Gymnema sylvestre extract	3380	O-H stretch (hydroxyl)	No shift
Gymnema sylvestre extract	1735	C=O stretch (ester)	No shift
Tinospora cordifolia (Berberine)	1610	C=N stretch (aromatic)	No shift
PVA	3300	O-H stretch (hydrogen bonded)	Slight broadening (compatible)
HPMC	3450	O-H stretch	No shift

3.5 Box-Behnken Design and Physicochemical Evaluation:

Fifteen formulations were developed utilising the Box-Behnken design matrix, with varying PVA (30-70%), ethanol (20-50%), and drying intervals (12-36 hours). The physicochemical examination results for all 15 formulations are presented

in Table 6. The formulation variables had a considerable influence on the evaluated parameters. A higher PVA content resulted in higher tensile strength, thickness, and folding endurance, while moisture absorption decreased. Extended drying time increased tensile strength and folding endurance while reducing moisture uptake. Ethanol concentration showed a moderate effect on drug release and surface pH.

Table 6: Box-Behnken Design Matrix and Physicochemical Evaluation of 15 Formulations:

Run	PVA (%)	EtOH (%)	Dry (h)	TS (kg/cm²)	MU (%)	Th (mm)	WV (g/m²/24h)	pH	FE
1	30	20	24	3.21 ± 0.12	4.2 ± 0.3	0.32 ± 0.02	± 4.1	5.8	110
2	70	20	24	3.45 ± 0.10	3.8 ± 0.2	0.34 ± 0.01	± 4.0	6.1	120
3	30	50	24	2.95 ± 0.11	5.0 ± 0.4	0.28 ± 0.02	± 4.3	5.6	100
4	70	50	24	3.72 ± 0.15	3.6 ± 0.3	0.36 ± 0.01	± 4.2	6.0	120
5	50	35	12	3.12 ± 0.13	4.5 ± 0.3	0.31 ± 0.02	± 4.5	5.7	110
6	50	35	36	3.65 ± 0.14	3.4 ± 0.2	0.35 ± 0.01	± 4.1	6.2	130
7	50	20	12	3.18 ± 0.12	4.8 ± 0.3	0.30 ± 0.02	± 4.4	5.9	110
8	50	20	36	3.60 ± 0.14	3.9 ± 0.2	0.34 ± 0.01	± 4.0	6.3	120
9	50	50	12	3.05 ± 0.11	4.9 ± 0.3	0.29 ± 0.02	± 4.2	5.5	100
10	50	50	36	3.58 ± 0.14	3.7 ± 0.2	0.35 ± 0.01	± 4.1	6.0	120
11	30	35	12	2.92 ± 0.10	5.2 ± 0.4	0.27 ± 0.02	± 4.5	5.6	103
12	30	35	36	3.50 ± 0.13	3.5 ± 0.2	0.33 ± 0.01	± 4.1	6.1	120
13	70	35	12	3.75 ± 0.15	3.3 ± 0.2	0.37 ± 0.01	± 4.0	6.4	130
14	70	35	36	3.80 ± 0.16	3.1 ± 0.2	0.38 ± 0.01	± 3.9	6.5	140
15	50	35	24	3.55 ± 0.13	3.6 ± 0.2	0.34 ± 0.01	± 4.1	6.0	120

3.6 In-Vitro Drug Release Study:

The in-vitro drug release profile of the optimized formulation (Run 14) showed sustained release over 24 hours with 96.2±1.5% cumulative drug release. The drug release was gradual and maintained, indicating controlled delivery through the matrix system. The release profile is presented in Table 7 and Figure 7.

Table 7: In-Vitro Drug Release Profile of Optimized Formulation (Run 14):

Time (h)	Cumulative Release (%)	Cumulative Amount (µg/cm²)	Flux (µg/cm²/h)
0	0	0	—
2	18.5 ± 0.9	74.0	37.0
4	36.7 ± 1.2	146.8	36.7
6	54.6 ± 1.4	218.4	36.4
8	69.8 ± 1.1	279.2	34.9
12	84.5 ± 1.3	338.0	28.2
24	96.2 ± 1.5	384.8	16.0

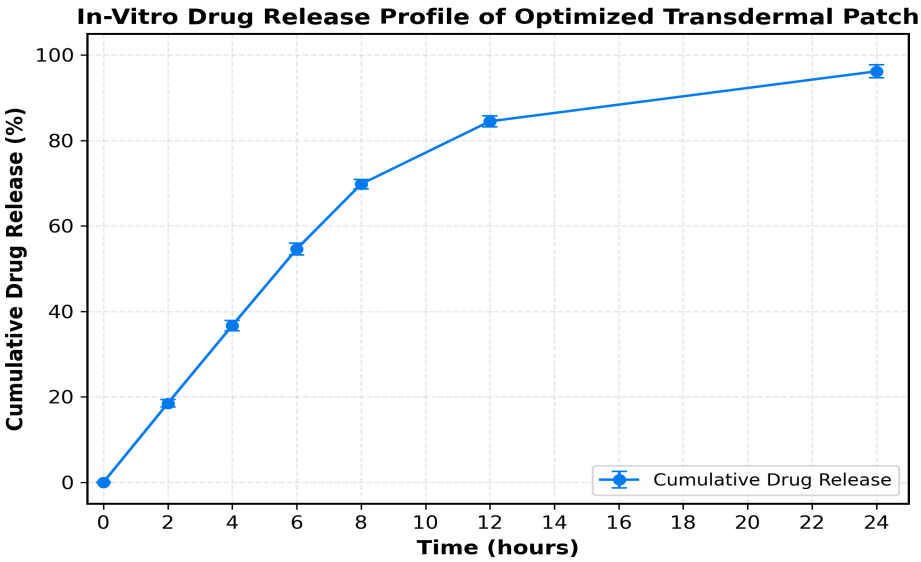

Figure 7: In-Vitro Drug Release Profile of Optimized Transdermal Patch.

3.7 Drug Release Kinetics:

To comprehend the drug release mechanism, the in-vitro data were fitted to several kinetic models. The results are presented in Table 8 and Figure 2. The zero-order model showed the highest correlation coefficient (R^2=0.981) and a release rate constant (K_0=3.998%/h), indicating concentration-independent drug release. The Korsmeyer-Peppas model had a good fit (R^2=0.984) with a diffusion exponent n=0.62, which falls between 0.5 and 1.0. This indicates non-Fickian (anomalous) transport, where both diffusion and polymer erosion contribute to drug release. The Higuchi model (R^2=0.976) suggested a diffusion-controlled procedure. The first-order (R^2=0.894) and Hixson-Crowell (R^2=0.921) models exhibited lower correlations, showing that drug release was not significantly affected by concentration or surface erosion. [23]

Table 8: Drug Release Kinetics of Optimized Formulation:

Kinetic Model	R^2	Rate Constant	Mechanism
Zero-order	0.981	K0 = 3.998 %/h	Controlled, constant rate release
First-order	0.894	K1 = 0.124 h-1	Concentration-dependent; less fitting
Higuchi	0.976	KH = 19.85 %/sqrt(h)	Diffusion-controlled matrix release
Korsmeyer-Peppas	0.984	KP = 14.28	Non-Fickian anomalous transport - BEST FIT
Hixson-Crowell	0.921	Ks = 0.018 h-1/3	Minor erosion contribution; less fitting

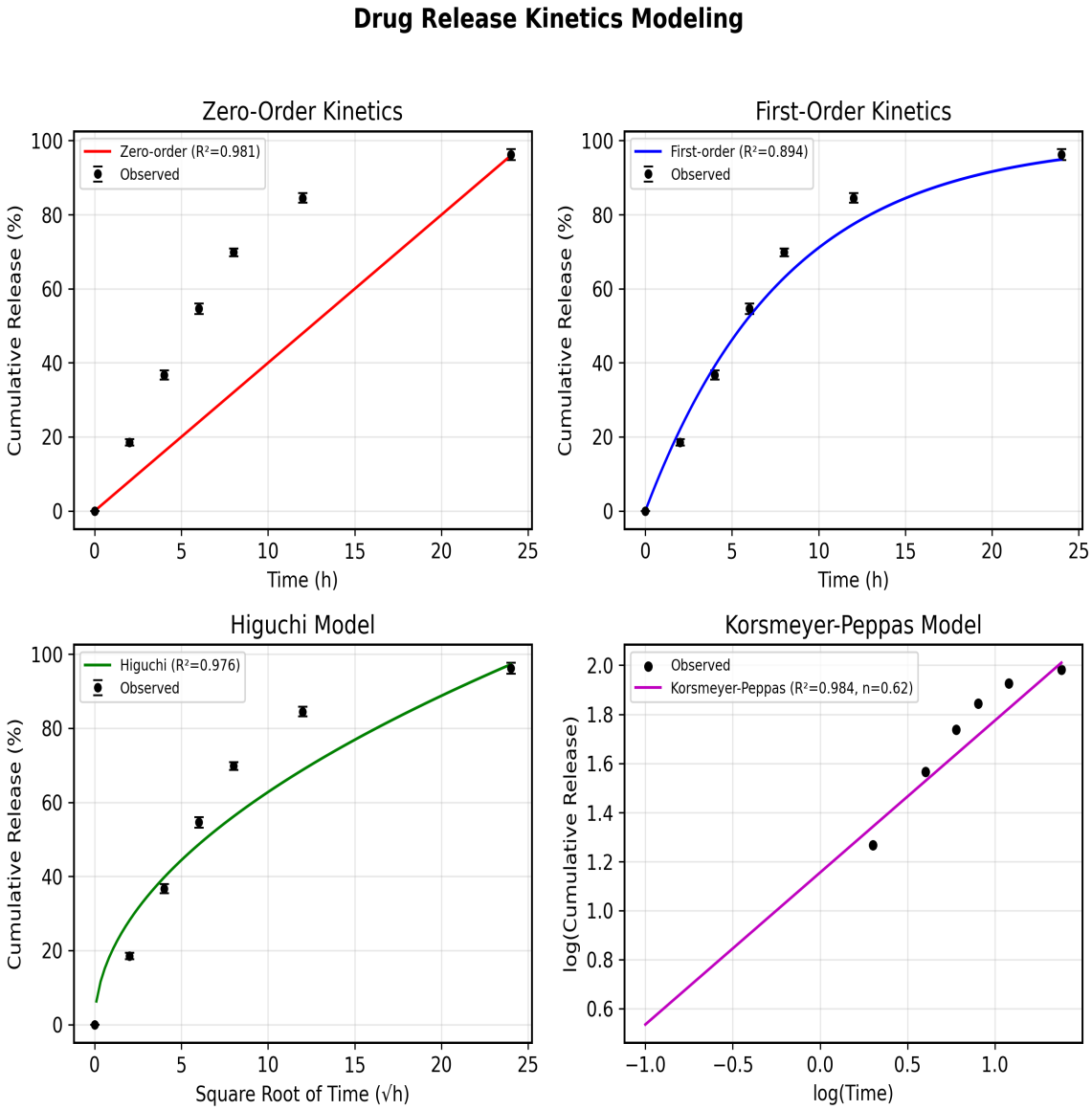

Figure 8: Drug Release Kinetics Modeling.

3.8 Comparative Evaluation of Optimized and Non-Optimized Formulations:

The improved formulation (Run 14: PVA 70%, ethanol 35%, drying 36 h) was compared with the non-optimized formulation (Run 11: PVA 30%, ethanol 35%, drying 12 hours. The results are shown in Table 9 and Figure 3. The optimum formulation performed better than the non-optimized formulation on the basis of physicochemical properties, notably greater tensile strength (3.80±0.16 vs 2.92±0.10 kg/cm²), folding endurance (>140 vs 103), drug content (99.1±0.7 vs 92.4±1.1%), and cumulative drug release (96.2±1.5 vs 84.3±2.1%).

Table 9: Comparative Evaluation of Optimized (Run 14) and Non-Optimized (Run 11) Formulations:

Parameter	Optimized (Run 14)	Non-Optimized (Run 11)	Significance
Thickness (mm)	0.38 ± 0.01	0.27 ± 0.02	p<0.001
Folding Endurance	>140 folds	103 folds	p<0.001
Tensile Strength (N/cm2)	3.80 ± 0.16	2.92 ± 0.10	p<0.001
Moisture Uptake (%)	3.1 ± 0.2	5.2 ± 0.4	p<0.001
Drug Content (%)	99.1 ± 0.7	92.4 ± 1.1	p<0.01
% Release at 24h	96.2 ± 1.5	84.3 ± 2.1	p<0.001

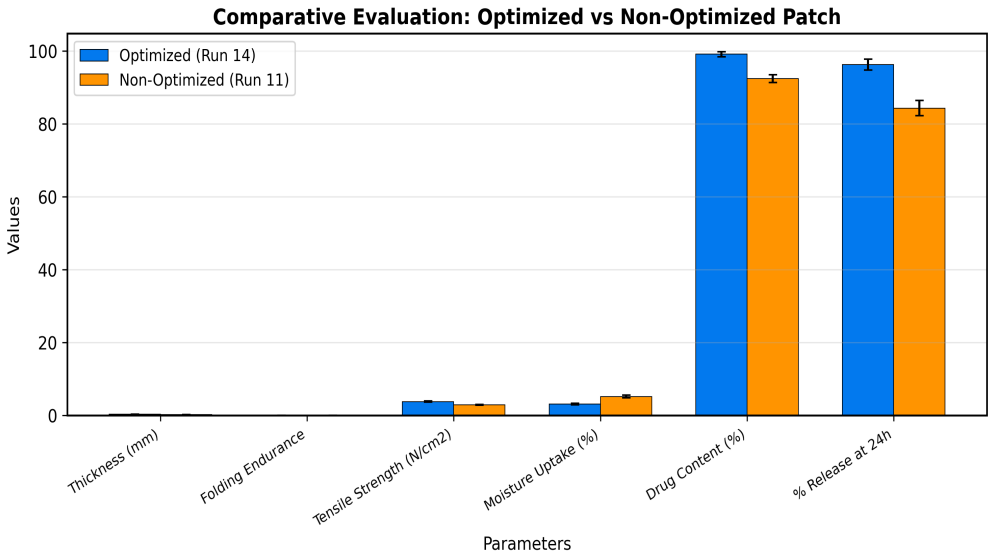

Figure 9: Comparative Evaluation of Optimized vs Non-Optimized Patch.

3.9 Stability Studies:

Stability tests performed on the improved formulation at 25°C/60% RH and 40°C/75% RH for 60 days revealed no significant changes in drug content or cumulative drug release. The results are presented in Table 10. At 25°C/60% RH, drug content diminished from 99.1±0.7% to 98.5±0.9% and cumulative release from 96.2±1.5% to 95.8±1.6% after 60 days. At 40°C/75% RH, drug content dropped to 96.9±1.2% and cumulative release to 94.5±1.8% at Day 60. Nevertheless, the changes were acceptable. The patches maintained their physical integrity, flexibility, and appearance throughout the testing period, confirming stability pursuant to the ICH requirements. [24]

Table 10: Stability Studies of Optimized Formulation:

Condition	Time Point	Drug Content (%)	Cum. Release (%)	Appearance
25C/60%RH	Day 0	99.1 ± 0.7	96.2 ± 1.5	Smooth, flexible, pale yellow
25C/60%RH	Day 30	98.9 ± 0.8	95.9 ± 1.4	No significant change
25C/60%RH	Day 60	98.5 ± 0.9	95.8 ± 1.6	No significant change
40C/75%RH	Day 0	99.1 ± 0.7	96.2 ± 1.5	Smooth, flexible, pale yellow
40C/75%RH	Day 30	97.8 ± 1.0	95.1 ± 1.7	Slight softening noted
40C/75%RH	Day 60	96.9 ± 1.2	94.5 ± 1.8	Slight reduction in flexibility

4. DISCUSSION:

The phytochemical screening results demonstrated the presence of multiple bioactive compounds in both *G. sylvestre and T. cordifolia* extracts, which validates their traditional use in diabetes management. The detection of alkaloids, glycosides, and flavonoids is particularly important because these molecule compounds have been extensively researched for their anti-diabetic properties [7, 8]. The incorporation of gymnemic acids in *G. sylvestre* and berberine in *T. cordifolia* provides a pharmacological basis for the resulting patch's antimicrobial effects [26, 27]. *Guduchi (T. cordifolia)* has been the focus of multiple experimental trials evaluating its therapeutic properties [52]. The effects of polymers on drug conveyance performance have been examined in comparable microsphere systems. [32]

The fluorescence inspection generated different fingerprints for the powdered pharmaceutical material, which acted as a quality control parameter for authentication and standardization [12]. The distinct colour changes observed with different reagents under visible and UV light are attributed to the presence of specific functional groups in the phytoconstituents that react with the reagents and produce coloured complexes or fluorescence. [28]

The FT-IR and DSC Preformulation studies revealed the absence of drug-excipient interactions, which is important for the formulation's stability and therapeutic efficacy [13]. The retention of identifiable FTIR peaks in physical mixtures indicates that the drug's functional groups did not change in the presence of excipients. Similarly, DSC thermograms indicated no further thermal events, showing

that the drug and excipients were physically compatible. [14]

The Box-Behnken design proved effective at minimizing the formulation variables. The optimum formulation (Run 14) with PVA 70%, ethanol 35%, and a drying time of 36 hours, provided the best overall performance. The high PVA concentration enhanced tensile strength and folding endurance by forming a dense polymer matrix with strong intermolecular hydrogen bonding [17]. The longer drying time allowed complete solvent evaporation and polymer chain relaxation, thereby resulting in a more uniform and mechanically robust layer [16]. The ethanol concentration of 35% demonstrated the ideal trade-off between polymer solubility and film synthesis properties [19]. Enhanced bioavailability through optimal formulation design has been demonstrated in numerous drug delivery techniques [34, 49], and carrier-mediated skin-based delivery principles complement the transdermal technique utilized here. [50]

The optimized formulation exhibits zero-order drug release kinetics (R^2=0.981), which renders it excellent for transdermal delivery. That ensures a steady release rate irrespective of concentration, which leads to steady plasma drug levels [29]. The Korsmeyer-Peppas exponent (n=0.62) suggests non-Fickian (anomalous) transport, indicating that drug release is mediated by both diffusion through the polymer matrix and polymer relaxation/erosion [30]. This dual mechanism is characteristic of hydrophilic polymer matrices which include PVA and HPMC. The resulting water penetration leads to polymer swelling, followed by drug diffusion through the expanded matrix. [31]

The contrast evaluation clearly demonstrated that an improved formulation outscored the non-optimized formulation, thus validating the Box-Behnken optimization approach. The improved formulation displayed a substantially higher drug content (99.1±0.7 vs 92.4±1.1%) and cumulative release (96.2±1.5 vs 84.3±2.1%) owing to better polymer entrapment and extended drying time, leading to a uniform distribution. [21]

The stability studies confirmed that the modified composition maintained its physical and chemical characteristics and drug diffusion profile under both long-term and accelerated storage conditions. The slight reduction in drug content and ejection at 40°C/75% RH coincides with the expected effect of elevated moisture and temperature on polymer matrices, but the changes were within acceptable limits according to ICH Q1A (R2) standards [24]. The stability results support a shelf life of at least 60 days under recommended storage conditions [25].

5. CONCLUSION:

A matrix-type antidiabetic herbal transdermal patch that included *G. sylvestre and T. cordifolia* extracts was successfully designed and improved using a Box-Behnken design. The Pharmacognostic study confirmed the presence of major bioactive compounds in both herbal extracts. Preformulation evaluations with FTIR and DSC demonstrated drug-excipient compatibility. The customised formulation (PVA 70%, ethanol 35%, drying 36 h) exhibited excellent physicochemical properties, including high tensile strength (3.80±0.16 kg/cm²), folding endurance (>140), drug content (99.1±0.7%), and sustained drug release (96.2±1.5% over 24 h) through the use of zero-order kinetics with a non-Fickian transport mechanism. The patch exhibited good stability when used in long-term and accelerated storage conditions. This information demonstrate the promising potential of the created herbal transdermal patch as an effective replacement to oral antidiabetic medication, giving sustained delivery of drugs, improved bioavailability, and improved bioavailability, and enhanced patient compliance. Further in vivo pharmacological study is needed to confirm the improved formulation's antidiabetic efficacy and pharmacokinetic improvements.

CONFLICT OF INTEREST:

The authors declare no conflict of interest.

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