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Preparation And Evaluation Of Transdermal Patch For Diabetes

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ABSTRACT: Transdermal patches offer a promising alternative route for the delivery of anti-diabetic drugs, aiming to improve glycemic control and patient compliance. The present work focuses on the development of a metformin-loaded transdermal patch using hydrophilic polymers such as HPMC and PVA to obtain a swell able matrix capable of providing zero-order release. Suitable plasticizers, permeation enhancers and backing membranes were selected to achieve adequate flexibility, skin adhesion and drug flux across the stratum corundum. The patches were prepared by solvent-casting technique and evaluated for thickness, drug content uniformity, folding endurance, moisture uptake and in-vitro drug release. In-vitro permeation studies through excised skin were performed to correlate release behavior with transdermal flux. The optimized formulation showed uniform drug loading, satisfactory mechanical properties and sustained permeation over an extended period, indicating its potential as a patient-friendly system for the management of diabetes.

Keyword: Metformin hydrochloride, Diabetes mellitus Antidiabetictherapy, Skin permeation enhancers, Oleic acid.

Introduction: Transdermal drug delivery has emerged as an attractive alternative to conventional oral and injectable routes for the long-term management of chronic diseases such as diabetes mellitus. In this approach, a medicated patch is applied to the surface of intact skin, from where the drug diffuses across the stratum corundum into the systemic circulation at a controlled rate.[1] This mode of delivery can maintain relatively constant plasma concentrations for an extended period, reduce dosing frequency, and improve patient adherence, which are particularly important in diabetic patients who often require lifelong therapy.[2-3]Metformin is one of the most widely prescribed first-line ant diabetic agents, but its oral administration is frequently associated with gastrointestinal side effects and variable bioavailability. Incorporating metformin into a transdermal patch system offers the possibility of bypassing the gastrointestinal tract and hepatic first-pass metabolism, thereby enhancing therapeutic efficacy while minimizing adverse effects.[4-6] To achieve sufficient permeation of this hydrophilic drug through the lipophilic skin barrier, suitable polymers, plasticizers, and skin-permeation enhancers must be carefully selected and optimized. In this context, hydrophilic polymers such as hydroxypropyl methylcellulose (HPMC) and polyvinyl alcohol (PVA) can form swell able matrices capable of providing controlled or nearly zero-order release, while enhancers like oleic acid or limonene temporarily increase skin permeability. The development of a metformin transdermal patch therefore involves not only the selection of appropriate excipients but also the design of a multi-layered system with adequate mechanical strength, flexibility, and adhesion. Critical quality attributes include uniform drug loading, folding endurance, moisture uptake, and an optimal moisture vapor transmission rate to ensure both patient comfort and formulation stability. Systematic formulation and

evaluation of such patches may lead to a patient-friendly, non-invasive dosage form that can improve glycemic control and overall quality of life in individuals living with diabetes.

1.2 MATERIAL AND METHOD

1.2.1MATERIAL

All chemicals used in the present study were of analytical grade and procured from reputed suppliers [7].

Table 1.1: List of Chemicals used in the experiment

S.NO	MATERIAL SUPPLIAR	MANUFACTURER
1.	Drug (Model drug for Transdermal Delivery	Central Drug House, New Delhi
2.	Hydroxypropyl Methylcellulose (HPMC)	Central Drug House, New Delhi
3.	Polyvinyl Alcohol (PVA)	Central Drug House, New Delhi
4.	Polyethylene Glycol 400 (PEG 400)	Loba Chemise Pvt. Ltd., Mumbai
5.	Dibutyl Phthalate	Loba Chemise Pvt. Ltd., Mumbai
6.	Methanol	Merck Pvt. Ltd., Mumbai
7.	Phosphate Buffer (pH 7.4)	Prepared in Laboratory
8.	Distilled water	Prepared in Laboratory

1.2.2 INSTRUMENTS

Table1.2: List of Instruments used in the study

S.NO.	Equipment	Manufacturer
1.	Digital Weighing Balance	Shimadzu Pvt. Ltd.
2.	Magnetic Stirrer with Hot Plate	Remi Instruments
3.	UV–Visible Spectrophotometer	Agilent Technology Cary 60
4.	FTIR Spectrophotometer	Perkin Elmer
5.	Franz Diffusion Cell	Electro lab, Mumbai
6.	pH Meter	Aqua sol
7.	Micrometer Screw Gauge	Mitutoyo
8.	Brookfield Viscometer	Brookfield
9.	Digital Melting Point Apparatus	Rexnord

1.2.3 METHODS

(a) *Preformulation Studies*

Preformulation studies were performed to determine the physicochemical characteristics of the drug and to evaluate its compatibility with excipients. [8-10].

(b) Organoleptic Properties

The color, odor, and appearance of the drug were observed visually and recorded using descriptive terms.

(c) Solubility Studies

The solubility of the drug was determined in various solvents such as methanol, ethanol, phosphate buffer (pH 7.4), and distilled water at room temperature. Description Parts of Solvent Required for One Part of Solute [12][24].

Table 1.3: Standard Solubility Table [IP]

Attributes	Range
Very Soluble	Less than 1
Freely Soluble	From 1 to 10
Soluble	From 10 to 30
Sparingly Soluble	From 30 to 100
Slightly Soluble	From 100 to 1000
Very Slightly Soluble	From 1000 to 10,000
Practically Insoluble	More than 10,000

(d) Drug–Excipient Compatibility Studies (FTIR Analysis)

Compatibility between drug and excipients was determined using Fourier Transform Infrared Spectroscopy (FTIR). Spectra were recorded between 4000–400 cm^{-1} and compared to identify any possible interactions.

2. PREPARATION DEVELOPMENT OF TRANSDERMAL PATCH

The transdermal patches were prepared by solvent casting technique.

Procedure:

1. Accurately weighed quantities of polymer(s) were dissolved in suitable solvent (methanol: water mixture).
2. Plasticizer (PEG 400 or Dibutyl Phthalate) was added to the polymeric solution to provide flexibility.
3. The accurately weighed amount of drug was incorporated into the polymeric solution and stirred continuously using a magnetic stirrer.
4. The solution was poured into a glass Petri dish and allowed to dry at room temperature for 24 hours.
5. After drying, the patches were carefully removed and stored in desiccators until further evaluation.

3. EVALUATION OF TRANSDERMAL PATCHES

3.1 Physical Appearance

The prepared patches were observed for color, transparency, smoothness, and flexibility.

3.2 Thickness

Measured at five different points using a digital micrometer screw gauge; mean thickness was calculated.

3.3 Weight Uniformity
Individual patch weights were determined and mean weight calculated.

3.4 Folding Endurance
The patch was repeatedly folded at the same place until it broke. The number of folds required to break the patch was noted.

3.5 Moisture Content
Patches were weighed, placed in a desiccator with calcium chloride for 24 hours, and reweighed to determine % moisture loss.

3.6 Moisture Uptake
Patches were exposed to a relative humidity chamber (75% RH) for 24 hours and % moisture uptake calculated.

3.7 Drug Content Uniformity
Each patch was dissolved in phosphate buffer pH 7.4, filtered, and analyzed spectrophotometric ally at λ max of the drug.

3.8 In-vitro Drug Diffusion Studies
Conducted using Franz diffusion cell with phosphate buffer (pH 7.4) as receptor medium, maintained at 37 ± 0.5°C with continuous stirring. Samples were withdrawn at specific intervals and analyzed spectrophotometric ally.

3.9 Skin Irritation / Compatibility Test:
Evaluated on suitable animal skin or synthetic membrane to check irritation potential.

4. RESULT AND DISCUSSION

4.1 Evaluation of Prepared Transdermal Patches
The developed transdermal patches[11] (F1–F6) were examined for several physicochemical characteristics including film thickness, uniformity of weight, folding endurance, percentage moisture content, percentage moisture uptake, and drug content.

Table 4.1 - Physicochemical Evaluation of Formulated Patches

Formulation code	Thickness (mm)	Weight uniformity (mg/cm2)	Folding endurance %	Moisture content %	Moisture uptake	Drug content
F1	0.25 ± 0.02	22.1 ± 0.5	285 ± 4	2.12 ± 0.04	3.40 ± 0.09	95.85 ± 0.40
F2	0.27 ± 0.03	23.0 ± 0.4	298 ± 5	2.05 ± 0.03	3.28 ± 0.07	96.42 ± 0.45
F3	0.28 ± 0.01	24.5 ± 0.6	310 ± 4	1.98 ± 0.04	3.12 ± 0.06	97.10 ± 0.48
F4	0.30 ± 0.02	25.2 ± 0.5	325 ± 5	1.90 ± 0.05	2.95 ± 0.08	97.85 ± 0.52
F5	0.26 ± 0.02	23.4 ± 0.3	302 ± 3	2.08 ± 0.04	3.20 ± 0.07	96.65 ± 0.50
F6	0.29 ± 0.02	24.0 ± 0.4	318 ± 4	1.95 ± 0.03	2.85 ± 0.05	98.10 ± 0.47

(i)Discussion on Physicochemical Parameters
All prepared patches showed acceptable uniformity in both thickness and weight, signifying even distribution of drug and excipients. Folding endurance values indicated good flexibility and resistance to mechanical stress. The low moisture content and uptake demonstrated better stability and protection from microbial contamination. Drug content analysis confirmed uniform dispersion of the active ingredient throughout the

polymeric matrix.

(j) In-vitro Drug Release Studies

The in-vitro diffusion of the drug from the prepared films was assessed using a Franz diffusion apparatus containing phosphate buffer (pH 7.4) maintained at 37 ± 0.5 °C. Samples were withdrawn at regular time intervals and analyzed spectrophotometric ally [12][14].

(k)In-vitro Drug Release Profile of Formulations (F1–F6)

Time(hr)	F1	F2	F3	F4	F5	F6
1	12.4	14.	16.3	10.5	15.2	17.1
2	23.	25.	28.1	20.2	27.3	29.5
4	39.	42.	46.8	36.1	45.2	48.9
6	56.	59.	63.5	52.0	61.8	65.4
8	70.	74.	78.6	68.2	76.1	80.5
10	83.	86.	90.2	81.4	88.6	92.4
12	91.	94.	97.6	89.8	95.2	98.9

Table 4.2

(l) Discussion on Drug Release

Among all batches, F3 exhibited the highest cumulative release (97.6 %) at 12 hours. The optimized polymer ratio of HPMC and PVA provided desirable film properties and effective drug diffusion. Lower release in F1 and F4 was attributed to higher polymer concentration, which increased matrix density and decreased permeability.

(m)Drug Release Kinetics

To understand the mechanism of drug diffusion, the release data were fitted to various kinetic [15].

Table 4.3: Drug Release Kinetics of Optimized Formulation (F3)

Model	R^2 value	Release mechanism
Zero order	0.983	Constant rate release
First order	0.942	Concentration denpendent release
Higuchi	0.988	Diffusion control
Korsmeyer peppas (n=0.62)	0.975	Anomalous (non fickian) diffusion

(n)Discussion on Release Mechanism

The release profile of the optimized batch followed the Higuchi diffusion model (R^2 = 0.988), indicating that diffusion through the polymer matrix governed the release. The Pappas exponent (n = 0.62) confirmed a non-Fiction (anomalous) pattern where both diffusion and polymer relaxation influenced the release process.

(o)*Stability Study*

The optimized formulation (F3) was kept under two storage conditions 25 °C / 60 % RH and 40 °C / 75 % RH for 30 days. No major variation in physical appearance, thickness, or drug content was found, suggesting good stability of the prepared patch [16][17].

5. CONCLUSION

The results of the present study indicate that the formulated transdermal patch for diabetic management exhibits promising performance in terms of drug release, permeation, and overall patch stability. The evaluation parameters including thickness, weight variation, folding endurance, moisture content, drug content uniformity, and in-vitro drug release confirmed that the optimized formulation maintained uniform physicochemical properties. The in-vitro permeation studies demonstrated a sustained and controlled release profile, which is essential for maintaining steady plasma glucose levels in diabetic patients. The stability studies further confirmed that the patches remained physically and chemically stable during the storage period, indicating suitability for long-term use. Overall, the findings suggest that the optimized transdermal patch possesses the potential to improve patient compliance, avoid first-pass metabolism, reduce dosing frequency, and provide sustained therapeutic action. Hence, this formulation can be considered a promising alternative to conventional oral diabetic therapies, offering a non-invasive and patient-friendly drug delivery approach.

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