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FORMULATION AND EVALUATION OF TRANSDERMAL PATCHES CONTAINING NIFEDIPINE

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ABSTRACT

This study aims to develop and assess transdermal patches incorporating nifedipine, a well-established medication for controlling hypertension and managing angina pectoris. Transdermal drug delivery systems offer a means of releasing drugs in a controlled and sustained manner through the skin into systemic circulation, enhancing both patient compliance and therapeutic outcomes. In this work, patches were fabricated via the mercury substrate technique, utilizing different blends of polymers, along with a penetration enhancer and plasticizer. Five distinct formulations (F1 to F5) were prepared using a combination of hydrophilic (HPMC) and hydrophobic (Ethyl cellulose) polymers. To confirm formulation stability, drug-excipient compatibility was thoroughly investigated. Among all formulations, F5 exhibited the most favorable evaluation parameters, including suitable thickness, consistent weight, excellent folding endurance, and appropriate moisture uptake. These findings underscore the promise of transdermal patches as an effective approach for the sustained systemic delivery of nifedipine.

KEYWORDS: Nefidipine, HPMC K4M, Ethyl Cellulose, Dibutyl phthalate, Polyethylene glycol, Mercury substrate method.

INTRODUCTION

Transdermal drug delivery systems (TDDS) are specialized drug delivery devices designed with a defined surface area and an adhesive backing, enabling them to deliver a controlled amount of drug across intact skin at a predetermined rate. These systems are intended to maintain consistent plasma drug concentrations within the therapeutic window, thereby enhancing treatment effectiveness. In recent years, transdermal delivery has gained significant attention for systemic therapy due to its ability to bypass hepatic first-pass metabolism, resulting in higher systemic bioavailability for drugs that are otherwise extensively metabolized in the liver. Additionally, TDDS can provide sustained drug release over an extended period, support self-administration, and allow rapid discontinuation of drug action when necessary, all of which contribute to improved patient compliance. However, despite these benefits, only a limited range of drugs are suitable for transdermal administration because most compounds exhibit poor permeability through the skin's layers. The stratum corneum, in particular, serves as a formidable barrier to drug penetration. To address this limitation, various strategies such as the use of vehicles, penetration enhancers, and electrically assisted methods have been explored to enhance drug permeation and expand the applicability of TDDS.[1.2]

Transdermal drug delivery systems (TDDS) are defined as self-contained, discrete dosage forms that, when placed on intact skin, enable the controlled release of a drug into the systemic circulation. The transdermal route has emerged as a promising option for both local and systemic drug administration. TDDS, commonly referred to as "patches," are specifically formulated to deliver a precise and therapeutically effective dose of medication through the skin barrier. This mode of delivery offers patients a safe, convenient, and pain-free method of self-administration.[3]

Currently, oral administration remains the most widely used method for drug delivery, primarily due to its ease of use. Nifedipine (NF) is a yellow crystalline compound that is practically insoluble in water but exhibits good solubility in ethanol. Pharmacologically, nifedipine is a selective calcium channel blocker and a peripheral arterial vasodilator that exerts its effect by acting directly on vascular smooth muscle. The present study focuses on the formulation and evaluation of nifedipine-loaded transdermal patches. These patches were prepared using various polymers and their combinations. The resulting transdermal systems were then assessed for key parameters such as weight variation, thickness, folding endurance, and percentage moisture uptake.

The suitability of nifedipine (NF) for development as an effective transdermal delivery system is supported by several factors, including its low molecular weight and low daily dose requirement (20–60 mg). Additionally, its poor water solubility, ability to bypass first-pass metabolism, and potential to maintain more consistent plasma drug levels all contribute to its promise as a transdermal candidate. These attributes can help reduce side effects and allow the formulation of patches with a dosing interval of 3 to 5 days, thereby enhancing patient adherence and convenience.[4]

Advantages

- Bypasses first-pass hepatic metabolism.
- Maintains steady plasma drug concentrations over an extended period.
- Reduces the required dosage.
- Minimizes undesirable side effects.
- Lowers gastrointestinal adverse effects.
- Allows prompt discontinuation if toxicity occurs.
- Enhances patient compliance and convenience.
- Enables modulation of biological barriers to improve drug absorption.

Disadvantages

- Local skin irritation or allergic reactions can occur at the application site.
- Not suitable for drugs that require high plasma concentrations.
- Drugs with long biological half-lives may not be ideal candidates for transdermal delivery.
- Some patients may find patches uncomfortable to wear for extended periods.
- Transdermal systems can be more expensive compared to conventional dosage forms.
- Limited to drugs with suitable physicochemical properties for skin permeation.

MATERIALS AND METHODS

Materials

Nifedipine was gift sample by Molychem Pvt. Ltd. Mumbai. HPMC K4M was produced by Molychem Pvt. Ltd. Mumbai. Ethyl Cellulose, Methanol, Ethanol, Chloroform, Polyethylene Glycol, Dibutyl Phthalate, produced by Research lab fine chem industries Mumbai.

Methods

Estimation of Nifedipine

Spectrophotometric method depends on the measurement of absorbance at 236 nm of U.V region in Distilled water and pH 6.8 was used for the estimation of Nifedipine.

Preparation of Calibration Curve for Nifedipine

An accurately weighed amount of nifedipine was dissolved in a suitable solvent to prepare a stock solution with a known concentration (e.g., 1 mg/mL). A series of standard solutions with different concentrations (e.g., 1 µg/mL, 2 µg/mL, 5 µg/mL, 10 µg/mL, etc.) were then prepared by appropriate dilution of the stock solution. The absorbance of each standard solution was measured at the maximum absorption wavelength of nifedipine (approximately 236 nm) using a UV-Visible spectrophotometer, with the solvent or buffer serving as the blank. A calibration curve was constructed by plotting the nifedipine concentrations (µg/mL) on the X-axis and the corresponding absorbance values on the Y-axis. A linear regression analysis was performed, and the resulting equation ($y = mx + b$) was used to calculate the concentration of nifedipine in unknown samples from their measured absorbance values.

Method for Preparation of Nifedipine Transdermal Patches

The transdermal patches of nifedipine were prepared by mercury substrate method. The required polymer was dissolved in a mixture of chloroform and methanol to form a clear solution. Nifedipine, along with the penetration enhancer and plasticizer, was then uniformly dispersed into the viscous polymer solution under continuous stirring to ensure homogeneity. The resulting mixture was carefully poured onto a leveled mercury surface contained in a Petri dish and covered with an inverted funnel to control the rate of solvent evaporation. The Petri dish was kept undisturbed at room temperature for 24 hours to allow complete solvent evaporation and film formation. The formed transdermal patch was then carefully removed intact by gently lifting it from the mercury surface.[5]

Characterization Methods

Fourier transform infrared spectroscopy (FTIR)

FTIR spectroscopy was performed to investigate and predict possible physicochemical interactions between the drug and other formulation components, facilitating the selection of chemically compatible, stable, and therapeutically acceptable ingredients. An IR matching approach was employed to detect any potential chemical interactions between nifedipine and the polymers used. A small amount of each sample was placed on the sample holder and scanned over a wavenumber range of 4000 to 400 cm^{-1} using an FTIR spectrophotometer. The IR spectra of the physical mixtures were compared with those of the pure drug and individual polymers. Peak matching was carried out to identify any shifts, appearance, or disappearance of characteristic peaks, which could indicate possible interactions.

Evaluation Parameter

I. Thickness of the patch

The thickness of the transdermal patch is measured at various points using a screw gauge or micrometer.[6]

II. Drug Content

A portion of the prepared patch was cut to a specified area (1 cm^2), dissolved in distilled water, treated in a sonication bath, and then centrifuged at 12,000 rpm for 15 minutes.[7]

III. Weight Variation

Before analysis, the prepared patches were dried at 60 °C for 4 hours. Each patch was then cut into equal sections, and the individual pieces were weighed using a digital balance. The average weight and standard deviation were calculated from the individual weights.[8]

IV. Folding Endurance

Folding endurance was determined by repeatedly folding the patch at the same location until it broke or developed cracks. The number of times the patch could be folded at the same spot without breaking was recorded as the folding endurance value.[9]

V. Moisture Uptake

The weighed patches were placed in a desiccator containing potassium chloride to maintain 84% RH. After 24 hours, the patches were reweighed, and the moisture uptake was calculated using the following formula:[10]

$$\% \text{ Moisture Uptake} = \frac{\text{Patch final weight-Patch initial weight} \times 100}{\text{Patch initial weight}}$$

RESULTS

Table 1: Standard calibration Curve of Nifedipine.

Sl. No	Concentration (µg/ml)	Absorbance (nm)
1.	0	0
2.	2	0.203
3.	4	0.406
4.	6	0.620
5.	8	0.840
6.	10	0.960

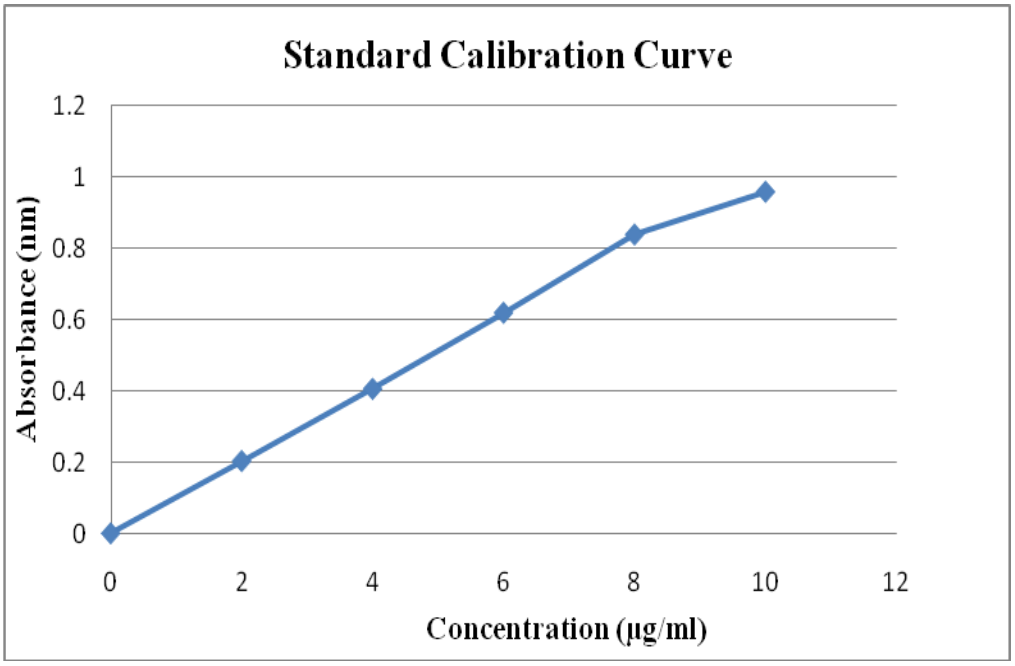

Figure 1: Standard calibration Curve of Nifedipine.

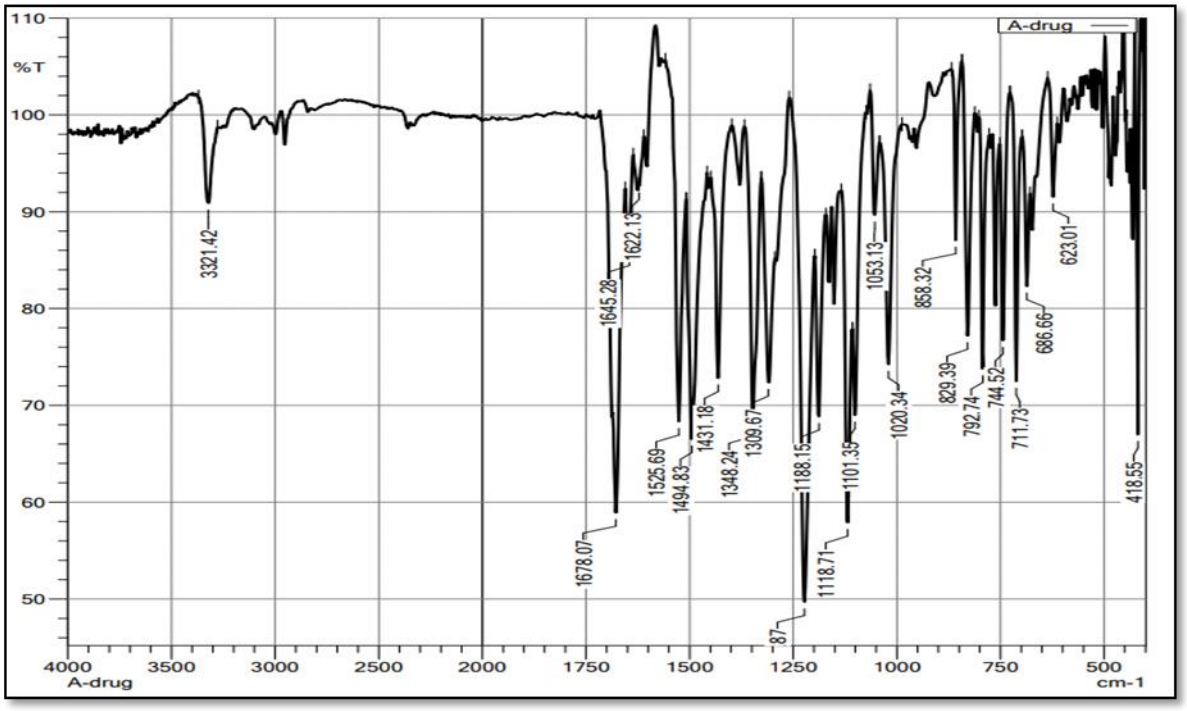

Figure 2: FT-IR of Nifedipine drug.

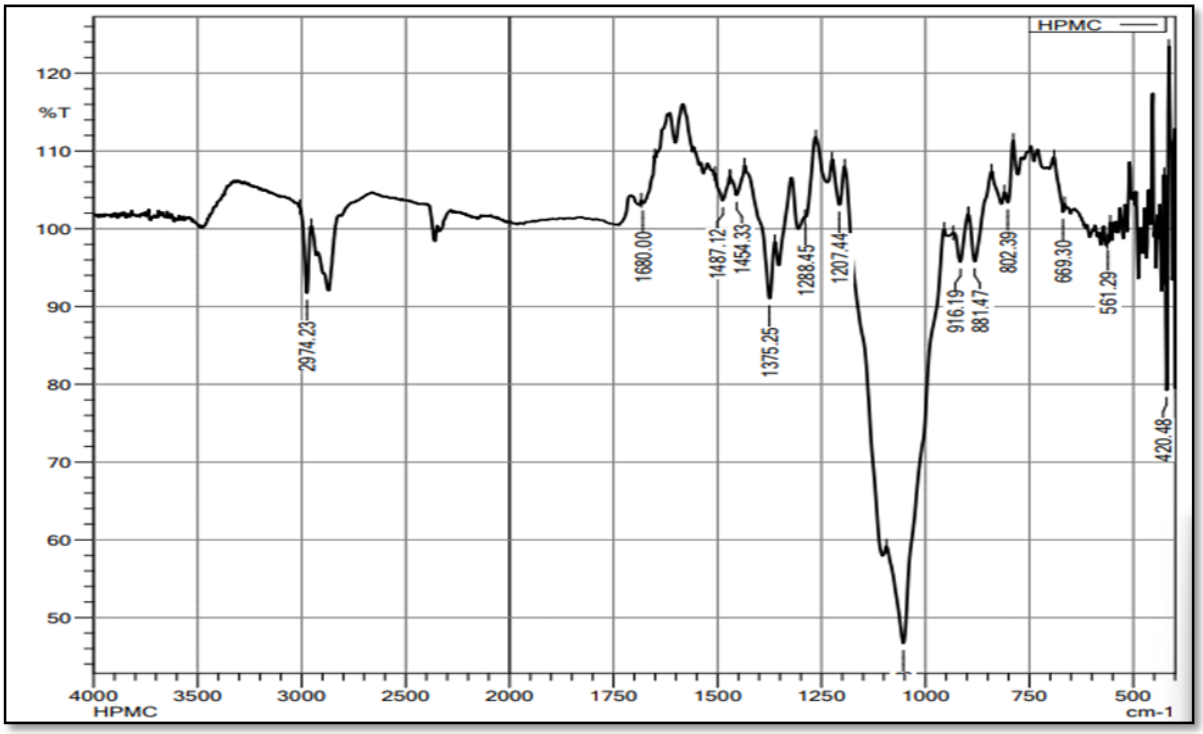

Figure 3: FT-IR of HPMC.

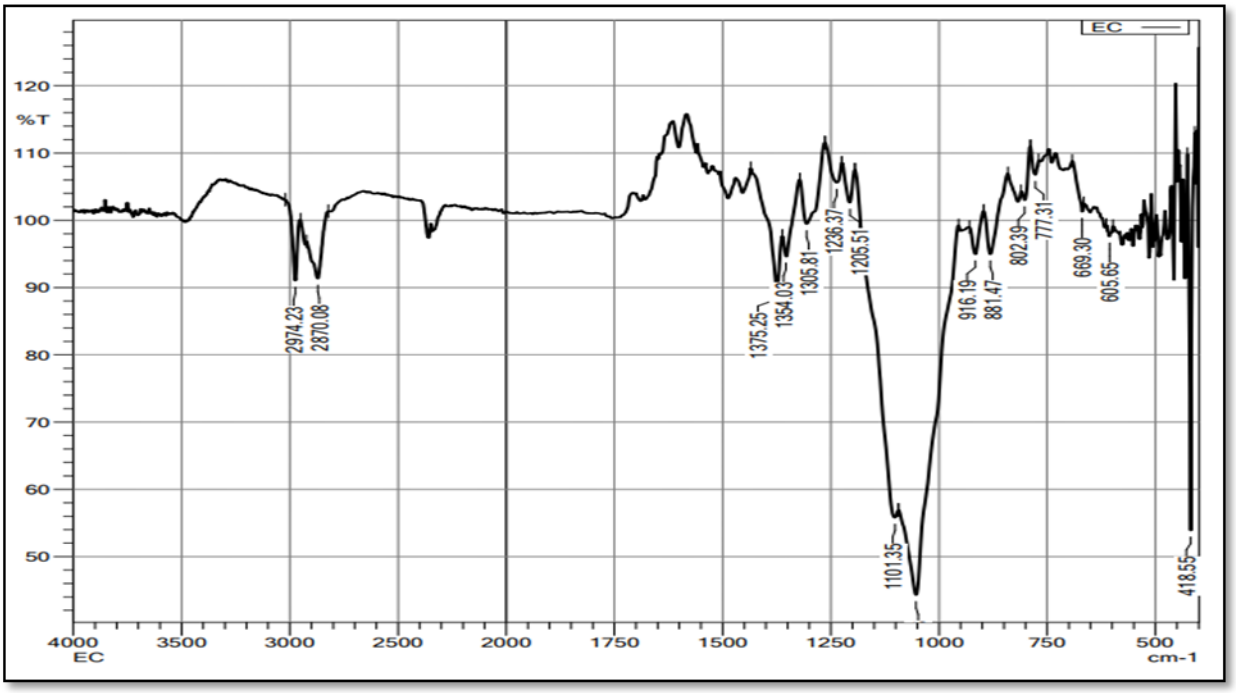

Figure 4: FT-IR of Ethyl Cellulose.

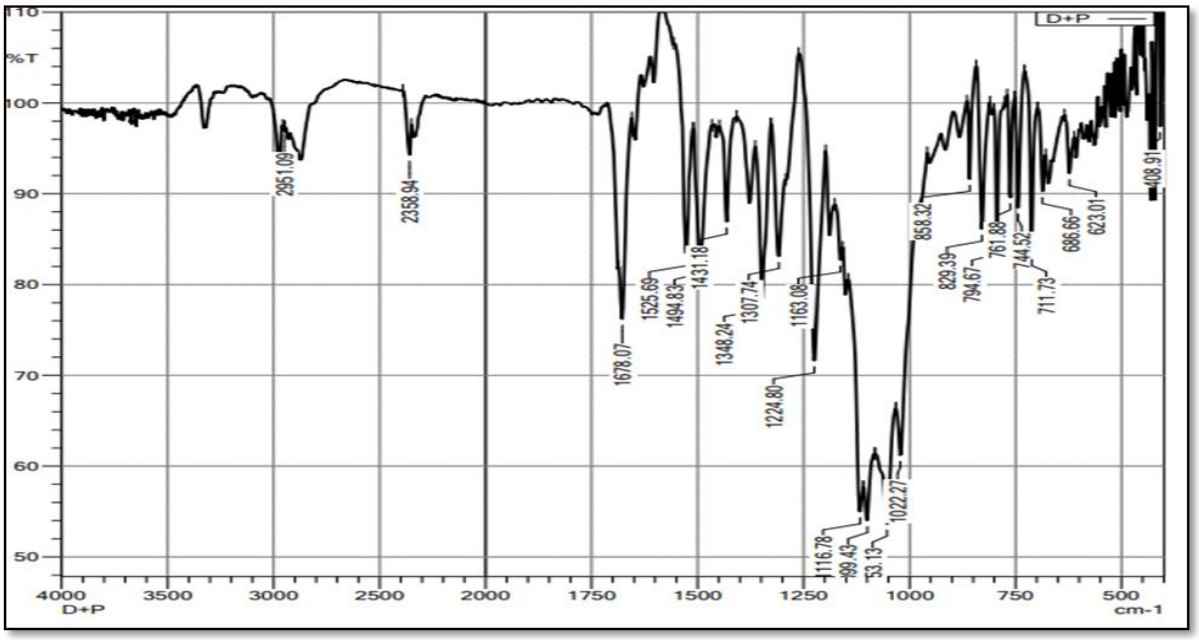

Figure 5: FT-IR of Drug and Polymers.

Table 2: Physico-chemical parameters of the nifedipine transdermal patches.

Parameters	F1	F2	F3	F4	F5
Folding Endurance	324	335	330	320	349
Thickness(mm)	0.30	0.35	0.40	0.50	0.65
Weight Uniformity (gm)	0.56	0.42	0.20	0.36	0.65
% Moisture Uptake	22.3	28.7	23.7	28.5	29.1
% Drug Content	96.5	97.6	95.7	98.3	98.5

DISCUSSIONS

The transdermal patches containing nifedipine were formulated and evaluated using HPMC K4M, ethyl cellulose by the mercury substrate method.

A standard calibration curve of nifedipine was prepared in phosphate buffer (pH 6.8), and it was found to obey Beer's law in spectrophotometric analysis. (Table: 1) (Figure: 1)

IR spectroscopy of the pure drug nifedipine exhibited characteristic peaks indicating the presence of an O–H group at 3300 cm^{-1}, an NH_2 group at 2946 cm^{-1}, an aromatic group at 3096 cm^{-1}, a carbonyl group at 1226 cm^{-1}, and a carboxylic group at 1680 cm^{-1}. The infrared spectra of the drug in combination with various polymers showed no evidence of any significant interaction between the drug and the polymers. The characteristic functional groups of the drug were clearly detected in both the pure drug and the drug–polymer spectra, confirming their compatibility. (Figure: 2, Figure: 3, Figure: 4 & Figure: 5)

The folding endurance was found to be in the range of 324 to 349, while the thickness varied between 0.30 mm and 0.65 mm. The weight variation ranged from 0.20 g to 0.65 g, and the percentage moisture uptake was observed to be between 22.3% and 29.1%. The percentage drug content was within the range of 96.5% to 98.5%. (Table: 2)

Among the formulations, F5 was optimized based on its good mechanical strength and satisfactory drug content, as confirmed by the various evaluation parameters.

CONCLUSION

The transdermal patches containing nifedipine were formulated and evaluated using different polymers, including ethyl cellulose and HPMC K4M, by the mercury substrate method. All evaluation parameters for the prepared formulations were found to be satisfactory. Based on the observations, it can be concluded that the formulated nifedipine transdermal patches were successful in providing sustained drug release over an extended period. Among the batches, formulation F5 demonstrated good mechanical strength and effective drug-release capability.

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