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"FORMULATION AND EVALUATION OF TRANSDERMAL PATCHES"

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ABSTRACT

The main objective of the present study was to formulate and evaluate matrix type Pioglitazone transdermal patches and to determine the drug release. Firstly, characterisation of the drug was done by performing FTIR compatibility studies and found that there was no interaction between the drug and polymers under study. Formulations (F1 to F6) were prepared using different ratios of HPMC E15 and Eudragit L 100 and penetration enhancer DMSO was incorporated to the above formulations (F7 to F12). These formulations were evaluated for weight variation, thickness variation, folding endurance, %moisture content, %moisture absorption studies, drug content, mechanical properties and exvivo permeation studies. In formulations F1 to F12, the drug permeation was maximum for F4 and F10 (ratio 10:2 HPMC E15: Eudragit L100). Among these, F10exhibited the required flux.

KEYWORDS: *Pioglitazone, Transdermal Patches, In-Vitro Release, In Vitro Permeation Study*

Article History

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INTRODUCTION

TRANSDERMAL DRUG DELIVERY SYSTEMS

Definition

Transdermal therapeutic systems are defined as self-contained discrete dosage forms which, when applied to the intact skin, deliver the drug(s) through the skin at controlled rate to the systemic circulation (USP 25, 2002).

A transdermal drug delivery device, which may be of an active or a passive design, is a device which provides an alternative route for administering medication. A drug is applied in a relatively high dosage to the inside of a patch, which is worn on the skin for an extended period of time. Through a diffusion process, the drug enters the blood stream directly through the skin. Since there is high concentration on the patch and low concentration in the blood, the drug will keep diffusing into the blood for a long period of time, maintaining the constant concentration of drug in the blood flow.

IDEAL CHARATERISTIC OF THE DRUG [2]

Table 1: Ideal Properties of Drug Candidate for Transdermal Drug Delivery

Parameter	Properties
Dose	Should be low (<10mg/day)
Half-life in hr	10 or less
Molecular weight	<500
Melting point	<200°C
Partition coefficient	Log P (octanol-water) between 1 and 4

pH of saturated solution	5-9
Skin permeability coefficient	$>0.5 \times 10^{-3}$ cm/h
Skin reaction	Non irritating and non sensitizing
Oral bioavailability	Low
Therapeutic index	Low

ADVANTAGES

Delivery via the transdermal route is an interesting option because transdermal route is convenient and safe. The positive features of delivery of drugs across the skin to achieve systemic effects are:

- Avoidance of first pass metabolism
- Avoidance of gastro intestinal incompatibility
- Predictable and extended duration of activity
- Minimizing undesirable side effects
- Provides utilization of drugs with short biological half lives
- Improving physiological and pharmacological response
- Avoiding the fluctuation in drug levels
- Avoiding inter and intra patient variations
- Maintain plasma concentration of potent drugs
- Termination of therapy is easy at any point of time
- Greater patient compliance due to elimination of multiple dosing profile
- Ability to deliver drug more selectively to a specific site
- Provide suitability for self-administration and enhance therapeutic efficacy

DISADVANTAGES

- The drugs that require high plasma levels cannot be administered.
- Not suitable for drugs with high molecular weight.
- Not suitable for drugs that undergo metabolism during the passage through the skin
- Not suitable for drugs that produce irritation and contact dermatitis.

1. Variation of absorption rate based on site of application, skin type and patient age.

EXPERIMENTAL WORK

Preformulation Study

Preformulation is a branch of pharmaceutical science that utilizes biopharmaceutical principles in determination of physicochemical properties of a drug substance. The goal of preformulation studies is to choose the correct form of the drug prerequisite for formulation. Therefore in preformulation substance, evaluated physical properties and generate a thorough

understanding of the material stability under various conditions, leading to the optimal drug delivery system. The preformulation study focus on the physicochemical parameters that to effect the development of efficacious dosage form thorough understanding of these properties may ultimately provide a rationale for formulation design. Also it will help in minimizing problems in later stages of drug development, reducing drug development cost and decreasing product time to market.

SCOPE OF THE STUDY

The use of preformulation parameters maximizes the chances in formulating an acceptable, safe, efficacious and stable product.

ANALYSIS OF THE PIOGLITAZONE

Description

The drug was observe for its general appearance

Solubility

The solubility of the pioglitazone was determine in phosphate buffer

Melting Point of the Drug Sample

Melting Point of the drug (Pioglitazone) was determined by taking a small amount of drug in a capillary tube closed at one end and it was placed in melting point apparatus and the temperature at which the drug melts was noted. Average of triple reading was taken and compared with the literature survey.

PREFORMULATION STUDY OF POLYMER

All polymers used in the formulation of Transdermal patch on which preformulation study was done and checked for if they complies the specification provided or not.

Analysis of Excipients Used in the Formulation:

The following excipients, HPMC E15, Eudrajit L100 as a plasticizer and chloroform, Methanol, Polyethylene glycol, Calcium chloride, Aluminium chloride, Potassium dihydrogen phosphate, Sodium hydroxide as a Solvent are selected for formulating patch and these have been evaluated and analyzed for the physic-chemical characters.

SPECTRUM MEASUREMENT OF PIOGLITAZONE

U.V Spectroscopy

Selection of Solvent

The phosphate buffer pH 7.4 was selected as a dissolution media because it represents the pH of plasma respectively.

Determination of λ Max:

The absorption maxima of pioglitazone was determined by scanning the sample drug solution concentration (0.5µg/ml) in double beam UV spectrophotometer for range of 220-280nm and compared with the standard specification given in Indian Pharmacopoeia or literature.

CONSTRUCTION OF STANDARD CALIBRATION CURVE OF PIOGLITAZONE:

Construction of Standard Calibration Curve of Pioglitazonein Methanol

The calibration curve is obtained by dissolving 100 mg of Pioglitazone in 100 ml of methanol to give 1000 µg/ml this was stock-I solution. From the above,1 ml solution was taken and made up to 10 ml with methanol to give 100 µg/ml this was stock- II. From stock-II 1, 2, 3, 4, 5, 6, 7 and 8 ml was taken and made up to 10ml with methanol this gave concentration 10, 20, 30, 40, 50, 60, 70 and 80 µg/ml. Absorbance was measured spectrophotometrically at 280nm against methanol as blank.

Construction of Standard Calibration Curve of Pioglitazonein Phosphate Buffer Ph 7.4

The calibration curve is obtained by dissolving 100 mg of Pioglitazonein 100 ml of pH 7.4 phosphate buffer to give concentration 1000 µg/ml, this was stock-I. From the above, 1ml solution was taken and made up to 10 ml with pH 7.4 phosphate buffer and this was stock- II. From stock-II 1, 2, 3, 4, 5, 6, 7 and 8 ml was taken made up to 10ml with pH 7.4 phosphate buffer this gave concentration 10, 20, 30, 40, 50, 60, 70 and 80 µg/ml. Absorbance was measured spectrophotometrically at 280nm against pH 7.4 phosphate buffer as blank.

PREPARATION OF PIOGLITAZONETRANSDERMAL FILMS:

Matrix type transdermal patches containing Pioglitazone were prepared by solvent evaporation technique, using different ratios of HPMCE 15 and EudragitL100. The polymers were weighed in requisite ratios and allowed for swelling for about 6hin solvent mixture (1:1ratio of methanol and chloroform) 15%v/w Polyethylene glycol was incorporate as plasticizer. Then the drug solution was added to the polymeric solution, casted on to anumbra petri plate of surface are about 66.44 cm^2 allowed for air drying overnight followed by vacuum drying for 8-10hr. The entire sheet was cut into small patches with an area of 4.9 cm^2 i.e. with a diameter of 2.5 cm. About 13 patches were obtained from each sheet.

Formulations F1 to F6 composed of HPMC E15andEudragit L100in different ratios. Formulations F7 to F12 were of same composition as the above but penetration enhancer DMSO was incorporated. All formulations carried 15% v/w polyethylene glycol as plasticizer.

Table 2: Composition of Pioglitazone Transdermal Patches

Formulation Code	Drug (mg)	HPMC E15 (mg)	EudragitL100 (mg)	DMSO (ml)
F1	30	600	-	-
F2	30	400	200	-
F3	30	450	150	-
F4	30	500	100	-
F5	30	550	50	-
F6	30	350	250	-
F7	30	600	-	0.03
F8	30	400	200	0.03
F9	30	450	150	0.03
F10	30	500	100	0.03
F11	30	550	50	0.03
F12	30	350	250	0.03

15% v/w polyethylene glycol - plasticizer.
5% v/w DMSO - penetration enhancer
Each patch 4.9 cm^2contains 3.67 mg of Pioglitazone

EVALUATION OF PARAMETER

Evaluation Parameters of Transdermal Films

Weight Variation

Six films from each batch of an area of 4.90 cm^2 were weighed individually and the average weight was calculated.

Thickness

The thickness of the film was measured at ten different points on one film using screw gauge. For each formulation three randomly selected films were used and average thickness was recorded.

Folding Endurance

Folding endurance of the patch was determined manually by repeatedly folding a small strip of the medicated patch at the same place until broke. The number of times the strip could be folded at the same place without breaking gave the folding endurance number.

Estimation of Drug Content in Polymeric Films

The formulated polymeric films were assayed for drug content in each case. Three polymeric films from each formulation were assayed for content of drug.

PROCEDURE

Films from each formulation were taken, cut into small pieces and was allowed to dissolve in a 100 ml solution containing 50 ml of methanol and 50 ml of chloroform. The solution was diluted suitably and the absorbance of the solution was measured using UV-Visible spectrophotometer at a wavelength of 338 nm against methanol chloroform mixture (1:1) as blank.

Moisture Absorption Studies

The patches were weighed accurately and placed in the desiccator containing 100ml of saturated solution of Aluminium chloride, which maintains 84 % RH. After 3 days, the patches were taken out and weighed. The percentage moisture absorption was calculated using the following formula

$$\%\text{Moisture absorption} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

Moisture Content Determination

The patches were weighed accurately and placed in a desiccators containing calcium chloride at 40°C for 24 h. Then the final weight was noted when there was no further change in the weight of individual patch. The percentage of moisture loss was calculated as difference between initial and final weight with respect to final weight.

$$\%\text{Moisture Content} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Mechanical Properties

Mechanical properties of the films were evaluated using a microprocessor based advanced force gauze (UltraTest, Mecmesin, UK) equipped with a 25 kg load cell. Filmstrip with dimensions 60x10 mm and free from air bubbles or physical imperfections were held between two clamps position data distance of 3 cm. During measurement, the top clamp at a rate of 2 mm/s pulled the strips to a distance till the film broke. The force and elongation were measured when the film broke. The mechanical properties were calculated according to the following formulae. Measurements were run in four replicates to reach formulation.

$$\text{Tensile strength (kg. mm}^{-2}) = \frac{\text{Force at break (kg)}}{\text{Initial cross sectional area of the sample (mm}^2)}$$

$$\text{Elongation at break (\% mm}^{-2}) = \frac{\text{Increase in length (mm)}}{\text{Original length (mm)}} X \frac{100}{\text{Cross sectional area}}$$

Force at corresponding strain (kg)

$$\text{Elastic Modulus} = \frac{1}{\text{Cross-sectional area (mm}^2)} X \frac{100}{\text{Corresponding Strain}}$$

$$\text{Strain} = \frac{\text{Tensile strength}}{\text{Elastic modulus}}$$

The tensile testing gives an indication of the strength and elasticity of the film, reflected by the parameters, tensile strength (TS) and elastic modulus (EM) and elongation at break (E/B). A soft and weak polymer mischaracterized by a low TS, EM and E/B; a hard and brittle polymer is defined by a moderate TS, high EM and low E/B; as often tough polymer is characterized by a moderate TS, low EM and high E/B; where as a hard and tough polymer is characterized by a high TS, EM and E/B. Another parameters train has been used as an indicator of the overall mechanical quality of the film. A high strain value indicates that the film is strong and elastic. Hence, it is suggested that a suitable transdermal films should have a relatively high TS, E/B and strain but low EM.

In Vitro Drug Release Studies:

In vitro drug release studies were performed by using a Franz diffusion cell with a receptor compartment capacity of 60ml. The cellulose acetate membrane was used for the determination of drug from the prepared transdermal matrix-type patches. The cellulose acetate membrane having a pore size 0.45µ was mounted between the donor and receptor compartment of the diffusion cell. The prepared transdermal film was placed on the cellulose acetate membrane and covered with aluminium foil. The receptor compartment of the diffusion cell was filled with phosphate buffer pH 7.4. The whole assembly was fixed on a hot plate magnetic stirrer, and the solution in the receptor compartment was constantly and continuously stirred using magnetic beads, and the temperature was maintained at 32+-0.5°C, because normal skin temperature of human is 32°C. The samples were withdrawn at different time intervals and analyzed for drug content spectrophotometrically. The receptor phase was replenished with an equal volume of phosphate buffer at each sample withdrawal.

Formula

First Step

Determine concentration of drug release by using formula

Y = mX+/-C

Where;

Y=Absorbance, M=Slope, C=Intercept, X=concentration (mcg/ml)

Second Step

Calculate amount of drug released

Amount of drug released (mg) = [Concentration × Dilution factor × Volume of Dissolution medium] / 1000

Final Step

%Drug release = Amt of drug released (mg) × 1000 / Dose (mg)

In Vitro Permeation Study

An in vitro permeation study was carried out by using Franz diffusion cell. Full thickness abdominal skin of male Wistar rat weighing 200 to 250g was used. Hair from the abdominal region was removed carefully by using an electric clipper; the dermal side of the skin was thoroughly cleaned with distilled water to remove any adhering tissues or blood vessels, equilibrate for an hour in phosphate buffer pH 7.4 before starting the experiment, and was placed on a magnetic stirrer with a small magnetic needle for uniform distribution of the diffusant. The isolated rat skin piece was mounted between the compartments of the diffusion cell, with the epidermis facing upward into the donor compartment. Sample volume of 5ml was removed from the receptor compartment at regular intervals, and an equal volume of fresh medium was replaced. Samples were filtered through watman filter and were analysed using Shimadzu UV 1800 double-beam spectrophotometer (Shimadzu, Kyoto, Japan). Flux was determined directly as the slope of the curve between the steady-state values of the amount of drug permeated (mg*cm^2) versus time in hours and permeability coefficient was deduced by dividing the flux by the initial drug load (mg*cm^2).

Formula for Determination of Percentage of Release of Drug from In Vitro Dissolution Testing:

Concentration of drug (µg/ml) = (slope × absorbance) + intercept

Amount of drug = Concentration × Dissolution bath volume × dilution factor

Release mg/ml 1000

Cumulative percentage = Volume of sample withdrawn (ml) × P(t-1) + Pt

Release (%) Bath Volume (V),

Where Pt = Percentage release at time t

Where P(t-1) = Percentage release previous to `t`

Steady-State Diffusion: Calculating Flux

Flux is proportional to concentration gradient= dC/dX

Fick's first law of diffusion

J= -D dc/dx

Where;

J=flux,

D=diffusion coefficient,

dC= change in concentration,

dx= change in linear distance.

RESULT AND DISCUSSIONS

Preformulation Study

Preformulation studies are primarily done to investigate the physicochemical properties of drug and to establish its compatibility with other excipients.

Preformulation Study of Pioglitazone

Organoleptic Properties of Drug:=

Pioglitazone was studied for organoleptic characters such as colour, odour, appearance and melting point. Results of organoleptic properties and melting point of received samples of pioglitazone were found

Table 3: Organoleptic Characterization of Drug

Identification Test	Observed Test
Appearance	Fine powder
Colour	White
Odour	Characteristics

- **Solubility:** Practically insoluble in water, freely soluble in acetone, methanol, Ethanol.
- **Melting Point:** The melting point was determined by open capillary method and the melting point was found to be 165-170°C.

Table 4: Melting Point of Drug

Identification Test	Observed Result
Melting Point	165-170°C

SPECTRUM MEASUREMENT

UV Spectroscopy

UV absorption spectrum of pioglitazone drug sample in phosphate buffer pH 7.4 shows maximum at nm specified in the range of to nm. Thus were found to be in specification of drug. So it is further selected as λ max of pioglitazone.

Compatibility Study

The drug polymer and mixture of both were subjected to Fourier Transform Infra-red (FTIR) studies to check drug polymer interaction using FTIR. The potassium bromide (KBr) disk method was used for preparation of sample. The infra-red spectrum of pure drug, HPMC E15, and Eudrajit shown in following figures. All the principle peak was retained in the physical mixture which indicates the compatibility between drug and polymer.

FTIR Compatibility Studies

In the FTIR spectra of pure drug and formulation with other ingredients (different polymers) it is observed that the peaks of major functional groups of Pioglitazone, which are present in spectrum of pure drug, are observed. It means there are no interactions between drug and other ingredients in a physical mixture and drug is compatible with other ingredients.

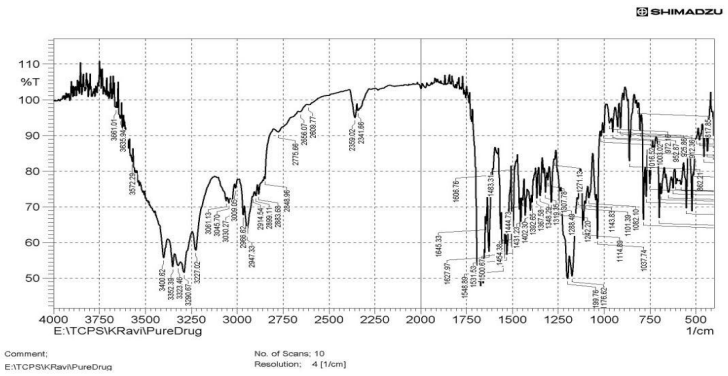

Figure 1: FTIR Spectra of Pioglitazone

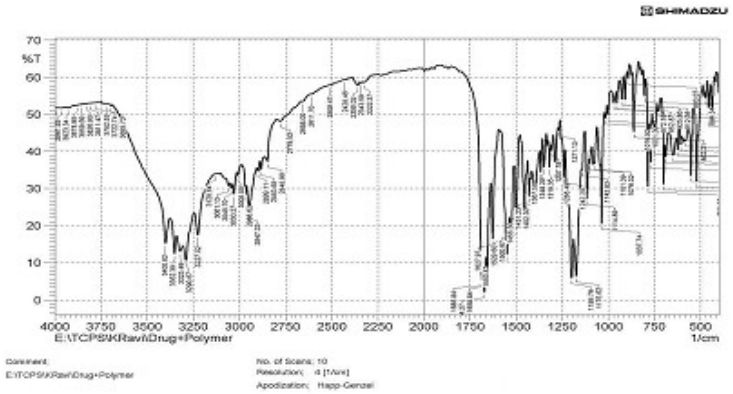

Figure 2: FTIR Spectra of Pioglitazone and HPMC E15 .

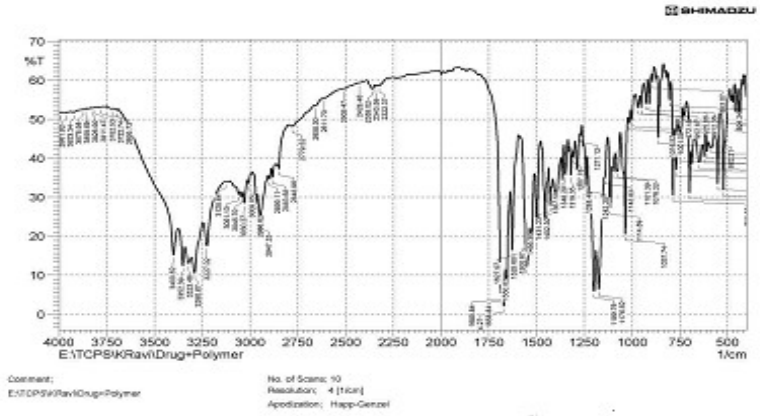

Figure 3: FTIR Spectra of Pioglitazone, HPMC E15 and EL 100.

CONSTRUCTION OF STANDARD GRAPH OF PIOGLITAZONE

Table 5: Standard Graph of Pioglitazone in Methanol

Concentration(µg/ml)	Absorbance
0	0
10	0.196
20	0.35
30	0.507
40	0.718
50	0.869

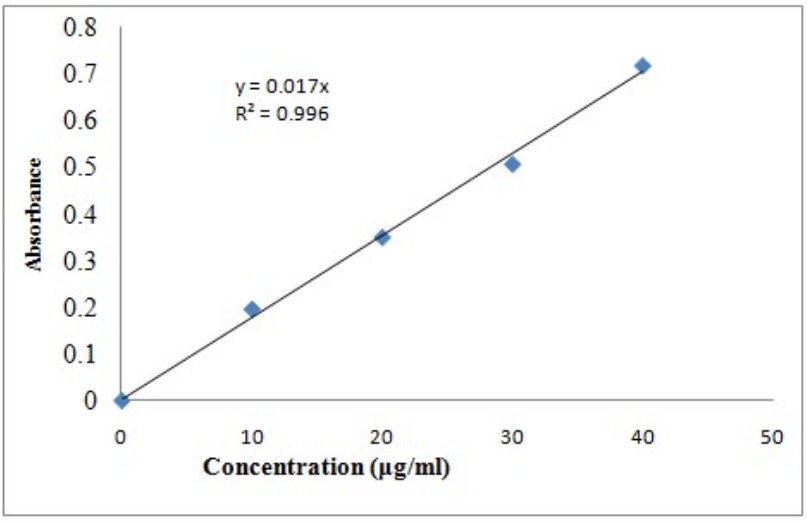

Figure 4: Standard Graph of Pioglitazone in Methanol.

Table 6: Standard Graph of Pioglitazone in pH 7.4 phosphate Buffer

Concentration(µg/ml)	Absorbance
0	0
10	0.127
20	0.278
30	0.36
40	0.497
50	0.649
60	0.767
70	0.936

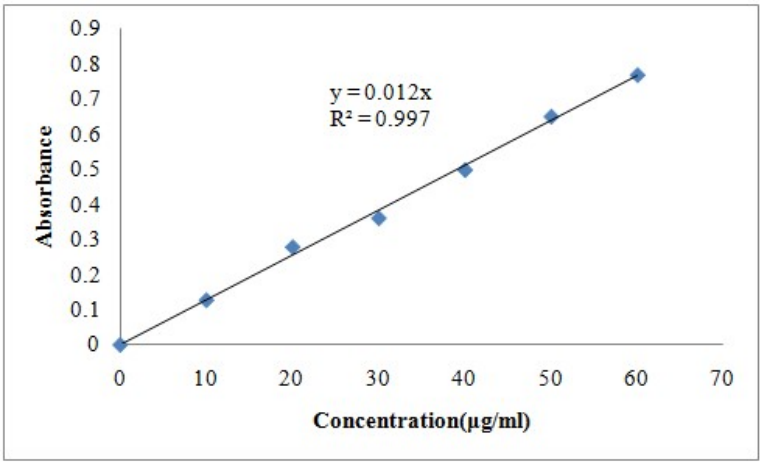

Figure 5: Standard Graph of Pioglitazone in pH 7.4 Phosphate.

Buffer

Table 7: Weight Variation, Thickness and Folding Endurance of Pioglitazone Transdermal Patches

Formulation	Weight Variation (mg)	Thickness (mm)	Folding Endurance
F1	46.9±1.53	0.25±0.79	562.45±0.53
F2	33.76±0.97	0.2±1.27	435.12±1.38
F3	38.26±0.59	0.22±0.95	489.57±0.75
F4	42.41±1.26	0.23±0.83	550.77±0.93
F5	45.75±0.78	0.24±0.56	558.98±0.88
F6	32.37±0.49	0.19±1.54	432.48±0.64
F7	47.55±0.55	0.26±0.67	566.92±1.29
F8	35.45±1.12	0.205±0.98	454.1±1.02
F9	39.62±1.43	0.21±1.38	490.7±0.74
F10	40.78±0.89	0.24±1.26	558.57±0.62
F11	43.51±0.95	0.25±0.58	563.46±1.14
F12	33.25±0.67	0.215±0.63	470.79±1.09

Table 8: Drug Content, % Moisture Absorbed, %Moisture Content of Pioglitazone Transdermal Patches

Formulation	Drug Content (mg)	% Moisture Absorbed	% Moisture Content
F1	3.35±0.96	10.87±1.58	9.34±0.96
F2	2.83±1.29	7.92±1.82	4.62±0.85
F3	3.05±0.84	9.67±0.95	5.97±1.17
F4	3.26±1.18	8.39±1.46	8.35 ±1.32
F5	3.29±1.04	10.45±0.93	8.45±1.95
F6	2.73±0.55	6.42±1.25	4.58±0.77
F7	3.42±1.37	11.44±1.03	9.35±0.94
F8	2.99±0.92	8.35±0.89	5.21±0.55
F9	3.16±0.75	8.86±0.64	6.32±0.79
F10	3.32±1.55	9.34±0.59	7.56±0.82
F11	3.38±1.27	10.48±1.19	9.12±0.93
F12	2.76±0.86	6.54±1.53	5.89±1.87

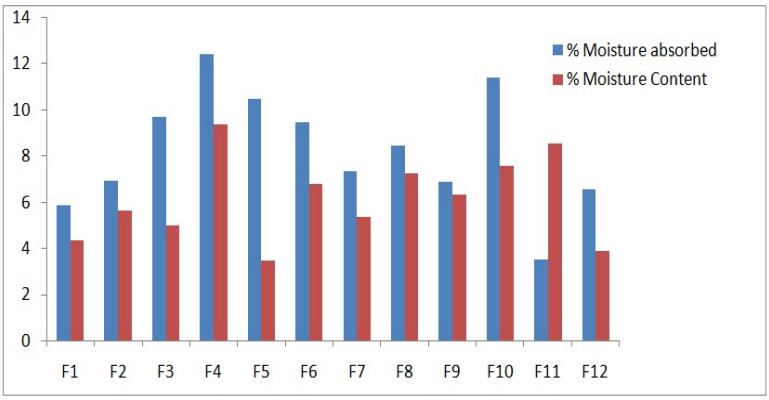

Figure 6: Moisture Absorbed and Moisture Content of Pioglitazone Transdermal Patches.

Table 6: Mechanical Properties of Optimized Formulations

Formulation Code	Tensile Strength(kg/m^2)	Elongation at Break (%mm^{-2})
F4	1.38±0.58	24.92±1.42
F9	0.76±0.34	43.18±1.03
F10	1.46±0.78	22.53±0.98

Table 9: Permeation of Pioglitazone from Transdermal Patches

Time (h)	Cumulative Amount of Drug Permeated (µg/cm^2)			
	F1	F2	F3	F4
0	0	0	0	0
1	234.11±7.42	329.99±7.5	351.21±9.3	269.01±10.5
2	356.83±9.93	4599.48±10.4	490.67±10.56	412.14±7.5
3	457.2±9.92	610.3±12.35	590.87±8.79	583.53±9.3
4	621.16±10.32	779.14±7.95	711.98±13.25	751.24±8.9
5	801.86±7.58	966.31±10.32	845.2±9.5	940.62±7.5
6	966.53±11.38	1115.68±9.56	1042.28±8.7	1143.93±9.92
7	1171.3±17.56	1302.85±11.5	1217.33±8.5	1351.66±9.35
8	1367.93±18.56	1518.27±12.32	1417.72±7.5	1545.07±13.56
9	1513.6±12.79	1679.75±13.5	1626.91±10.5	1773.71±14.5
10	1686.8±8.97	1865.46±10.5	1831.33±7.32	2001.25±9.58
12	1909.33±12.1	2145.84±15.4	2243.28±10.2	2252.27±12.12
24	2357.3±19.46	2530.67±9.3	2754.54±9.1	3062.63±14.2
Flux J_{ss}	**26.54± 1.05**	**29.4± 0.93**	**29.74 ±0.72**	**32.82 ±1.36**

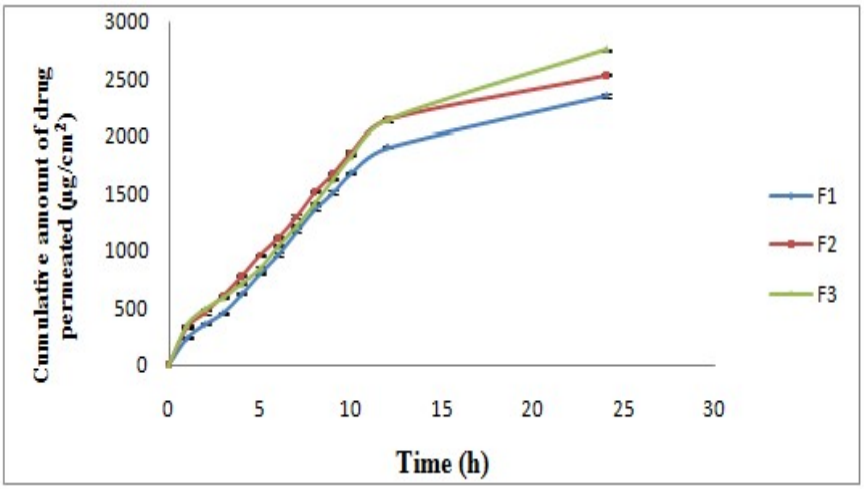

Figure 7: Permeation of Pioglitazone from Transdermal Patches.

Table 10: Permeation of Pioglitazone from Transdermal Patches

Time (h)	Cumulative Amount of Drug Permeated (µg/cm^2)			
	F5	F6	F7	F8
0	0	0	0	0
1	198.18±5.5	259.1±7.45	291.03±12.4	500.9±5.92
2	319.29±3.8	346.08±6.51	444.8±5.53	608.48±7.5
3	452.52±9.2	554.17±5.83	568.48±3.82	768.13±10.42
4	562.61±4.5	748.68±2.52	726.66±9.52	941.3±8.55
5	713.08±12.5	925.94±7.58	865.01±7.3	1058.06±9.31
6	886.67±10.5	1086.32±7.49	1080.08±7.84	1226.88±6.55
7	1080.08±3.6	1278.26±10.5	1272.38±5.3	1393.49±11.42
8	1258.81±4.7	1437.17±2.97	1487.45±2.68	1527.82±4.8
9	1451.85±8.5	1612.23±4.91	1690±4.72	1680.86±13.52
10	1655.17±2.5	1835±9.73	1816.65±8.35	1938.86±2.7
12	1905.83±3.9	2064.74±12.81	2063.6±6.7	2206.77±8.9
24	2269.35±6.7	2437.82±8.32	2597.64±10.5	2695.45±7.7
Flux J_{ss}	**25.47± 0.85**	**28.32± 0.64**	**29.15± 1.54**	**31.04± 1.13**

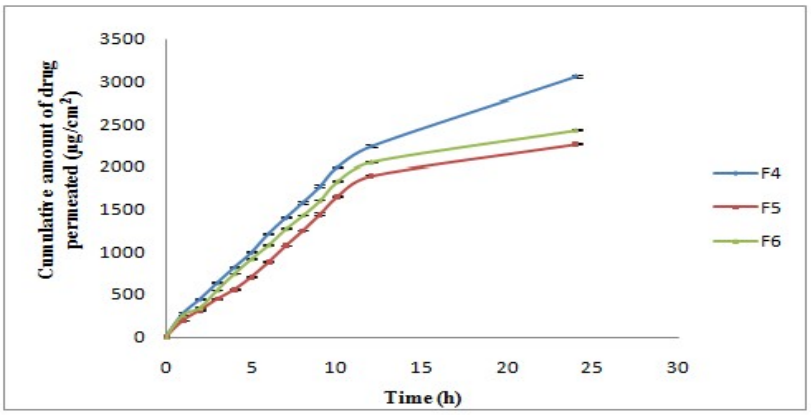

Figure 8: Permeation of Pioglitazone from Transdermal Patches

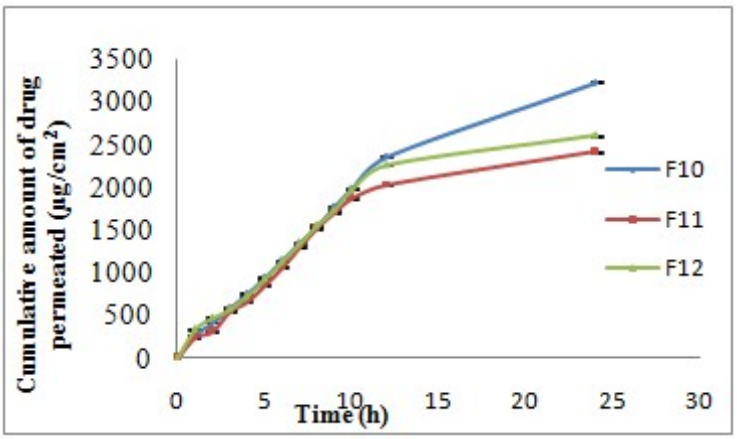

Figure 9: Permeation of Pioglitazone from Transdermal Patches.

Table 11: Permeation of Pioglitazone from Transdermal Patches

Time (h)	Cumulative Amount of Drug Permeated (µg/cm²)			
	F9	F10	F11	F12
0	0	0	0	0
1	422.05±6.81	276.35±4.2	243.32±10.53	335.07±8.56
2	529.58±11.6	447.74±10.55	307.62±2.85	467.19±4.98
3	615.09±13.68	638.58±7.93	543.16±6.82	566.28±9.58
4	778.04±9.65	822.08±2.95	656.93±4.78	724.09±2.43
5	929.61±10.77	997.13±8.52	848.87±9.56	920.06±4.69
6	1142.47±4.37	1221±3.78	1054.39±13.87	1125.58±5.65
7	1362.67±5.68	1405.61±6.45	1294.4±12.54	1332.21±7.12
8	1567.09±6.45	1585.4±12.56	1518.27±9.55	1549.84±8.34
9	1776.28±9.52	1775.17±9.7	1696.64±10.23	1728.57±9.17
10	1986.57±10.55	1987.14±10.69	1861.79±8.94	1962.34±3.21
12	2284.94±7.45	2358.7±5.38	2021.06±6.52	2252.27±11.45
24	2963.54±3.24	3227.78±6.74	2411.93±9.25	2600.4±10.95
Flux J_{ss}	**31.6± 0.56**	**33.4± 0.97**	**28.24± 1.28**	**30.2± 1.18**

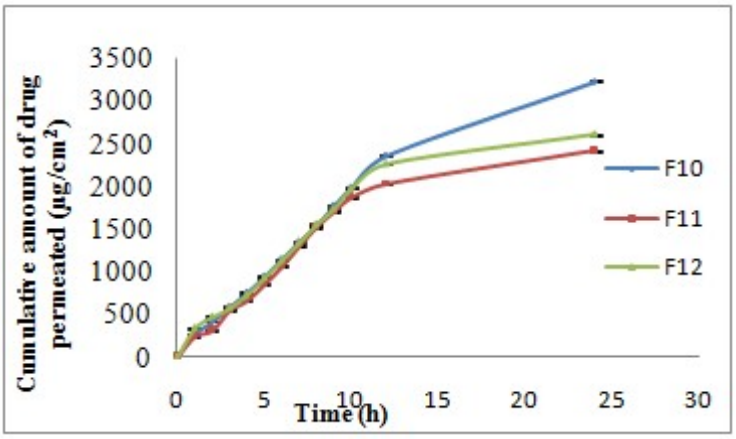

Figure 10: Permeation of Pioglitazone from Transdermal Patches.

Table 12: Comparative Study of Pioglitazone Permeation

Time (h)	Cumulative Amount of Drug Permeated (µg/cm²)	
	F4	F10
0	0	0
1	269.01±10.5	276.35±4.2
2	412.14±7.5	447.74±10.55
3	583.53±9.3	638.58±7.93
4	751.24±8.9	822.08±2.95
5	940.62±7.5	997.13±8.52
6	1143.93±9.92	1221±3.78
7	1351.66±9.35	1405.61±6.45
8	1545.07±13.56	1585.4±12.56
9	1773.71±14.5	1775.17±9.7
10	2001.25±9.58	1987.14±10.69
12	2252.27±12.12	2358.7±5.38
24	3062.63±14.2	3227.78±6.74
Flux J_{ss}	**32.82±1.36**	**33.4±0.97**

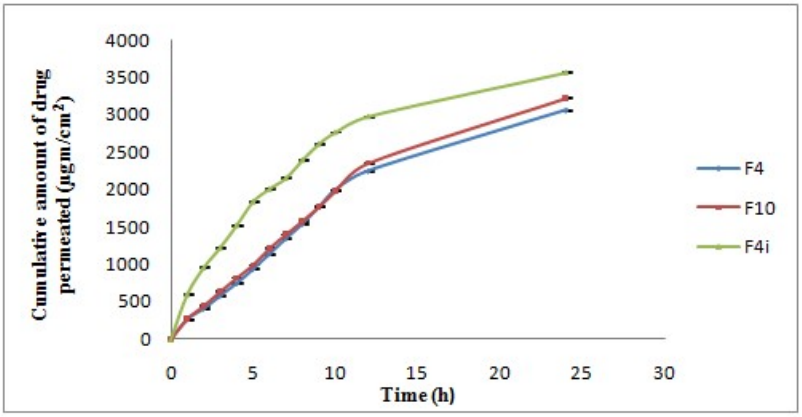

Figure 11: Permeation of Pioglitazone from Transdermal Patch.

CONCLUSIONS

- In the present study, an attempt was made to formulate an anti-hypertensive drug Pioglitazone in the form of transdermal patches using different ratios of HPMC E15 and Eudragit L100.

- From the results obtained, DMSO enhanced the drug release from the Pioglitazone transdermal patches compared with the normal films
- The transdermal patches of Pioglitazone with required flux could be prepared with suitable mechanical properties, further studies are recommended to find their therapeutic utility in humans by pharmacokinetic and pharmacodynamic studies.

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