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DEVELOPMENT, CHARACTERIZATION AND EVALUATION OF TRANSDERMAL PATCH OF PRAZOSIN HYDROCHLORIDE

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Abstract:
In today's world about 74% of drugs are taken orally and are found not to be as effective as desired in the present scenario. So to overcome or to improve such character transdermal drug delivery system was emerged in form of transdermal patches. Transdermal drug delivery represents the most rapidly advancing areas of novel drug delivery. To overcome the difficulties of drug delivery through oral route easier way was introduced known as transdermal drug delivery system for example poor bio-availability, first pass metabolism and sometime responsible for rapid blood level. The present study was carried out to develop transdermal patches of prazosin hydrochloride with different ratio of HPMC (hydroxyl propyl methyl cellulose), EC (ethyl cellulose) by solvent casting method. Propylene glycol 3% is used as a plasticizer and Span 80 as permeation enhancer. The recognition of drug and the possible drug polymer relations were studied by FTIR spectroscopy. Formulated transdermal patches were evaluated with regard to physicochemical characteristics (thickness, folding endurance etc.) and In-vitro permeation studies were performed using Franz diffusion cell.
The figures obtained from in- vitro permeation studies was treated by different conventional mathematical models (zero order, first order, Higuchi and Korsmeyer- peppa's) to determine the release mechanism from the transdermal patches formulations. Selection of a appropriate release model was based on the values of R^2 (correlation coefficient), k (release constant) obtained from the curve fitting of release data. It was found that all the formulations follow the first order kinetics. The regression coefficients (R^2) for the all formulations F1 to F4 of Higuchi plot was found to be almost linear.
Keywords: *Transdermal patches, prazosin hydrochloride, Permeation enhancer, In-vitro permeation study.*

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INTRODUCTION:

Transdermal drug delivery system [1,2,3,4]

Transdermal drug delivery system is defined as the topically administered medications which when applied to the skin membrane in the form of patches and delivers the drug, through the skin at a predetermined and controlled rate. Transdermal drug delivery system can improve the therapeutic efficacy and safety of the drugs because drug delivered through the skin at predetermined and controlled rate. For application of the drug skin is the important site for both systemic and local effect. However, it was the twentieth century when the skin became used as route for long term drug delivery. Today about two third of drugs (available in market) are taken orally, but these are not as effective as required. To improve upon the features the transdermal drug delivery system was emerged. In transdermal delivery system drug injects directly into the plasma stream from the skin layers by the process termed as diffusion. As on one hand the concentration of the patch is high in comparison to the concentration of plasma which is low in its concentration, this condition will help the drug to diffuse for longer period of time by maintaining the persistent concentration of plasma. Over the last few decades, transdermal delivery system has become an appealing and patient compliance technology as it minimizes and overcomes the limitations concerned with conventional as well as parenteral route of drug administration.

Physiology of skin[5]:

The skin is the largest organ tissue of the human body. Most of the topical preparations are designed to be useful to the skin. So for scheming topical preparation basic knowledge of the skin and its physiology function are very significant. The skin of an average adult body covers a surface area approximately $2m^2$ and receives about one third of the blood circulating through the body. The pH of the skin varies from 4 to 5.6. Sweat and fatty acid secreted also get influence the pH of the skin surface.

Structure of skin:

The skin can be considered to have mainly three distinct layers:

- Epidermis.
- Dermis.
- Subcutaneous connective tissue.

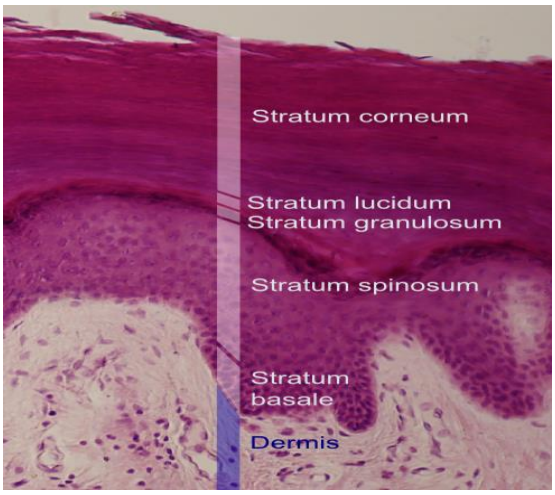


Fig 1: Layers of skin.

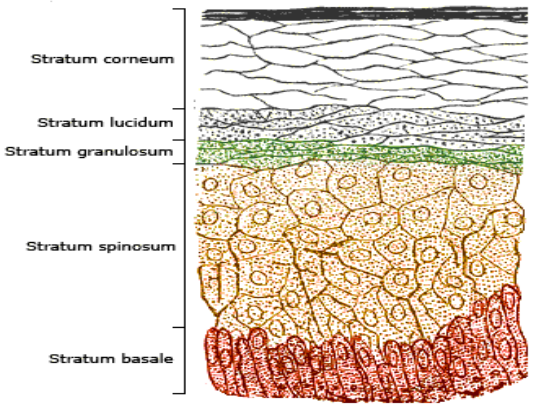


Fig 2: Epidermis layer and its sub layers.

Epidermis: The multilayered envelope of the epidermis varies in thickness, depending on the cell size and number of cell layers, which ranges from 0.8mm on palms and soles down to 0.06mm on the eyelids. It further consists of two layers:

a) Stratum corneum: It is the outermost layer of the skin and also termed as horny layer. It is approximately 10mm thick when in dry conditions but swells to several times the thickness when fully hydrated. It is flexible but relatively impermeable and known as the principal barrier for penetration. It constitutes of 75 to 80% proteins, 5 to 15% lipids and 5 to 10% ondansetron material on the dry weight basis.

b) Viable epidermis- Situated beneath the stratum corneum and varies in thickness from 0.06mm on the eyelids to 0.8mm on the palms. As we go more deep it consists of few layers as stratum lucidum, stratum basale, and stratum spinosum and stratum granulosum.

Dermis: Dermis is composed of a matrix of a connective tissue which contains lymphs, blood vessels and nerves and is about 3 to 5mm thick layer. On one hand it provides nutrients and oxygen to the skin and on other hand it removes toxins and waste products too. The blood supply thus keeps dermal concentration of permeation very low, and the resulting concentration difference across the epidermis provides the vital driving force for transdermal permeation.

Subcutaneous connective tissue: The subcutaneous fat tissue or hypodermis supports the dermis and epidermis. This layer serves as fat storage area, and helps to regulate temperature and provides nutritional support too. For transdermal drug delivery drug has to penetrate through all the three layers of the skin and reach into systemic circulation while in case of topical drug delivery, only penetration through stratum corneum is important and then retention of drug in skin layers is desired.

Methods for preparation of TDDS

Asymmetric TPX membrane method[6]:

The heat sealable polyester sheet which has a concave of 1cm diameter will be used as a backing laminate. For these types of methods a fabricated prototype patch can be used. A sample of the medicament is then distributed into the concave membrane, which is enclosed by a TPX [poly (4 methyl-1-pentene)] asymmetric membrane and then sealed by an adhesive.

Circular Teflon mould method [7]:

Solutions containing polymers in a different ratio in organic solvent are used. Drug in a calculated quantity is mixed in half the amount of same organic solvent, on the other hand enhancers in different concentrations are mixed with the other half of the organic solvent and then added. In a drug polymer solution Di-N-butyl phthalate is added as a plasticizer. Firstly all contents are to be mixed or stirred for 12 hours and then shifted into a circular Teflon mould. The mould then placed on a flattened surface and enclosed with inverted funnel to control solvent vaporization as expressed in the laminar flow hood model with an air speed of 0.5m/s. Further in next step the solvent is then permitted to evaporate for 24hrs. At 25±0.5°C the dried films are stored for again another 24 hours in a dessicator containing silica gel. The type films are to be evaluated within one week of their preparation.

Mercury substrate method [8]:

In this method firstly the polymer solution is prepared and drug along with plasticizer is mixed. Then the solution is mixed or stirred for 10-15min in an order to generate a homogenous dispersion and shifted into a leveled mercury surface, which is then furtheren closed with inverted funnel to control solvent evaporation.

By using IPM membranes method [9]:

In this method thedispersed form of a drug mixed in a combination of propylene glycol and water comprising carbomer940 polymers and agitated for 12hrs in a magnetic stirrer. The dispersion gets to be neutralized and to enhance its viscosity addition of triethanolamine is done. In order to achieve solution gel buffer pH 7.4 can be used and if the solubility of the drug in aqueous solution is very poor. The gel formed will be merged in the IPM membrane.

By using EVAC membrane method [10]:

In this method ethylene vinyl acetate co-polymer (EVAC) membrane can be used as rate controlling membrane. If the drug is immiscible in water, propylene glycol; carbopol resin will be added to the above solution and gets neutral by using 5% w/w sodium hydroxide solution. The drug (in gel form) is then positioned on a sheet of backing layer cover the quantified area. A rate controlling membrane will be placed over the gel and to achieve a leak proof device the ends is then sealed by heat.

Types of transdermal patch [11]

Single-layer Drug-in-Adhesive [12]

A single layer drug in adhesive system is categorized by the addition of the medicament right within the skin containing adhesive. In this type of transdermal system design, the adhesive not only assist to attach the system to the skin but on the other hand it is also help as the foundation of the formulation which contain the medicament with all its excipient beneath a single backing layer. In this type of drug delivery system the diffusion of medicament across the skin membrane mainly dependent on rate of release of medicament.

Multi-layer Drug-in-Adhesive [13]

Multi-layer Drug-in-Adhesive patch alike to the Single-layer Drug-in-Adhesive system. In this type of adhesive system one of the both layer is liable for immediate release of medicament and on the other hand the other layer responsible for controlled release of medicament from the reservoir.

Reservoir [14]

As compared to single layer and a multiple layer adhesive system, the drug reservoir in adhesive system consist of a separate layer, in this the medicament layer consists of a liquid compartment is contained a medicament solution or suspension separated by the adhesive layer from the diffusion

membrane(semi-permeable membrane). The rate of release is zero order for these type of systems. These patches assisted by the backing layer.

Matrix [14]

These Matrix design has the medication layer of a semisolid matrix comprising of a medicament solution or suspension. The outer adhesive layer of this patch atmospheres the medicament layer moderately covering the patch. Drug matrix in adhesive system design is also categorized or termed as monolithic device.

Advantages [15, 16]

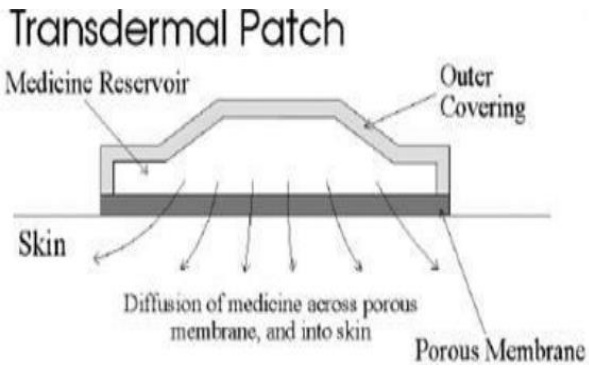
- They avoid gastrointestinal drug absorption difficulties caused due to gastrointestinal pH, enzymatic activities, etc. with foreign particles (food, water, etc.) and orally administered drugs.
- They can substitute oral route of administration of drugs which when administrated through oral route, as in case of vomiting and diarrhea.
- Avoids first pass effect.
- They are non-invasive, avoiding the convenience of parenteral therapy.
- Drug administration can be terminated rapidly by instant removal of its application from the surface of the skin.
- It is also a positive route for the patients who are unconscious.
- They provide extended therapy with a single application, improving compliance over other dosage forms.

Disadvantages[15]

- Its use may be uneconomical.
- The delivery systems can't be used for drug requiring high blood levels.
- May cause allergic reactions.

The transdermal patch used is not appropriate when:

- Medication for acute pain is essential.
- Where rapid dose titration is essential.
- Where necessity of dose is equal to or less than 30 mg/24 hrs.



Identification of drug through Fourier transforms infrared (FTIR)

Sample drug is identified by FTIR. FTIR spectra of sample drug are compared with the FTIR spectra of standard drug. FTIR of standard Prazosin hydrochloride is shown in figure 2 and FTIR spectrum of sample Prazosin hydrochloride is shown in figure 1.

Preparation of Calibration Curve of Prazosin hydrochloride

By dissolving 50mg of per standard sample of the drug were made from the stock solution in 50ml volumetric flask separately and the volume was prepared up with 7.4 phosphate buffer to achieve a concentration of 1mg/ml. different dilutions were prepared in 7.4 phosphate buffer to achieve working standard solution of 0-40µg/ml for Prazosin hydrochloride was observed at 275nm. The graph was plotted between absorbance v/s concentrations to obtain the calibration curve.

Preparation of Transdermal patch:

Transdermal patch of Prazosin hydrochloride was prepared by solvent casting technique in a Petridis. Four types of transdermal patch were prepared. First two formulations were prepared by using HPMC, EC and alone having drug and polymer ratio 1:2 using methanol and chloroform as a solvent and other two formulation F3 and F4 is formulated using HPMC and EC and alone having drug and polymer ratio 1:3 using methanol and chloroform. All four formulations contain span 80 (1%) as permeation enhancer and propylene glycol (3%) as plasticizer.

Table 1: Composition of Transdermal Patch

S. No	Constituent	Formulation Code			
		F1	F2	F3	F4
1	Drug(mg)	10	10	10	10
2	HPMC	20	-	30	-
3	EC	-	20	-	30
4	Span 80%	1%	1 %	1%	1%
5	Propylene Glycol	3%	3 %	3%	3%

Evaluation of TDDS

Thickness of the patch [16, 15]:

The thickness of prepared transdermal patch using a digital micrometer on different point and from the prepared patch determined to ensure the average thickness and standard deviation. The thickness of transdermal film is determined by travelling microscope dial gauge, screw gauge or micrometer at different points of the film.

Folding endurance [16]

Cut the particular area of the patch consistently and repeatedly folded at the same place till it breaks. The numerous times the film could be folded at the same place until it gets breaked, results in the value of folding endurance.

Percentage (%) Moisture content [17, 15]

The prepared separately weighed film that to be set aside in a desiccators consisting of a fused calcium chloride at room temperature for 24 hrs. In the next step the films are to be reweighed and determine the percentage moisture after 24 hrs. From the below mentioned formula

Percentage (%) moisture absorbed =

$$\frac{\text{(Final weight) – (Initial weight)}}{\text{(Initial weight)}} \times 100$$

Percentage (%) of moisture lost [18]:-

To calculate the percentage (%) moisture lose from freshly prepared film, the accurately weighed film are placed in a desiccators containing fused anhydrous calcium chloride for 72hrs, After 72hrs films were re-weighed percentage moisture is calculated using by the following formula

Percentage (%) moisture lost =

$$\frac{\text{(Initial weight) – (Final weight)}}{\text{(Initial weight)}} \times 100$$

Drug content uniformity [19]:-

By the use of diffusion medium a pieces of patch which were cut in a manner and placed in a dissolution of 100ml respectively is mixed or stirred repeatedly using a mechanical stirrer and after the ends of 3hrs the sample is withdrawn the drug content to be determined by U.V spectroscopy at 330 nm.

***In-vitro* Diffusion Study:-**

By using Franz Diffusion Cell the study of *in-vitro* release studies of patch is carried out. Egg membrane is used the purpose of semi-permeable membrane for diffusion. Franz diffusion cell has a receptor compartment with an effective volume around 60 ml and effective surface area of permeation 3.14cm^2.

In-vitro release studies were carried out using Franz diffusion cell.

Drug release kinetic study[20]

The mechanism of drug release from the transdermal patches is analyzed by fitting the release data to following equations

Zero – order equation:

$$Q = k_0 t$$

Where, Q is the amount of drug released at time t

K, is the zero – order release rate.

First – order equation:

$$\text{In } (100 - Q) = \text{In } 100 - k_1 t$$

Where, Q is the percent (%) of drug release at time t

K_1 is the first – order release rate constant.

Higuchi's equation:

$$Q = k_2 \sqrt{t}$$

Where, Q is the percent (%) of drug release at time t

$K_2$is the diffusion rate constant.

Mathematical model for transdermal drug delivery system:-

The drug release mechanism and kinetics are two important characters of delivery system for the drug dissolution profile. Some kinetics models are given in Table no. 5.

Table 2: Mathematical model for transdermal drug delivery system

Kinetic model	Mathematical relation	System that follows the model
First order	In Q_t = in Q_0+k(release proportionate to amount of drug remaining)	Water soluble drug in porous matrix
Zero order	$F_t = k_0 t$(release independent of drug concentration)	Transdermal system
Higuchi's square root of time equation	$F_t = k_h^{1/2}$	Diffusion matrix formulation
Korsmeyer-peppas power law equation	$M_t/M_\infty = kt^n$	Swellable polymeric device

Where,

F_t=fraction of drug release in time t

K, k_h, k_0, k_t=release rate constant

M_t=amount release at time t

M_∞=amount release at infinite time

Q_0=drug amount remaining to be release at 0 hours

Q_t=drug amount remaining to be release at t hours

RESULT AND DISCUSSION:

Preformulation studies

Identification of pure drug by FTIR

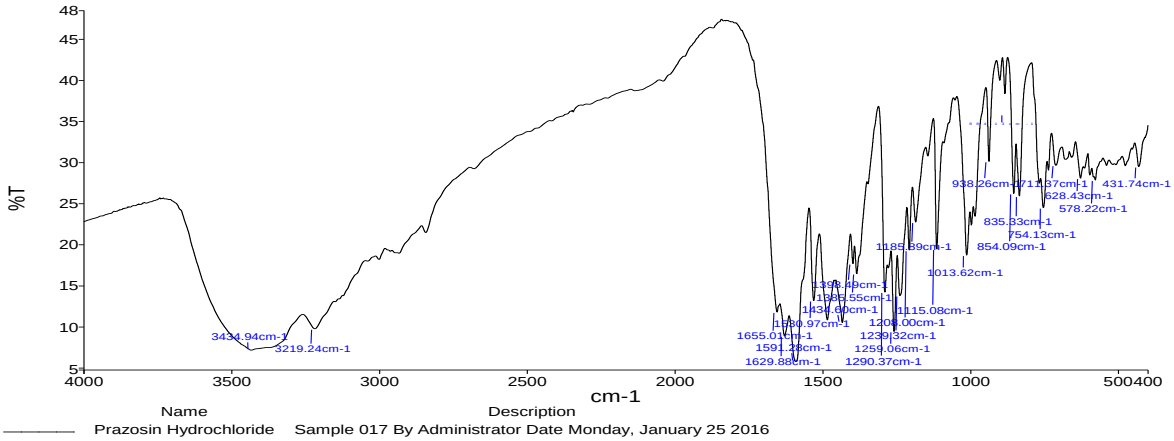


Fig 3: Identification of Sample through FTIR

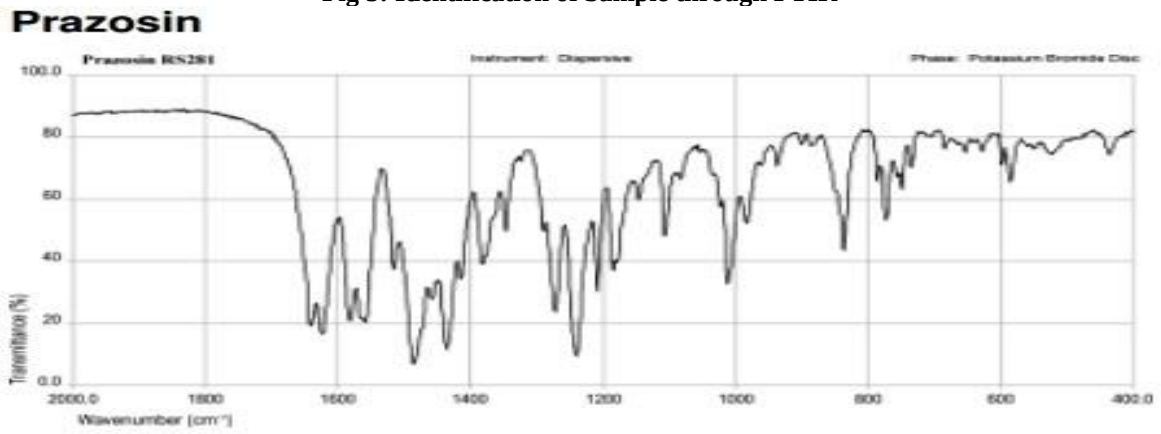


Fig 4: FTIR Spectrum of Standard Prazosin hydrochloride (with references of B.P. -2009)

Table 3: Characteristics peaks of Prazosin hydrochloride

S.No.	Reference peaks (cm^{-1})	Theoretical peak of Prazosin hydrochloride	Obtained peaks (cm^{-1})	Functional Group	Stretching/ Bending
1	1750-1680	1529.92	1529.92	C=O	Stretching
2.	1650-1580	1651.70	1651.70	N-H	Bending
3.	1335-1250	1385.08	1385.08	C-N	Stretching
4.	1320-1000	1146.18	1146.18	C-O	Stretching
5.	900-800	884.13	884.13	C-C	Stretching

The comparison between the peak of two graph shows that the characteristic peak of Prazosin hydrochloride (Reference) was found similar to the given sample, which shows that the drug is Prazosin hydrochloride.

Organoleptic characteristics of drug:
Organoleptic properties like colour, Odour, and taste of Prazosin hydrochloride were characterized by descriptive terminology, and shown in table below.
Organoleptic properties of Prazosin hydrochloride was observed by physical and visual method.

Table 4: Organoleptic characteristics of Prazosin hydrochloride

S. No.	Properties	Result
1	Description	White to tan powder
2	Colour	White to off white
3	Odour	Odourless
4	Taste	Bitter

Solubility:
Prazosin hydrochloride is very soluble in chloroform, soluble in methanol, slightly soluble in Distilled water.

Table 5: Solubility of Prazosin hydrochloride

S.No	Solvent	Solubility (mg/ml)	Remark
1	Water	27	Sparingly soluble soluble
2	Methanol	117	Slightly soluble
3	Ethanol	1597	Very soluble
4	Chloroform	13	Sparingly soluble
5	Acetone	12	Slightly soluble

Melting Point Determination:
Determination of Melting Point: the sample was loaded in to sealed capillary (melting point capillary) which was then placed in melting point apparatus. The sample was then heated and as the temperature increase the sample was observed to detect the phase change from solid to liquid phase. The temperature at which the phase changes occur gives the melting point.
The melting point of prazosin hydrochloride is 268-272^{o}c.

Table 6: Results of Melting point determination

1	Experimental value	271-273°C
2	Literature value	268-272°C

Partition coefficient: The partition coefficient of the drug was found to 0.128.

Spectral studies

Drug-excipient compatibility study:

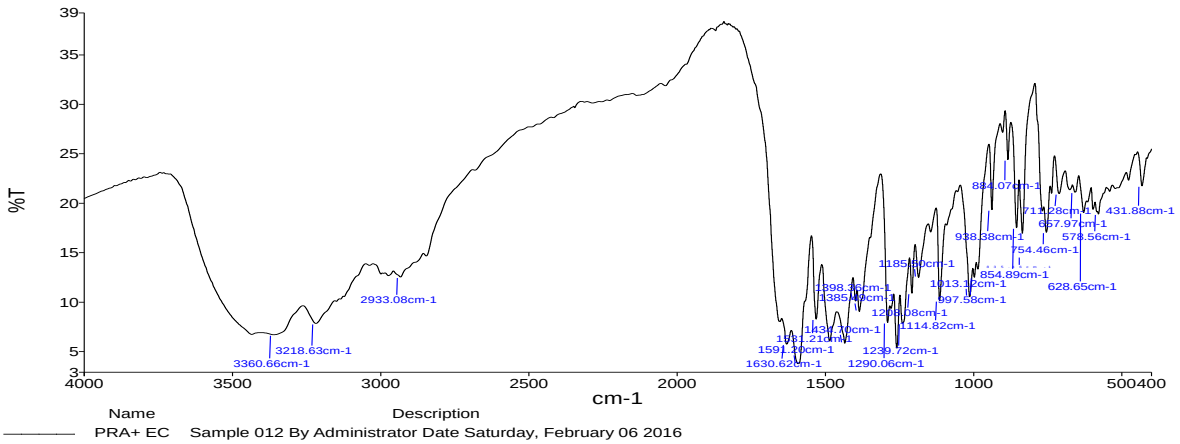


Fig 5: FTIR of prazosin hydrochloride + Ethyl Cellulose

Table 7: FTIR interpretation of prazosin hydrochloride +Ethyl Cellulose

S. No.	Wave number cm^{-1}	Peaks of drug(cm^{-1})	Functional Group	Stretching/Bending
1.	1651.55	1651.67	C=O	Stretching
2.	1416.96	1416.98	C=C	Stretching
3.	1072.39	1072.37	C-O	Stretching

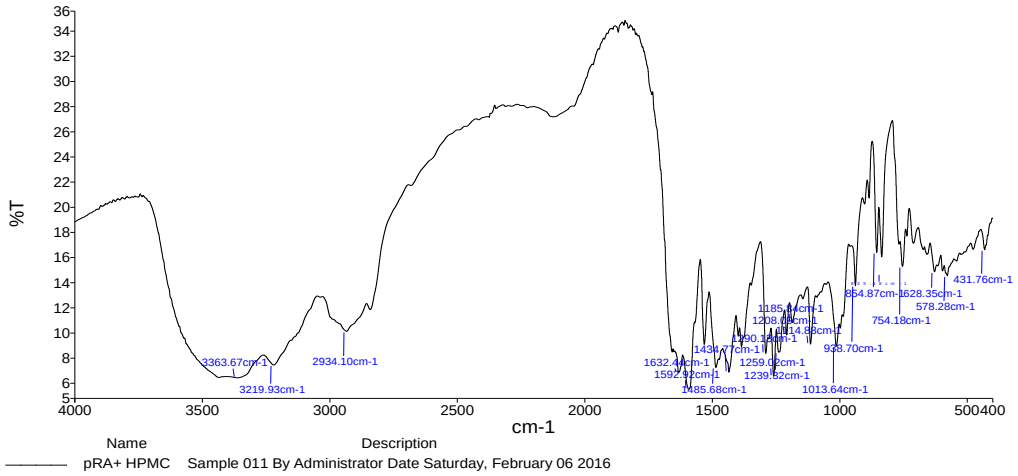


Fig 6: FTIR spectra of Prazosin + HPMC

Preparation of Calibration curve of prazosin hydrochloride

Determination of λ_{max} of prazosin hydrochloride
Exhibited peak absorbance at 330nm (λ_{max}) in methanol.

Standard solution
50mg of standard drug was accurately weighed and placed in 250ml of volumetric flask and 50 ml methanol was added to it and shakes for few minutes to prepare 1000microgram/ml.

Stock solution
From this solution the stock solution was prepared by taking 1 ml from standard solution and made the volume to 100 by ethanol and then prepare the solution of 0-10µg/ml and check the absorbance at 330 nm in UV spectrum. Absorbance v/s concentration were plotted to obtain the calibration graph. The drugs obeyed beer's law with the above concentration range with 'r' value of 0.997 for prazosin and line of equation:-

Wavelength of maximum absorption (λ_{max}) of drug (**Prazosin Hydrochloride**) in phosphate buffer 7.4was found to be 330nm.

Table 8: Data for calibration curve of prazosin hydrochloride:

S. No.	Concentration (µg/ml)	Absorbance
1	0	0
2	2	0.12
3	4	0.24
4	6	0.35
5	8	0.46
6	10	0.55

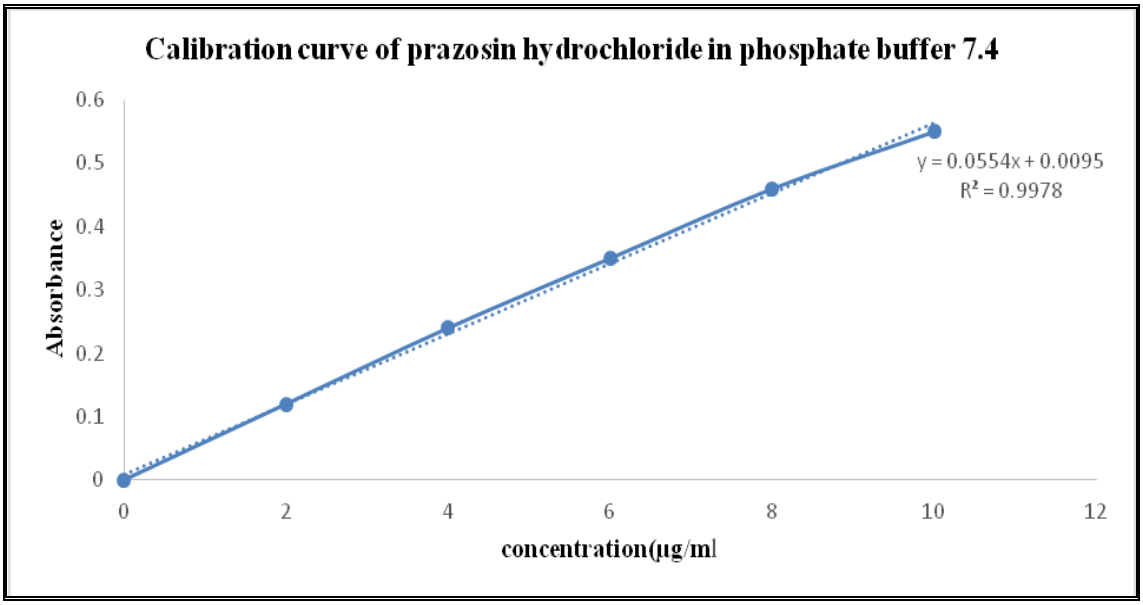


Fig 7: Calibration curve of Prazosin hydrochloride

Line of Equation: y = 0.055x+0.009

Beer's Range: 0-10 µg/ml

R^2 Value: 0.997

λ_{max}: 330 nm

Evaluation parameters of transdermal patches of prazosin hydrochloride

The evaluation of prepared transdermal patches was done under following parameters:

- Thickness
- Folding endurance
- Percentage (%) moisture absorbed
- Percentage (%) moisture lost
- Drug content

Table 9: Evaluation parameters of transdermal patches of prazosin hydrochloride

S.No	Formulation Code	Thickness(mm)	Folding endurance	%Moisture absorbed	%Moisture lost
1	**F1**	0.25±0.032	68	2.45±0.012	1.28±0.01
2	**F2**	0.26±0.054	65	2.35±0.034	1.26±0.04
3	**F3**	0.27±0.026	72	2.25±0.086	1.56±0.43
4	**F4**	0.29±0.036	70	2.56±0.054	1.35±0.02

Mean ± SD (n=3)

Thickness determination:
The thickness of prepared transdermal patches was found to be range of 0.25± 0.032mm to 0.29 ± 0.036mm, thus the patch prepared were uniform in thickness.

Folding endurance:
Folding endurance of transdermal patches was found to be range of 65 to 72.

% Moisture absorption determination:
The range of % Moisture absorption of transdermal patches lies within the range 2.25 ± 0.086 to 2.56± 0.054.

% Moisture loss determination:
The range of % Moisture loss determination of transdermal patches lies within the range 1.26 ± 0.04 to 1.56 ± 0.43.

Table10: Drug Content Uniformity

Formulation	Percentage (%) of drug in 3.14 sq.cm			
	1st	2nd	3rd	Mean
F1	93.56	93.76	93.54	93.62
F2	91.15	91.30	91.29	91.25
F3	90.25	90.32	90.36	90.31
F4	95.14	95.08	95.24	95.15

Drug content uniformity:

All formulation contained good amount of content of drug which lies within the range 90.31% to 95.15%.

***In-vitro*release study:**

Table 11: *In-vitro* diffusion profile of prazosin hydrochloride formulation

S.No	Time (hrs.)	Percentage (%) Cumulative drug release			
		F1	F2	F3	F4
1.	0	0	0	0	0
2.	1	12.02	8.31	15.74	9.37
3.	2	21.32	17.45	23.65	18.25
4.	4	26.65	25.04	32.25	26.64
5.	6	32.61	28.19	36.17	32.15
6.	8	37.68	31.26	41.61	36.38
7.	10	42.63	36.23	46.35	40.32

Table 12: *In- vitro* diffusion profile of Prazosin hydrochloride from Formulation F1

S.No	T	√T	Log T	Cumulative Percentage %drug release	Cumulative percentage %drug remain	Log Cumulative percentage % drug release	log Cumulative percentage %drug remain
1	0	0	-	0	100	-	2
2	1	1	0	12.02	87.98	1.07	1.94
3	2	1.414	0.3	21.32	78.68	1.32	1.89
4	4	2	0.6	26.65	73.35	1.42	1.86
5	6	2.449	0.77	32.61	67.39	1.51	1.82
6	8	2.828	0.9	37.68	62.32	1.57	1.79
7	10	3.16	1	42.63	57.37	1.62	1.75

Table13: *In- vitro* diffusion profile of Prazosin hydrochloride from Formulation F2

S.No	T	√T	Log T	Cumulative percentage % drug release	Cumulative percentage % drug remain	Log Cumulative percentage %drug release	Log Cumulative percentage %drug remain
1	0	0	-	0	100	-	2
2	1	1	0	8.31	91.69	0.91	1.96
3	2	1.414	0.3	17.45	82.55	1.24	1.91
4	4	2	0.6	25.04	74.96	1.39	1.87
5	6	2.449	0.77	28.89	71.11	1.46	1.85
6	8	2.828	0.9	31.26	68.74	1.49	1.83
7	10	3.16	1	36.23	63.77	1.55	1.80

Table 14: *In- vitro* diffusion profile of Prazosin hydrochloride from Formulation F3

S.No	T	√T	Log T	Cumulative percentage% drug release	Cumulative percentage% drug remain	Log Cumulative percentage% drug release	Log Cumulative percentage% drug remain
1	0	0	-	0	100	-	2
2	1	1	0	15.74	84.26	1.19	1.92
3	2	1.414	0.3	23.65	76.35	1.37	1.88
4	4	2	0.6	32.25	67.75	1.50	1.83
5	6	2.449	0.77	36.17	63.83	1.55	1.80
6	8	2.828	0.9	41.61	58.39	1.61	1.76
7	10	3.16	1	46.35	53.65	1.66	1.72

Table 15: *In- vitro* diffusion profile of Prazosin hydrochloride from Formulation F4

S.No	T	√T	Log T	Cumulative percentage% drug release	Cumulative percentage% drug remain	log Cumulative percentage% drug release	log Cumulative percentage% drug remain
1	0	0	-	0	100	-	2
2	1	1	0	9.37	90.63	0.97	1.95
3	2	1.414	0.3	18.25	81.75	1.26	1.91
4	4	2	0.6	26.64	73.36	1.42	1.86
5	6	2.449	0.77	32.15	67.85	1.50	1.83
6	8	2.828	0.9	36.38	63.62	1.56	1.80
7	10	3.16	1	40.32	59.68	1.60	1.77

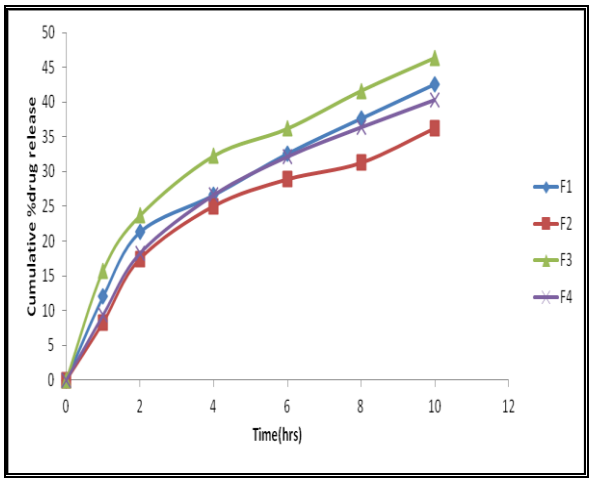


Fig 8: Zero order release plot of prazosin hydrochloride Transdermal Patches

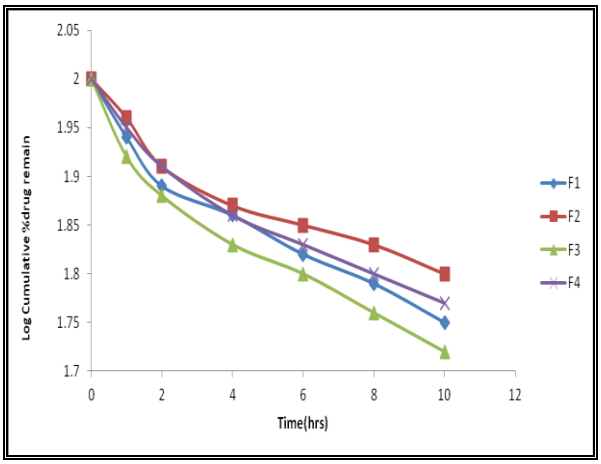


Fig 9: First order release plot of prazosin hydrochloride Transdermal Patches

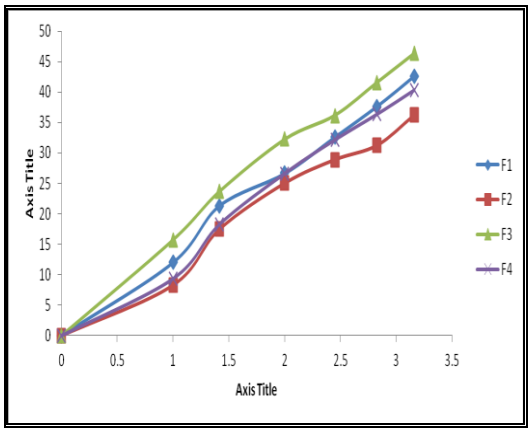


Fig 10: Higuchi plot of prazosin hydrochloride Transdermal Patches

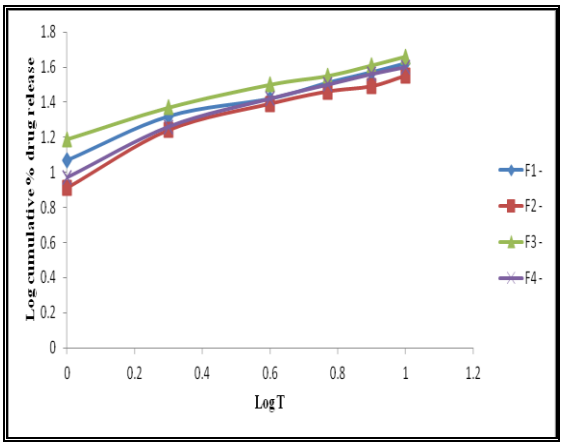


Fig 11: Korsmeyer Peppa's plot of prazosin hydrochloride Transdermal Patches

Mathematical modelling:

Table 16: Model fitting release profile of Formulation F1 to F4

Formulation code	Regression coefficient (R^2)			Korsmeyer-Peppas	
	Zero order	First order	Higuchi model	R^2	N
F1	0.877	0.918	0.993	0.990	0.452
F2	0.915	0.948	0.994	0.977	0.521
F3	0.915	0.948	0.991	0.971	0.61
F4	0.891	0.934	0.983	0.971	0.61

The calibration curve of pure Prazosin hydrochloride was plotted phosphate buffer 7.4 to get a concentration 1mg/ml. from this suitable dilution were made in phosphate buffer 7.4 to get the working standard solution of 0-20µg/ml for Prazosin spectrum measured at 330 nm. The graph was plotted between concentration v/s absorbance to obtain a calibration graph shown in figure 7 and data obtained from U.V spectrophotometer were shown in table 8. The compatibility study of drug and polymer studied are carried out by using FTIR. The absorption spectrum of compatibility studied shown in figure 3-6.The preliminary study conducted on compatibility between Prazosin with HPMC EC revealed that there is no interaction between the drug and polymer as from FTIR spectra. Prepare four formulations using different polymer HPMC and EC with the ratio 1:2 and 1:3 along with span 80 (1%) as permeation enhancer and propylene glycol (1%) as plasticizer. The various physico-chemical characteristics such as thickness of the patch, folding endurance, percentage of moisture absorbed, percentage of moisture lost, and drug content analysis were found to be within the acceptable limits. The patches were found to be stable to withstand the stress. In vitro Diffusion studies of Transdermal patches: The study of in-vitro diffusion is carried out by using Franz Diffusion Cell. Using Franz diffusion cell In-vitro release studies were carried out. Drug release from prepared dermal patch F1, F2, F3, and F4 was 42.63%, 36.23%, 46.35%, and 40.32% respectively in 10 hrs.

CONCLUSION:

Transdermal drug delivery is most applicable route of drug administration, which is used to deliver the drug into the site of action at the predetermined and control rate .through this route drug can applied in the form of thick transdermal patch that's why the drug release easily from the patch and maintain therapeutic effect. The main purpose of making transdermal patches is to overcome the steps present in oral drug delivery like first pass

metabolism, GI irritation, etc. Manufacturing transdermal patch of prazosin hydrochloride contains HPMC and EC as polymer with different ratio, PG as plasticizer and Span 80 as permeation enhancer for control release of the drug over an extended period of 8 hrs. Greater appreciative of the different polymers and different mechanism of biological interactions are essential to optimize this drug delivery system. Prepare four formulations using different polymer HPMC and EC with the ratio 1:2 and 1:3. The prepared formulation were studied their estimation parameter like thickness, folding endurance and moisture content, moisture loss and *in-vitro* drug release study. Formulation F2 show minimum *in-vitro* drug release, So, in general it was fulfilled that topical formulation prepared with polymer HPMC (1:3) was the formula of choice as it showed enhanced drug release.

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