RESEARCH ARTICLE

FORMULATION CHARACTERIZATION AND IN-VITRO EVALUATION OF CLASS 1C ANTIARRHYTHMIC AGENT: PROPAFENONE INTO TRANSDERMAL PATCHES

*Dr. P. Shashidhar, Dr. M. Sunitha, Dr. D. Ramakrishna and Ms. Mariyam Ali

Shadan Women's College of Pharmacy, Kahirtabad, Hyderabad

ABSTRACT

In the present research work PROPAFENONE an anti-arrhythmia agent was selected for the formulation and preparation of transdermal patches as a model drug, using HPMC-15 cps and Methocel K100 as release controlling agents from patches along with sodium alginate are used. Transdermal patches were prepared using HPMC-15cps from trials T-1 to t-5, in which concentrations of HPMC-15 cps used in increasing concentrations. Similarly same in case of trials T6 to T10 was used with Methocel K 100. In-house films were taken for in-vitro evaluation tests and found to be 109 mg to 365 mg. whereas folding endurance test was found to be 56 times for TRIAL-1 and 126 times for TRIAL-10. In case of moisture content test TRIAL -10 showed less percent of moisture with 1.14 and TRIAL-4 Showed 3.54. For water uptake studies patches of TRAIL-10 absorbed 0.98 percent and TRIAL -2 of 1.63 percent. When comes to tensile strength of in-house prepared patches lease of TRIAL-6 with 63 and maximum of TRIAL-10 with 106. Release kinetics was also determined for optimized trial T10 and the drug release was found to be in following order, Zero order-0.995>Koresmeyer Peppas plot-0.972>First order>0.932>Higuchis plot-0.923. Based on the above R^2 values it has been concluded that the release of PROPAFENONE was following Zero order rate kinetics with R^2 value 0.995.

INTRODUCTION

The improvement of novel drug delivery structures for present drug molecules and their dosage has been a concern of hobby due to the fact beyond few years .greatest therapy calls for no longer most effective proper drug selection however also proper efficacy of the drug and safety. The pharmacological response, each the preferred therapeutic effect and the unfavorable results, of a drug is depending on the awareness of the drug at the website online of action, which in turn relies upon at the side of the dosage form and the volume of absorption of the drug on the web page of action. This improvement in novel shipping system for present drug molecules now not simplest improves the drug's overall performance in phrases of efficacy and protection but additionally improves affected person compliance and ordinary therapeutic advantage to a giant extent. Transdermal drug transport is becoming an increasing number of popular and a hit to that traditional methods of medicinal drugs being given thru pills and injections . Transdermal Drug transport machine (TDDS) is a self contained, discrete dosage shape of medication (Gaur *et al.,* 2009).

That are administered in the form of "patches" on the surface of the skin. The drug is administered thru transdermal course through the patches in the circulatory device at a pre-decided fee with minimum inter and intra patient version .It gives controlled management of capsules, alongside with non-stop enter of drugs with short biological 1/2 lives and doing away with pulsed access into systemic move, which often reasons unwanted aspect effects (Singh, 2010). A transdermal drug shipping device it can be active or passive designed administered to the affected person thru a permeable membrane overlaying a reservoir of medication or via the frame warmth melting thin layers of the medication deposited in the adhesives. The most important disadvantage to transdermal transport stems shape the fact that the pores and skin being a totally lively barrier as a result simplest allowing prescriptions whose atoms are sufficiently little to enter pores and skin can be presented by this approach. It enhances bioavailability, giving more noteworthy uniform plasma stages, longer time of movement resulting in a decrease in measurements recurrence, diminished angle impacts and ventured forward treatment because of insurance of plasma levels up to the stop of the dosing c program dialect period when contrasted with a decrease in plasma ranges with that of customary oral dose administration.

Corresponding author: **Dr. Pshashidhar,**
Shadan Women's College of Pharmacy, Kahirtabad, Hyderabad.

A wide type of endorsed drugs right now are to be had fit as a fiddle of transdermal fix .the essential economically accessible medicine fix move toward becoming allowed by methods for the us sustenance and Drug administration in December 1979, which progress toward becoming directed for scopolamine for movement illness. A transdermal patch is a medicated adhesive patch that is positioned topically at the skin to supply a specific dose of drugs thru the pores and skin and into the bloodstream recuperation to an injured area or area of the body. Skin is the largest organ in a body the pores and skin of an average person body covers of about 2 m2 of the floor and gets approximately one-third of the blood circulating via the frame. For the delivery of a drug into the frame via transdermal layer of pores and skin, it is vital to apprehend approximately the pores and skin. It is one of the most quite simply to be had organs of the frame with a thickness of few millimeters (2.ninety seven 0.28 mm) which,

- It separates the underlying blood flow network from the outdoor environment.
- It acts as a barrier against bodily, chemical and microbiological attacks.
- Acts as a thermostat and helps in preserving body temperature.
- Plays a position in the law of blood strain.
- Protects human body in opposition to the penetration of UV rays.
- Pores and skin is a primary factor in figuring out the various drug delivery aspects like permeation and absorption of drug across the epidermis. The diffusional resistance of the pores and skin is substantially depending on its anatomy and ultra shape (Aarti *et al.,* 1995).

Mechanism of drug transportation (Chien, 1992)

Membrane permeation controlled structures

In this sort of gadget, the medication store is completely epitomized in a shallow compartment shaped from a medication impermeable steel plastic overlay and an expense controlling layer made of polymer. e.g. Ethylene vinyl acetic acid derivation with portrayed medication penetrability. The medication particles are endorsed to dispatch handiest through the rate-controlling film. In the medication store compartment, the medication solids are both scattered in a solid polymer grid or suspended in a thick fluid medium to shape a glue like suspension. a thin layer of glue polymer is done to the outside floor of the expense controlling film to acquire a private touch of the transdermal machine and the skin floor

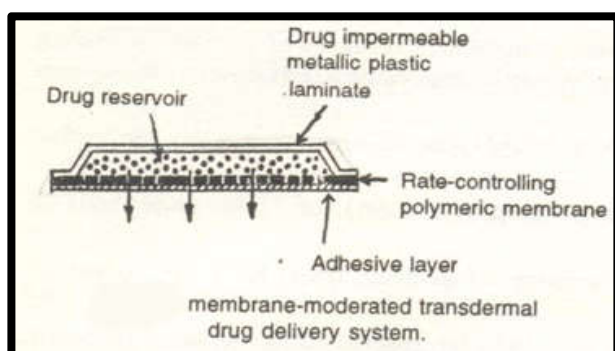**Example:** Transderm-Nitro, Transderm-Scop, Catapress, Estraderm

Figure 1. Membrance perm`eation controlled device

Matrix diffusion-controlled device

In this sort, the medication store is set up by method for homogenously scattering drug trash in a hydrophilic or lipophilic polymer framework. The resultant sedated polymer is then shaped into a cured plate with a portrayed surface place and controlled thickness. This medication store containing polymer circle is then glued on to an occlusive base plate in a compartment created with a medication impermeable plastic support. The cement polymer is then spread along the boundary to frame a piece of cement edge around the sedated circle. Illustration: Nitro-Dur gadget.
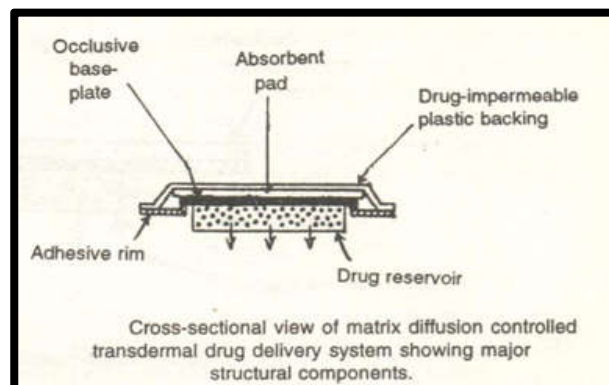

Figure 2. Matrix diffusion controlled systems

Adhesive dispersion

That is a streamlined type of the layer pervasion oversaw machine. The medication supply is planned by method for without a moment's delay scattering the medication in a cement polymer eg. Poly-isobutylene after which spreading the sedated glue, through dissolvable throwing or hot relax onto a level sheet of medication impermeable metallic plastic support to shape a thin medication store layer. at the apex of the medication repository layer, thin layers of non-cured, charge controlling glue polymer of a chose porousness are connected to create a glue dispersion – controlled transporting gadget. Example: Deponit, Frandol Tape
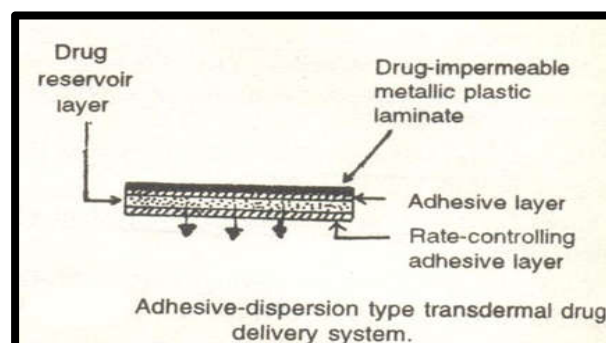
Figure 3. Adhesive dispersion

Micro reservoir type or micro-sealed dissolution controlled systems

Ideal here, the medication supply is designed by methods for first suspending the medication solids in a fluid answer of a water dissolvable fluid polymer after which scattering the medication suspension homogenously in a lipophilic polymer through over the top shear mechanical power to shape a substantial scope of smaller scale repositories. These are inaccessible minuscule circles of medication supplies. This thermodynamically unpredictable scattering is balanced out

quick by methods for moment expansion of cross connecting polymers like Gluteraldehyde the polymer which creates a sedated polymers plate with unfaltering floor region and an immovable thickness. A transdermal recuperating framework is created by utilizing situating the sedated circle on the middle and encompassing it with a glue edge and afterward it's miles spread on to the occlusive base plate with cement froth cushion.
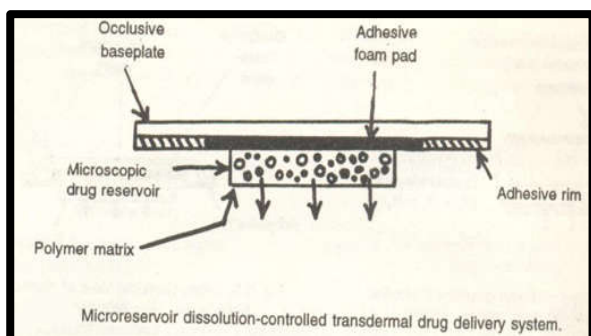
Example: Nitro-Disc device

Figure 4. Dissolution of patches form micro-reservoir

Table 1. Polymers used in TTS (Misra *et al.,* 1997)

Natural Polymers	Synthetic Elastomers	Synthetic Polymers
Cellulose derivatives, Zein, Gelatin, Waxes, Proteins,.	Polybutadiene, Hydrin rubber polyoxane, silicone rubber, Neoprene.	Polyvinylpyrrolidone, Polymethyl methacrylate, Epoxy, Polyurea, etc.

Ideal molecular properties for transdermal drug delivery (Kumar *et al.,* 2010)

- Melting point of the drug required is low (<200ºC).
- The saturated solution used should have the ph in the choice of 5-9.
- To obtain good therapeutic action optimal partition coefficient is required.
- Adequate solubility is required to obtain better permeation of the drug in lipid and water. (1mg/ml).

MATERIALS AND METHODS

API Propafenone used in the present research work us procured as gift sample form Gland Pharma Limited, Hyderabad and all other excipients are procured from SD fine chemical, Hyderabad.

Methodology

Pre-formulation Studies

Determination of Melting Point (Shaila *et al.,* 2006)

Melting point of the Probenced was determined by using open capillary tube technique in digital melting point apparatus.

Method: In this method, the capillary tube is closed by gently heating from one end. Then the little amount of the drug Probenced was filled into the sealed capillary tube.

Then this tube was tied to the tube having the oil phase in such that the sealed part of the capillary containing the drug was dipped into the oil. Gently the oil bath was heated. When powder starts melting, the heating was stopped and the temperature is noted down at which the drug melts starts melting.

Determination of Partition Coefficient

The partition coefficient of the drug Probenced was known by using equal volumes of 1-octanol and aqueous solution in a separating funnel. For water soluble drugs, drug solution was prepared in distilled water, and for water insoluble drugs, drug solution was prepared using 1-octanol. 1-octanol (100 ml) is added to the equal volume of the drug solution prepared in separating funnel by using distilled water and the solutions were allowed to separate with shaking at irregular intervals. Then the drug solution was separated and assayed for drug content.

$$Partition\ Coefficient = \frac{Concentration\ of\ drug\ in\ organic\ phase}{Concentration\ of\ drug\ in\ aqueous\ phase}$$

Determination of Drug Excipients Compatibility

During the preparation of patch formulation, drug and polymers interact when they in contact with each other, which may cause instability of the drug. FT-IR spectroscopy is employed to confirm the compatibility between the polymer and Probenced. The pure drug and drug with all the excipients are scanned separately. KBr Pellet method is used and the samples were mixed with dry powder KBr crystals. The blend was compacted to make a disc. This disc was kept in spectrophotometer and spectrum was recorded. Chemical contact among drug and polymers was found by using the FT-IR spectra.

Color, whiff, tang and structure

The color, aroma, taste as well as manifestation of the drug were recorded using descriptive terminology.

Determination of solubility

The solubility of Propafenone was determined by adding excess amount of drug in the solvent and equilibrium solubility was determined by taking the supernatant and analyzing it spectro-photo metrically with water, 0.1N HCL, Methanol, 6.8pH buffer, chloroform and Alcohol by using the following formula:

%solubility=sample absorbance/ standard absorbance *dilution factor*100

Description

Description of Propafenone was determined

PH: Propafenone was resolute according to IP study. Amid 5.0 to 6.5 within an aqueous solution.

Analytical Methods Development of Propafenone:

Preparation of standard stock solution using distilled water: Accurately weighed 5mg of the drug Propafenone is taken in a volumetric flask, and it is completely solubilized in distilled water and then the volume is made up to 100ml which gives a concentration of 50µg/ml.

Preparation of calibration curve using Distilled water

From the above standard stock solution (50µg/ml), appropriate aliquots are taken into different volumetric flasks and make up the volume to 10 ml by using distilled water which gives concentration of 10, 20, 30, 40µg/ml. The absorbance of the solution was measured at 247nm using UV-Visible spectrophotometer. The standard graph is plotted with concentration on x-axis and absorbance on y-axis.

Table 2. Absorbance for calibration curve

Concentration	Absorbance
0	0
10	0.135
20	0.27
30	0.41
40	0.54
50	0.675

Formulation of Propafenone transdermal Patches

The test tube is touched to the superficial layer of the distilled water (50 ml) taken in a beaker. The beaker is magnetically stirred on magnetic stirrer. The samples of 5ml were withdrawn at time interval of 1, 2, 3, 4, 5, 6, 7, 8, up to 24h, analyzed for drug content spectro-photo metrically at 289 nm against blank. Then it is exchanged with the equal quantity of distilled water at every time of sample withdrawal.

General Procedure of Preparation of Propafenone Transdermal Patch

Drug-loaded matrix-type transdermal patches of Propafenone were prepared by using solvent casting method. A petri dish with a total area of 44.15 cm^2 was used. Polymers were accurately weighed and dissolved in 10 mL of water, methanol (1 : 1) solution and kept aside to form clear solution. Drug was dissolved in the above solution and mixed until clear solution was obtained. Polyethylene glycol 400 (30% w/w of total polymer) was used as plasticizer and propylene glycol (15% w/w of total polymer) was used as permeation enhancer.

Table 3. Ingredients used in formulation of patches for all trials

INGRIDENTS	trial-1	trial-2	trial-3	trial-4	trial-5	trial-6	trial-7	trial-8	trial-9	trial-10
DRUG	40	40	40	40	40	40	40	40	40	40
HPMC-15 CPS	25	50	75	100	125	-	-	-	-	-
SODIUM ALGINATE	25	50	75	100	150	100	125	150	175	200
METHOCEL K 100	-	-	-	-	-	20	30	40	50	60
ETHANOL	3	3	3	5	7	7	10	15	15	15
WATER	5	5	10	15	20	20	25	25	30	30
PEG-400	1	1	1	2	2	2	5	5	5	7
GLYCEROL	2	2	2	2	2	2	2	2	2	2
TOTAL WEIGHT	101	151	206	264	346	191	237	277	317	354

In-Vitro Evaluation of Transdermal Patches

Physical Appearance

All the formulated transdermal patches are visually checked for its color, clarity, elasticity and flatness.

Folding Endurance

The transdermal patch of each type of the formulation is cut into small strips of 2×2 cm and they are folded at the exact point until it breaks or cracks. The total of times it is folded at the same point indicates the value of the folding endurance.

Uniformity of weight

The formulated transdermal patches are weighed using digital weighing machine. Three readings for each transdermal patch are taken. Average of the weight is then calculated.

Drug Content Uniformity

The transdermal patches are cut into pieces of 1 ×1 cm for the formulations made and placed in 50ml of distilled water. The contents are stirred for 2h by using magnetic stirrer. The solution is then sifted by using Whatmanns filter paper and diluted suitably by using distilled water. The solution is then analyzed for its absorbance at 289nm. From the above absorbance values, the drug content is determined.

In-vitro drug release studies

The transdermal patches prepared are cut into piece of 1 ×1 cm for all the formulations made and are placed in the middle of the egg membrane and it is tied to the inverted test tube.

The resulted uniform solution was cast on the petri dish, which was lubricated with glycerin and dried at room temperature for 24 h. An inverted funnel was placed over the petri dish to prevent fast evaporation of the solvent. After 24 h, the dried patches were taken out and stored in a desiccator for further studies.

In-Vitro Evaluation Parameters of Transdermal Patch

Folding Endurance

A strip of specific area (2 cm*2 cm) was cut evenly and repeatedly folded at the same place till it broke. The number of times the film was folded at the same place without breaking gave the value of the folding endurance.

Tensile Strength

The tensile strength of the patch was evaluated by using the tensiometer (Erection and instrumentation, Ahmedabad). It consists of two load cell grips. The lower one was fixed and upper one was movable. Film strips with dimensions of 2*2 cm were fixed between these cell grips, and force was gradually applied till the film broke. The tensile strength was taken directly from the dial reading in kg.

Percentage Elongation Break Test

The percentage elongation break was determined by noting the length just before the break point, the percentage elongation was determined from the below mentioned formula.
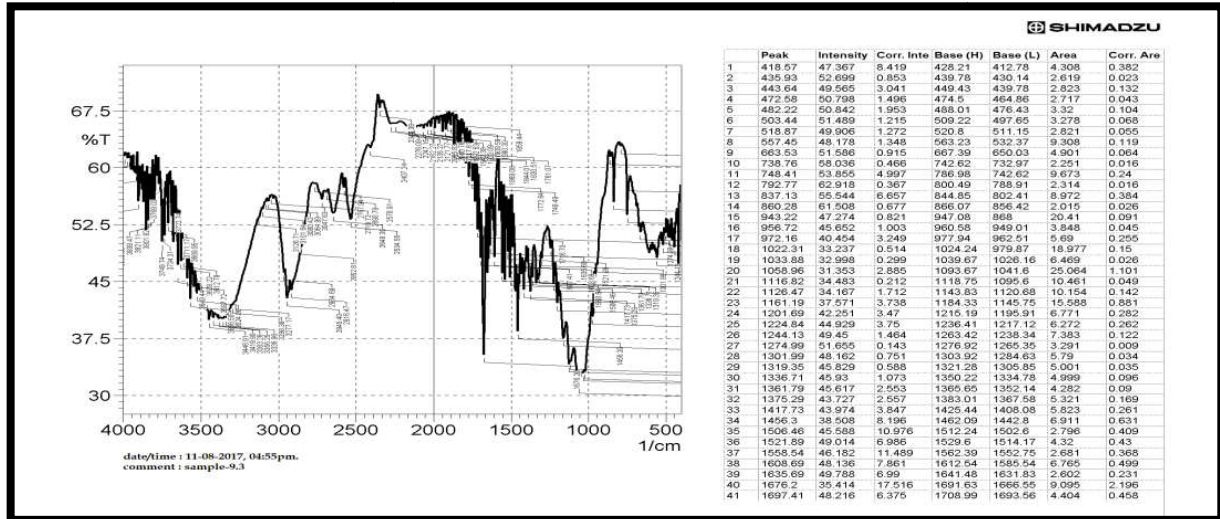
PURE PROPAFENONE
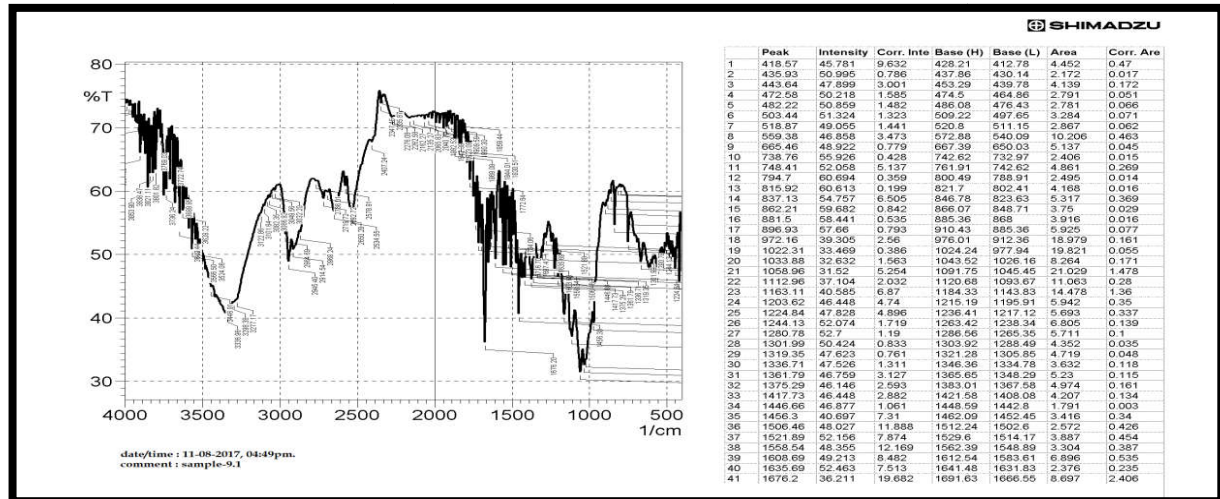

Figure 5. FTIR spectra of PROPAFENONE

SODIUM ALGNATE

Figure 6. FTIR spectra of Sodium Alginate
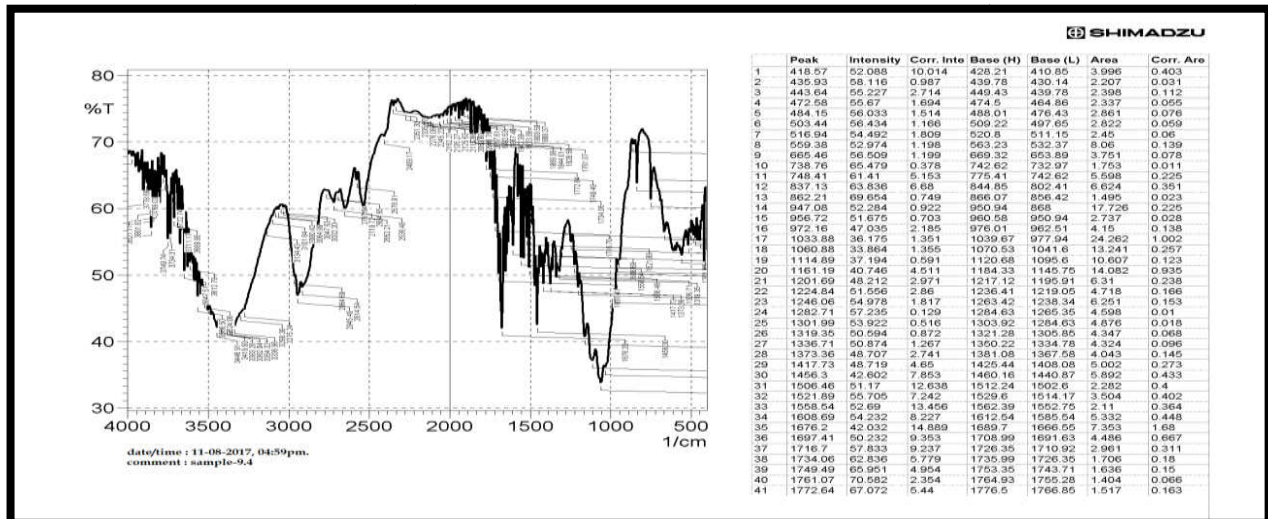
METHOCEL K100

Figure 7. FTIR spectra of Methocel K 100
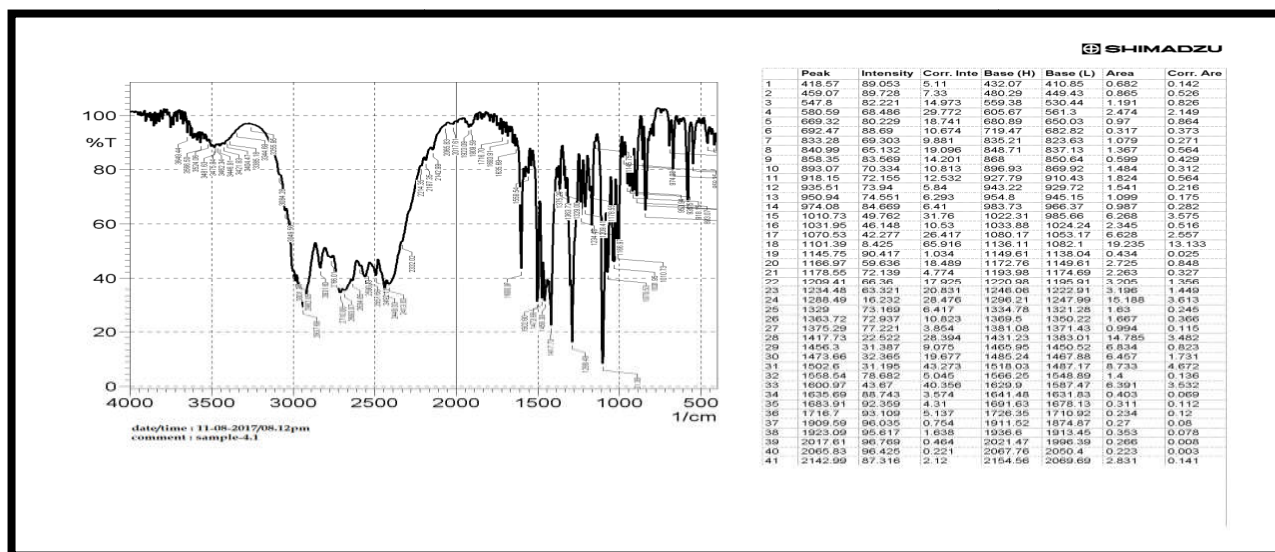
OPTIMIZED TRIAL T-10

Figure 8. FTIR spectra of Optimized trial T10

Table 4. FTIR spectra peaks of pure drug and polymers used in present work

S.NO	METHOCEL	SODIUM ALGINATE	DRUG	OPTIMIZED TRIAL
1	466.79	503.44	459.07	472.58
2	540.09	594.1	516.94	569.02
3	605.67	644.25	619.17	651.96
4	756.12	889.21	761.91	754.19
5	954.8	1016.52	798.56	947.08

The drug and the polymers do not show interaction with each other.

Elongation percentage=[(L1-L2)/L2]x100]

Where $L1$ is the final length of each strip, and $L2$ is the initial length of each strip

Thickness

Patch thickness was measured using digital micrometer screw gauge at three different places, and the mean value was calculated.

Drug Content

A specified area of patch (2 cm*2 cm) was dissolved in 100 mL methanol and shaken continuously for 24 h. Then the whole solution was ultra-sonicated for 15 min. After filtration, the drug was estimated spectrophotometrically at wavelength of 281 nm and determined the drug content.

Percentage Moisture Content

The prepared films were weighed individually and kept in a desiccators containing fused calcium chloride at room temperature for 24 h. After 24 h, the films were reweighed and determined the percentage moisture content from the below mentioned formula

Percentage moisture content = (Initial weight−Final weight)/Final weight x100

Percentage Moisture Uptake

The weighed films were kept in desiccators at room temperature for 24 h containing saturated solution of potassium chloride in order to maintain 84% RH.

After 24 h, the films were reweighed and determine the percentage moisture uptake from the below mentioned formula.

Percentage moisture uptake = (Final weight−Initial weight)/Initialweight×100.

In-Vitro Drug Release Studies

In Vitro drug release studies were performed by using a Franz diffusion cell with a receptor compartment capacity of 60 mL 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 0.45 μ 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 aluminum 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 the 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.

Kinetic Modeling of Dissolution Data

The release profile of all batches were fitted to various mathematical models such as Zero order, First order, Higuchi, and Koresmeyer et al, to ascertain the kinetic of drug release.

One month accelerated stability studies

Optimized trial T10 was taken for one month accelerated stability studies at 60^0C and 60% Relative Humidity and at room temperature.

RESULTS AND DISCUSSION

Preformulation Studies

Determination of Melting Point

Melting point of the Propafenone was determined by using open capillary tube technique in digital melting point apparatus. The melting point of the Propafenone was found to be: 175ºC

Determination of Partition Coefficient

The partition coefficient of the drug Propafenone was known by using equal volumes of 1-octanol and aqueous solution in a separating funnel. The partition coefficient of the Propafenone was found to be 36.96

Determination of Drug Excipients Compatibility

During the formulation of transdermal patch, drug and polymers interact when they in contact with each other, which may cause instability of the drug. FT-IR spectroscopy is employed to confirm the compatibility between the polymer and Propafenone. The pure drug and drug with all the excipients were scanned separately. KBr Pellet method is used and the samples were mixed with dry powder KBr crystals. The blend was compacted to make a disc. This disc was kept in spectrophotometer and spectrum was recorded. Chemical contact among drug and polymers was found by using the FT-IR spectra.

Uniformity of weight

The patches are exposed to weight variation test by balancing the patches by using digital weighing machine. The values are calculated in triplicate for each preparation. Average values of the weight and standard deviation values are then measured. All the patches showed uniformity in the weight

Table 5. Determination of Weights of Trials

Trials	Theoretical Weight	Practical Weight
1	101	109
2	151	165
3	206	217
4	264	274
5	346	354
6	191	198
7	237	243
8	277	285
9	317	327
10	354	365

Folding Endurance

The transdermal patch of the formulation is cut into small strips of 2×2 cm and they are folded at the exact point til it breaks or cracks The quantity of times it is folded at the same point indicates the value of the folding endurance.

Drug content uniformity

Pieces of 1 × 1 cm size are cut from every kind of preparation and kept in 50 ml of water. The solution is magnetically

agitated for 2h. The solution is then sifted through Whatmanns filter paper and diluted suitably with distilled water. The solution is then analyzed for its absorbance at 289 nm. From the above values, the drug content is determined.

Table 6. Folding Endurance Test for T-01 to T-10

FORMULATION TRIALS	NUMBER OF FOLDINGS
T1	56
T2	74
T3	63
T4	92
T5	113
T6	75
T7	84
T8	92
T9	106
T10	126

Table 7. Content uniformity results of from trial 01 to 12

Trials	Conc. In patch	Trials	Conc. In patch
0	00	6	36.18
1	32.92	7	34.18
2	32.92	8	31.24
3	36.16	9	33.42
4	34.81	10	37.39
5	34.28		

Thickness of Propafenone Films

Table 8. Thickness of all trials

Formulation Code	Thickness (mm) ± S.D
T1	0.145±0.0024
T2	0.165±0.0045
T3	0.185±0.0073
T4	0.275±0.0036
T5	0.289±0.0028
T6	0.135±0.0077
T7	0.145±0.0030
T8	0.157±0.0031
T9	0.165±0.0064
T10	0.187±0.0086

Moisture content in patches

Table 9 Moisture Content in all trials

Trials	Moisture Content
T1	2.34±0.032
T2	3.45±0.046
T3	3.14±0.021
T4	3.54±0.083
T5	1.14±0.094
T6	2.53±0.043
T7	1.65±0.098
T8	3.47±0.047
T9	2.34±0.056
T10	1.24±0.024

Water uptake studies

Table 10 Water uptake of all trials

FORMULATION TRIALS	WATER UPTAKE
T1	1.12±1.022
T2	1.63±1.54
T3	1.04±0.13
T4	1.54±0.021
T5	1.14±0.094
T6	1.53±0.16
T7	1.72±0.10
T8	1.47±0.17
T9	1.34±0.16
T10	0.98±0.15

Tensile Strength

Table 11. Tensile strength of all trials

Formulation Trials	Tensile Strength %
T1	75
T2	86
T3	75
T4	86
T5	92
T6	63
T7	78
T8	84
T9	92
T10	106

Table 12. Drug release date from trial T1 to T5

TIME	T-1	T-2	T-3	T-4	T-5
0	0	0	0	0	0
30	12.34	10.23	8.34	12.12	5.74
60	24.82	19.27	12.84	28.23	12.84
120	38.28	29.73	28.81	34.23	21.85
180	52.84	41.83	37.71	54.23	32.91
240	63.63	64.72	59.62	76.93	38.63
300	81.92	78.28	78.58	88.83	41.64
360	95.71	87.43	81.63	97.34	52.84
420	99.27	93.67	89.63	99.30	68.37
480	94.17	99.63	98.57	95.73	71.22

In-vitro drug release studies

Piece of 1×1 cm size is cut from every kind of preparation and is placed in the middle of the egg membrane and it is tied to the inverted test tube. The test tube is touched to the surface of the distilled water (50 ml) taken in a beaker. The beaker is magnetically stirred on magnetic stirrer. The samples of 5ml were withdrawn at time interval of 1, 2, 3, 4, 5, 6, 7, 8, …up to 24h, analyzed for drug content spectro-photometrically at 289 nm against blank. Then it is replaced with a same volume of distilled water at every time of sample removal. In-vitro Release of Propafenone from Transdermal Patches:
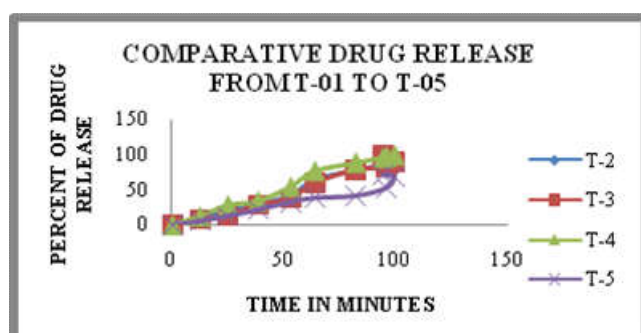

Figure 9. Drug release from T1 to T5

Table 13. Comparative drug release profile from trial T-06 to T-10

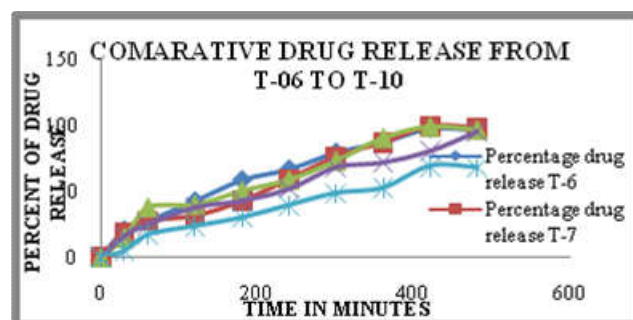| time interval	Percentage drug release				
TIME	T-6	T-7	T-8	T-9	T-10
0	0	0	0	0	0
30	20.81	18.72	14.83	16.28	5.18
60	27.52	27.62	37.71	24.91	17.28
120	42.81	31.72	39.62	37.81	23.81
180	58.71	42.82	50.18	42.84	30.18
240	66.91	59.52	58.63	51.83	39.71
300	79.51	76.46	72.81	68.17	48.72
360	87.52	87.56	90.17	71.82	52.74
420	97.82	99.82	98.72	80.48	69.27
480	96.72	98.56	96.28	95.27	68.27

Figure 10. Drug release from T6 to T10

Based on the drug release profile from all the 10 trials trial T-05 and trial T-10 was optimized, as the drug release from these two trials T-05 and T-10 were showing constant release, along with drug release other physical evaluation parameters were also showing better results from these two trials, but when compare to these two trials T-05 and T-10, trial T-10 was showing stability in sense of tensile strength, folding endurance test, content uniformity etc… Trial T-10, considered as optimized trials in this present research work, and taken for further studies, one month accelerated stability studies.

Results after one month stability studies at room temperature

Physical characterization

Table 14. In-vitro evaluation of T10 after stability studies

Trials	Thickness (mm)	MOISTURE CONTENT	TENSILE STRENGHT	WATER UPTAKE
T10	0.197	1.04	113	1.56

Drug release studies after one month

Table 15. Drug release after one month

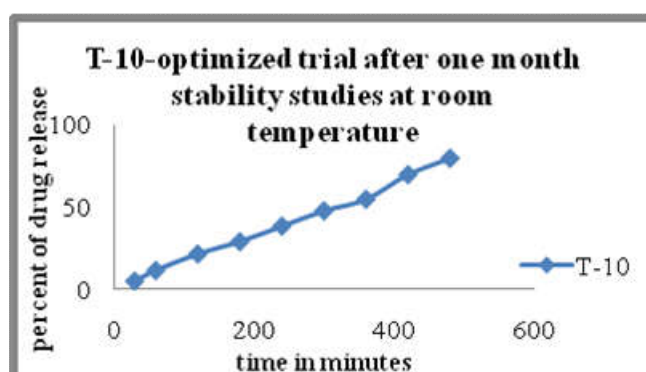| Sampling interval	T-10
0	00
30	5.30
60	11.83
120	21.81
180	29.27
240	38.62
300	47.92
360	54.92
420	69.92
480	79.82

Figure no 11. Drug release from optimized trial-T10

Drug Release Rate Kinetics

Table 16. Release kinetic data from all models

ZERO ORDER		FIRST ORDER			HIGUCHIS	KORESMEYER PEPPAS PLOT	
Time	% Drug undissolved	Time	100-Q	Sq. time	Mean % drug dissolved	Log time	Log cumulative % drug dissolved
0	100	0	2	0	0	0	0
30	94.7	30	1.98	5.48	5.3	1.48	0.72
60	88.17	60	1.95	7.75	11.83	1.78	1.07
120	78.19	120	1.89	10.95	21.81	2.08	1.34
180	70.73	180	1.85	13.42	29.27	2.26	1.47
240	61.38	240	1.79	15.49	38.62	2.38	1.59
300	52.08	300	1.72	17.32	47.92	2.48	1.68
360	45.08	360	1.65	18.97	54.92	2.56	1.74
420	30.08	420	1.48	20.49	69.92	2.62	1.84
480	20.18	480	1.30	21.91	79.82	2.68	1.90

Graphical Representation of Release Rate Kinetics From Different Kinetics Models
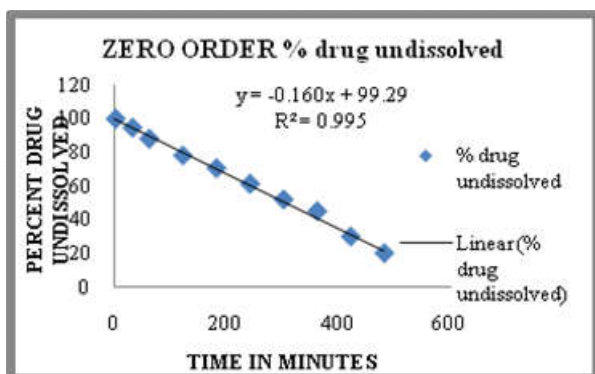
ZERO ORDER
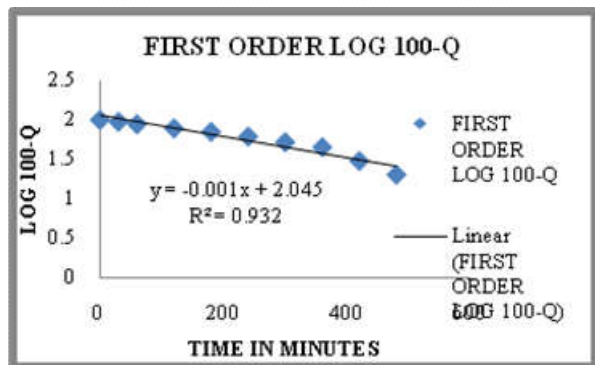

Figure 12. Zero Order Rate Kinetics

FIRST ORDER

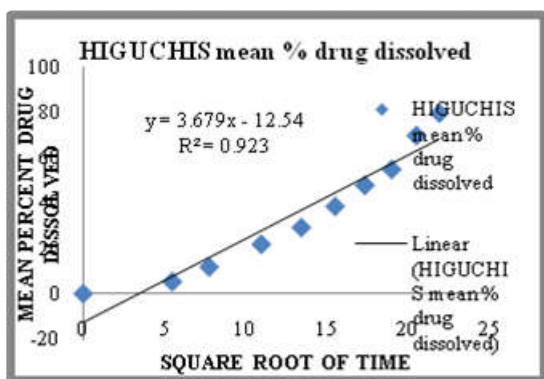Figure 13. first order rate kinetics

HIGUCHIS MODEL

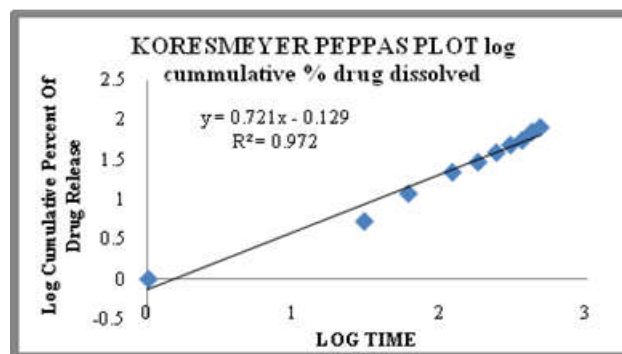Figure 14. Higuchis model

Koresmeyer Peppas Plot

Figure 15. Koresmeyer Peppas plot

DISCUSSION

Initiation of the present research work of done with FTIR compatibility studies and the spectra of pure drug with that of HPMC, Sodium Alginate and with other excipients gave no much interaction between them based on FTIR spectra. The prepared patches were evaluated for weight variation test and found to be 109 mg to 365 mg. Where as folding endurance test was found to be 56 times for TRIAL-1 and 126 times for TRIAL-10. In case of moisture content test TRIAL -10 showed less percent of moisture with 1.14 and TRIAL-4 Showed 3.54. For water uptake studies patches of TRAIL-10 absorbed 0.98 percent and TRIAL -2 of 1.63 percent. When comes to tensile strength of in-house prepared patches lease of TRIAL-6 with 63 and maximum of TRIAL-10 with 106.

In Vitro Drug Release Study

The drug release characteristics of the formulation were studied in in vitro conditions by using artificial semi-permeable membrane. The drug release was found to be varying with change in concentration of polymers. From trial T1-T5, the drug release was found to be decreasing order, obeying the principle of controlled release patches, from 94.17 IN T-1, 99.63-T2, 98.53-T3, T4-95.73 and in T5-71.22, where change in HPMC-15 cps was done in its concentrations. From trials T-6 to T-9 the drug release was found to be 96.72 in T6, 98.3-T7, 96.28-T8, 95.27-T9 and 68.27 in T10. After one month stability studies of trial T10, the in-vitro evaluation parameters were found to be, thichness-0.197mm, moisture content-1.04%, tensile strength was found to be 113, water uptake studies shows 1.56 percent, whereas drug release was found to be 79.82 percent after 480 minutes.

Drug Excipients Compatibility Study

Drug-excipients interactions play a vital role in the release of drug from formulation. The pure Propafenone and its mixture with different grade of HPMC and sodium alginate and Methocel k 100 were mixed separately with IR grade KBR and were scanned over a range of 400–4500 cm^{-1} using FTIR instrument (FTIR-1700, Shimadzu, Kyoto, Japan). The drug exhibits peaks due to ketonic group, alcohol group, secondary amine, terminal CH_3 group, and C=O stretching in COOH and CONH. It was observed that main peaks of Propafenone were present in mixture of drug and polymer, and no change in main peaks of the drug IR spectra in a mixture of drug and polymers was found. The FTIR study revealed no physical or chemical interactions of Propafenone with each grade of HPMC-15 cps, sodium alginate and Methocel K-100

Conclusion

To achieve the objective of present research work various trials were attempted for preparation of transdermal patches of PROPAFENONE using polymers of HPMC-15 CPS, SODIUM ALGINATE and METHOCEL K 100. Transdermal patches were prepared using HPMC-15cps from trials T-1 to t-5, in which concentrations of HPMC-15 cps used in increase in concentration for trial T1 to T5. Similarly same in case of trials T6 to T10 was used with Methocel K 100. Physical characteristic properties and drug release of patches for five trials were evaluated and were found to be satisfactory as mentioned in discussion. Release kinetics was also determined for optimized trial T10 and the drug release was found to be in following order, Zero order-0.995>Koresmeyer Peppas plot-0.972>First order>0.932>Higuchis plot-0.923. Based on the above R^2 values it has been concluded that the release of PROPAFENONE was following Zero order rate kinetics with R^2 value 0.995.

Acknowledgement

REFERENCES

Aarti N, Louk A.R.M.P, Russel.O.P and Richard H.G. 1995. Mechanism of monounsaturated fatty acid evoked skin permeation improvement invivo in humans. *Jour.control. unharness,* 37: 299-306.

Chien YW, 1992. Novel drug delivery systems, medication and therefore the Pharmaceutical sciences, Vol.50, Marcel Dekkar, New York, NY;797.

Gaur PK, Mishra S, Purohit S and Dave K. 2009. Stratum Drug Delivery System: A Review. *Asian Journal of Pharmaceutical and Clinical analysis,* 2(1): 14-20.

Kandavalli S, Nair v, Panchagnula R. 2008. Polymers in stratum drug delivery systems, pharmaceutical technology 2002, 62-78. offered from: web.pharmatech.com. Accessed on fifteen Gregorian calendar month.

Kumar JA, Pullakandam N, Prabu SL, Gopal V. 2010. Stratum drug delivery system: an outline. *International Journal of Pharmaceutical Sciences Review and analysis.* 3(2): 49-54.

Misra AN. 1997. Stratum Drug Delivery, In: Jainist N. K., editor, Controlled and Novel Drug Delivery, initial edition, CBS publication, pp one hundred – 129.

Patel D, Chaudhary A S, Parmar B. 2012. stratum drug delivery system: A review. *The Pharm Innovation.,* 1(4):66-75.

Shaila L, Pandey S and Udupa N. 2006. Style and analysis of matrix sort membrane controlled stratum drug delivery system of nicotin appropriate to be used in smoking stop. *Indian Journ. Pharm.Sci.,* 68: 179-184.

Shingade metric weight unit, Aamer Q, Sabale PM, Grampurohit ND, Gadhave MV, Jadhav SL, Gaikwad D. Review on: Recent Trends on stratum Drug Delivery System. J Drug Delivery medicine 2012;2(1):66-75.

Singh MC, 2010. Naik AS and Sawant Mount Rushmore State. stratum Drug Delivery Systems with major stress on stratum patches : A Review. *Journal of Pharmacy analysis* 3(10): 2537-2543.

****