Research Article

Formulation and Evaluation of Transdermal Patch of Benazepril hydrochloride using Acryl coat L100 and Acryl coat S100

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ABSTRACT

The purpose of this research was to develop a matrix-type transdermal therapeutic system containing drug Benazepril hydrochloride (BH) with different ratios of Acryl coat L100 and Acryl coat S100 with hydroxypropyl methyl cellulose (HPMC) polymeric systems (F1-F10) by incorporating 5 % w/w of polyethylene glycol (plasticizer) and 30% w/w methanol (permeation enhancer). The physicochemical compatibility of the drug and the polymers studied by FTIR spectroscopy suggested absence of any incompatibility. Formulated transdermal films were physically evaluated with regard to thickness, weight variation, drug content, flatness, folding endurance, percentage of moisture content and water vapor transmission rate and *In-vitro* permeation studies of formulations were performed by using Franz diffusion cells. Thickness (79.625± 1.111 to 83.613 ± 1.359 µm), percentage of moisture content (1.671± 0.012 to 5.690 ± 0.015), moisture uptake (2.569± 0.22 to 7.895± 0.22), water vapor transmission rate (1.623 ± 0.622 to 4.122 ± 0.662 g/cm. day), drug content analysis (95.857 ± 0.2073 to 97.770 ± 0.1992%). F5 exhibits highest (89.58%) *In vitro* % permeation profile after 10 h and considered as an optimized formulation. Release kinetic profile and scanning electron microscopy (SEM) of F5 were undertaken and concluded that release follows zero-order kinetic and SEM study reveals the uniformity of drug distribution.

Keywords: Benazepril hydrochloride, Transdermal patch, Permeation enhancer, *In-vitro* permeation study.

INTRODUCTION

Transdermal drug delivery system (TDDS) offers controlled release of the drug into the patient, it enables a steady blood-level profile resulting in reduced systemic side effects, offers multi-day dosing, penetrate the skin barrier and reach the target site[1-2]. Because of its great advantages, it has become one of the highly research field among the various drug delivery system. The skin as a site of drug delivery has a number of significant advantages over many other routes of drug administration, including the ability to avoid problems of gastric irritation, pH and emptying rate effects, avoid hepatic first-pass metabolism thereby increasing the bioavailability of drug, reduce the risk of systemic side effects by minimizing plasma concentrations compared to oral therapy, provide a sustained release of drug at the site of application; rapid termination of therapy by removal of the device or formulation, the reduction of fluctuations in plasma levels of drugs, and avoid pain associated with injections. The transdermal delivery can also eliminate pulsed entry into the systemic circulation, which might often cause undesirable side effects[3].

Hypertension, a cardiovascular diseases account for a large proportion of all deaths and disability worldwide. Global Burden of Disease study reported that there were 5.2 million deaths from cardiovascular diseases in economically developed countries and 9.1 million deaths from the same causes in developing countries. Transdermal systems are ideally suited for diseases that demand chronic treatment. Despite the suitability of TDDS in the treatment of chronic disease like hypertension, the high cost of antihypertensive patches than conventional products made the target patients to think twice. In spite of the high cost of transdermal patches for hypertension treatment, antihypertensive patches with the established

dosage forms reduced the occurrence of hospitalization and diagnostic costs[4].

Benazepril hydrochloride (BH) is chemically (3-[[1-(ethoxy-carbonyl)-3-phenyl-(1S)propyl]amino] -2,3,4,5-tetrahydro-2-oxo-1H-1-(3S)-benzazepine -1-acetic acid monohydrochloride) (Fig. 1) is a medication used to treat high blood pressure (hypertension) congestive heart failure, and chronic renal failure.

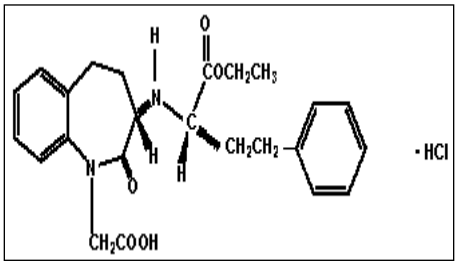

Fig. 1: Structure of Benazepril hydrochloride

Upon cleavage of its ester group by the liver, benazepril is converted into its active form benazeprilate, a non-sulfhydryl angiotensin-converting enzyme (ACE) inhibitor. The empirical formula of BH is $C_{24}H_{28}N_2O_5 \cdot HCl$ with a molecular weight of 460.96 g/mole[5]. So our aim to develop a transdermal drug delivery system for BH to reduce the dose frequencies and minimize the side effects.

MATERIAL AND METHODS

Pure samples of Benazepril hydrochloride (BH) were obtained as gift from Aurobindo Pharmaceuticals, Ltd., Hyderabad. Acrylcoat S100 (AS) and Acrylcoat L100 (AL) were obtained from Corel Pharma Chem., Ahmedabad. Methanol was obtained by SD Fine Chem. Ltd., polyethylene glycol 400 (PEG-400), Span 80 and Tween 80 obtained from Karnataka Fine Chem., Bengaluru. Chloroform were procured from CDH Pvt. Ltd., Hydrochloric acid purchased from Merck Ltd., Mumbai, India. All the other chemicals were of analytical grade.

CHARACTERIZATION OF DRUG

1. Physiochemical properties of BH

1.1. Organoleptic evaluation

It refers to the evaluation by sensory characters-taste, appearance, odor, feel of the drug.

1.2. Solubility (at room temperature)

Solubility is determined in different solvents like water, methanol 0.1 N HCL, 0.1 N NaOH and different buffers.

1.3. Identification test

FTIR spectroscopy[6]

Infra- red spectrum is an important record which gives sufficient information about the structure of a compound. This technique provides a spectrum containing a large number of absorption band from which a wealth of information can be derived about the structure of an organic compound.

1.4. Loss on drying

Loss on drying directly measuring by IR moisture balance. Firstly calibrate the instrument by knob then take 1 gm sample (powder) and set the temp at 100°C-105°C for 5 min and constant reading set the knob and check % moisture.

1.5. Determination of pH (1% w/v solution in water)

1g of the powder was taken and dissolved in 100ml of distilled water with sonication and filtered, pH of the filtrate was checked with standard glass electrode.

1.6. Melting point

A small quantity of powder was placed into a fusion tube. That tube is placed in the melting point determining apparatus containing castor oil. The temperature of the castor oil was gradual increased automatically and read the temperature at which powder started to melt and the temperature when all the powder gets melted.

1.7. Bulk properties

Bulk density is defined as the mass of powder divided by the bulk volume. Bulk density largely depends on particle shape, as the particles become more spherical in shape, bulk density is increase. In addition as granules size increase, bulk density decrease.

A known quantity of powder was poured into the measuring cylinder carefully level the powder without compacting, if necessary and read the unsettled apparent volume, Vo, to the nearest graduated unit. Calculate the bulk density, in gm per ml gm/cc, by the formula

Bulk density = Bulk Mass/ Bulk Volume

1.8. Compressibility index (Carr's index)

Compressibility index (C.I.) is an important measure that can be obtained from the bulk and tapped densities. Carr's index a material having values of less than 20% to 30% is defined as the free flowing material.

It can be calculated as per given formula:

$$\frac{\text{Tapped density- Bulk density}}{\text{C I}} \times 100$$

1.9. Hausner ratio

It indicates the flow properties of the powder and is measured by the ratio of tapped density to bulk density.

Hausner ratio = Tapped density / Bulk density

1.10. Angle of repose

The angle of repose is a relatively simple technique for estimating the flowability of a powder through a funnel and fall freely onto a surface. The height and diameter of the resulting cone is measured and using the following equation, the angle of repose can be calculated.

$$\text{Tan } \theta = h/r$$

Where h, r is the relatively height and radius of the powder cone.

1.11. Moisture content determination

Principle: The titrimetric determination of water is based upon the quantitative reaction of water with an anhydrous solution of sulphur dioxide and iodine in the presence of a buffer that reacts with hydrogen ions.

1.12. Determination of $\lambda_{max.}$

Accurately weighed 10 mg of drug was dissolved in 100 ml of 0.1 N HCl in 100 ml of volumetric flask and prepare suitable dilution to make it to a concentration of 100µg/ml make adequate of sample with concentration range of 5-25µg/ml. The spectrum of this solution was run in 200-400 nm range in U.V spectrophotometer (LABINDIA UV 3000 +).

2. DEVELOPMENT OF TRANSDERMAL PATCHES

2.1. Preparation of rate controlling membrane

Rate controlling membranes were prepared using Acryl coat L100 and Acryl coat S100. The polymeric solution was prepared in chloroform where the polymer was first dissolved, along with (30%) plasticizer. 5 ml of the solution was then poured into a glass Petri dish of 18 cm² area containing liquid mercury. The solvent was allowed to evaporate under room temperature for 24 h.

2.2. Preparation of matrix type transdermal patches

Transdermal patches composed of different polymers like Acryl coat L100 and Acryl coat S100 containing BH were prepared (Table 1). PEG 400 was used as plasticizer whereas methanol and water was incorporated as a permeation enhancer.

The polymers (total weight: 250 mg) and drug (20 mg) were weighed in requisite ratios (L 100 and S 100 --5.0:1, 4.0:1.0, 3.0: 1.0, 1.0:3.0, 1.0:4.0, and 1:5.0) and dissolved in 5 ml of water and methanol (30%w/w of polymers) and PEG 400 (5% w/w of polymers). The solution was poured on mercury placed in a glass Petri dish of 18 cm² area and dried at room temperature for 24 h. (The solvent was completely evaporated in 24 h). Aluminum foil was used as the backing membrane that was cast by pouring and then evaporating 4%w/v solution of PVA at 60ºC for 6 h[7, 8].

Table 1: Formulation design of BH transdermal patch

Formulation code	Drug (% w/w) of total polymer	Ratio of Acryl coat L100:HPMC	Ratio of Acryl coat S100: HPMC	Total polymer weight (mg)	Plasticizer % w/w of total polymer (PEG 400)	Permeation enhancer % w/w of total polymer (methanol, water)
F1	20	5:1	-	250	5	30
F2	20	4:1	-	250	5	30
F3	20	3:1	-	250	5	30
F4	20	2:1	-	250	5	30
F5	20	1:1	-	250	5	30
F6	-	-	5:1	250	5	30
F7	20	-	4:1	250	5	30
F8	20	-	3:1	250	5	30
F9	20	-	2:1	250	5	30
F10	20	-	1:1	250	5	30

2.3. Preparation of transdermal membrane patch

Aluminium foil was used as backing membrane and Acryl coat L100 and Acryl coat S100 with plasticizer was used as the rate controlling membranes. Transdermal patches of BH were prepared by sandwiching the gel (1g) containing drug in between the two membranes. The rate controlling membrane was placed over the gel and it was fixed by applying chloroform on the edge of the controlling membrane.

3. EVALUATION OF TRANSDERMAL PATCHES

3.1. Thickness

The thickness of patches was measured at three different places using an Absolute Digimetic (Mitutoyo) from Medreich Lab, Bangalore[9].

3.2. Folding endurance

This was determined by repeatedly folding one film at the same place until it broke. The number of times the film could be folded at the same place without breaking / cracking gave the value of folding endurance[9].

3.3. Percentage of moisture content

The films were weighed individually and kept in desiccators containing activated silica at room temperature for 24 hrs. Individual films were weighed repeatedly until they showed a constant weight. The percentage of moisture content was calculated as the difference between initial and final weight with respect to final weight[9].

3.4. Percentage of moisture uptake

A weighed film kept in desiccators at room temperature for 24 h was taken out and exposed to 84% relative humidity (a saturated solution of aluminium chloride) in a desiccator until a constant weight for the film was obtained. The percentage of moisture uptake was calculated as the difference between final and initial weight with respect to initial weight.

3.5. Water vapor transmission (WVT) rate [10]

The film was fixed over the brim of a glass vial, containing 3 g of fused calcium chloride as desiccant, with an adhesive type. The vial was weighed and kept in desiccators containing saturated solution of potassium chloride to provide relative humidity of 84%. The vial was taken out and weighed at every 24 h intervals for a period of 72 h. The water vapor transmission rate was calculated from the plots of amount of water vapor transmitted versus time.

3.6. Drug content analysis

The patches (n = 3) of specified area were taken into a 100 ml volumetric flask and dissolved in methanol and volume was made up with phosphate buffer pH 7.4. Subsequent dilutions were made and analyzed by UV spectrophotometer at 242.0 nm.

3.7. In *Vitro* skin permeation study[11]

The in vitro skin permeation experiments were conducted using a Franz diffusion cell (receptor compartment capacity: 100 ml: surface area: 3.799 cm^2). Full thickness skin from dorsal region of Swiss albino mice, whose hair had been removed by razor, was used as membrane. The mice were sacrificed by cervical dislocation and dissected skin was used immediately. The receiver compartment was filled with 100 ml of phosphate buffer, pH 7.4. The Transdermal patch was firmly pressed onto the center of the mouse skin and then the skin was mounted on the donor compartment. The donor compartment was then placed in position such that the surface of dermis side skin just touches the receptor fluid surface. The whole assembly was kept on a water bath maintained at 37± 0.5ºC. The samples were withdrawn at different time intervals up to 10 h and analyzed for drug content. Receptor phase was replenished with an equal volume of buffer solution at each time interval.

3.8. Scanning electron morphology (SEM)

The external morphology of the transdermal patches was analyzed using a scanning electron microscope (JSM 6100 JEOL, Tokyo, Japan). The samples placed on the stubs were coated finely with gold palladium alloy and examined under the microscope.

RESULT AND DISCUSSION

Our present work comprises the formulation and evaluation of BH transdermal patches for sustained or extended release for a prolonged period of time. Transdermal patches were prepared by matrix diffusion method. Totally, ten formulations trials (F1-F10) were done with the aim to achieve the successful matrix type transdermal patches.

1. Physico-chemical properties of BH

1.1 Organoleptic evaluation

Organoleptic studies concludes the specific color, odor and taste of pure drug.

Table 2: Organoleptic properties of BH

Color	white to off white powder
Odor	Odorless
Taste	Tasteless

1.2 Solubility

Solubility study of BH has been done in various solvent such as water, phosphate buffer pH 6.8 and 0.1N HCl solution. We were found that a solubility of BH is good in a 0.1N HCl solution (Table 2).

1.3. Identification test by FTIR

Identification of BH by FTIR spectroscopy and pure drug-excipients were analyzed and were depicted in Fig. 2 which clearly indicates that there was very slight interaction between drug and excipients. In case of pure drug sharp peaks were observed at 1735.39 (C=O stretching), 1669.76 (strong C=C stretching), 1519.74 (weak C=C stretching), 1363.08 (C-H bending), 1321.65 (C-N stretching), 1204.21 (C-N stretching), 1003.44 (C-O stretching) and 838.39cm^{-1} (=C-H bending) (Fig. 2).

Whereas, in case drug-excipient sharp peaks were observed at 1793.54 (C=O stretching), 1645.16 (C=C stretching), 1490.09 (C-N stretching), 1361.15 (C-H bending), 1242.14 (C-N stretching), 946.20 (=C-H bending) and 842.36 cm^{-1} (=C-H bending).

1.4. Loss on drying (LOD)

The percentage of loss on drying for BH was found **0.004**% w/w respectively.

1.5. Determination of pH (1% w/v solution in water)

The pH determination of BH was done by Digital pH meter and found to be **3.09.**

1.6. Melting point determination

The melting point of the drug sample range of the drug is 200-205^{o}C. Hence complies with USP standards thus indicating the purity of the drug sample.

Table 3: Solubility studies of BH in different solvent

Sl. No.	Descriptive term	Parts of solvent required for parts of soluble	Solvent used	Solubility
1	Very soluble	Less than 1	Water	Freely soluble
2	Freely soluble	From 1to 10	0.1 N HCl	Freely soluble
3	Soluble	From 10 to 30	Ethanol	Freely soluble
4	Sparingly soluble	From 30to 100	Methanol	Freely soluble
5	slightly soluble	From 100 to1000	Acetone	Freely soluble
6	Very slightly soluble	From 1000 to 10000	Buffer, pH 7.4	Freely soluble
7	Practically insoluble	10000 or more	-	-

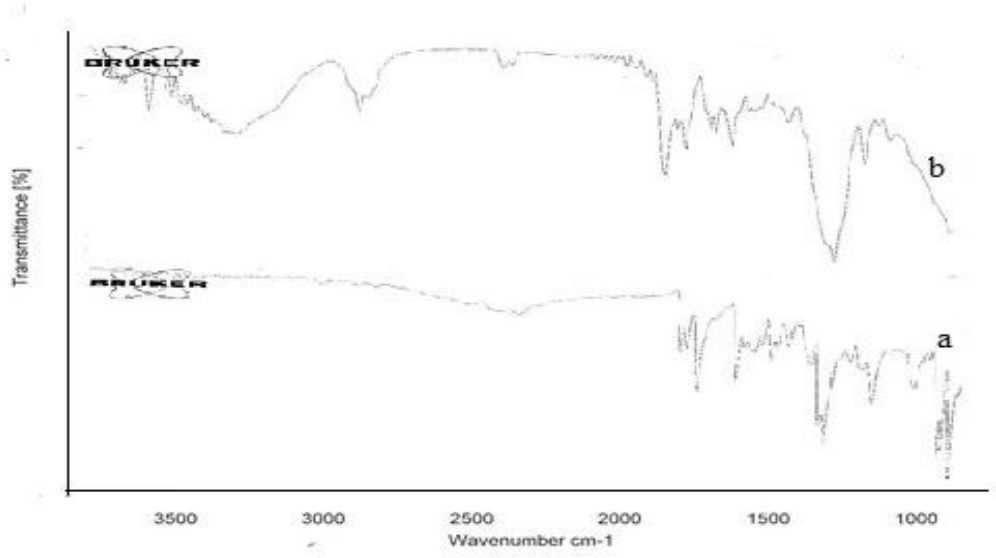

Fig. 2: FTIR spectroscopy study of pure drug BH (a) and drug-excipient (b)

1.7. Bulk density

Table 4: Bulk density of BH

S.No.	Density	BH
1	Untapped Density	**3.0 g/cc**
2	Tapped Density (after 50 tapping)	**0.416 g/cc**

1.8. Compressibility index (%)

The compressibility index of BH was found **20.673 %.**

1.9. Hausner's ratio

The Hausner ration of BH was found 1.260**.**

1.10. Angle of repose

The Angle of repose of BH is **43.56** degree.

1.11. Moisture by Karl-Fischer apparatus (KF)

The Moisture content of BH is **0.75%.**

1.12. Determination of λ max.

Preparation of SGF

Accurate weight 2g of sodium chloride was dissolved in 7ml of concentrated hydrochloric acid and resulting solution is diluted with 1000ml of distilled water and the final pH of solution was adjusted to 1.2.

Preparation of standard solution BH

Weight of Benazepril hydrochloride = 10mg
Volume made up to 100 ml
Concentration of standard solution = 100µg/ml
The λ_{max} found for Benazepril hydrochloride is 240.0 nm as shown in **Fig.3.**

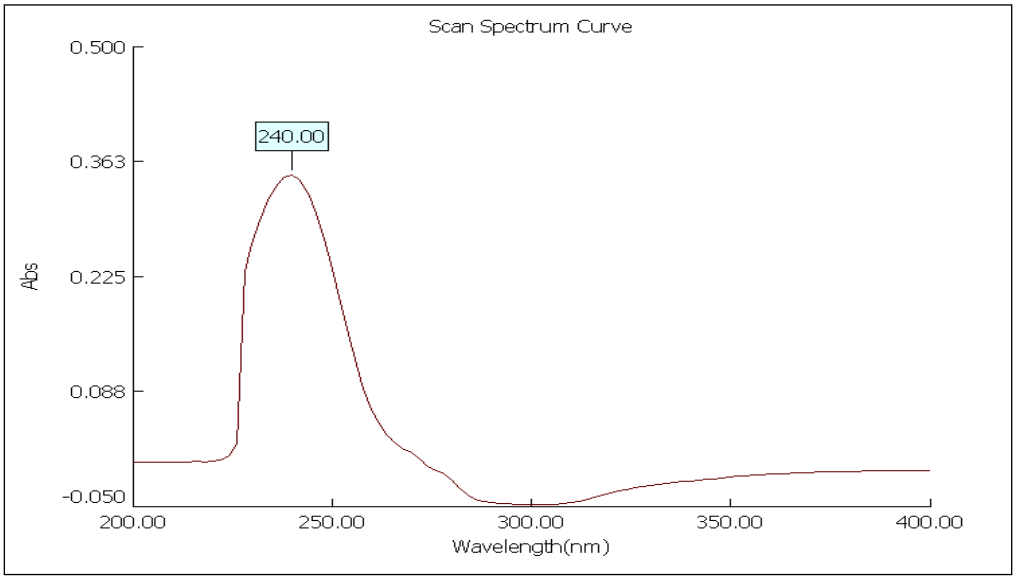

Fig. 3: Determination of λ_{max} of Benazepril hydrochloride

Table 5: Calibration curve of BH

Replicate	5	10	15	20	25
1	0.106	0.223	0.327	0.450	0.545
2	0.105	0.224	0.328	0.452	0.544
3	0.107	0.225	0.329	0.451	0.546
Mean	0.106	0.224	0.328	0.451	0.545
S.D.	0.001	0.001	0.001	0.001	0.001
% RSD	0.943	0.446	0.305	0.222	0.183

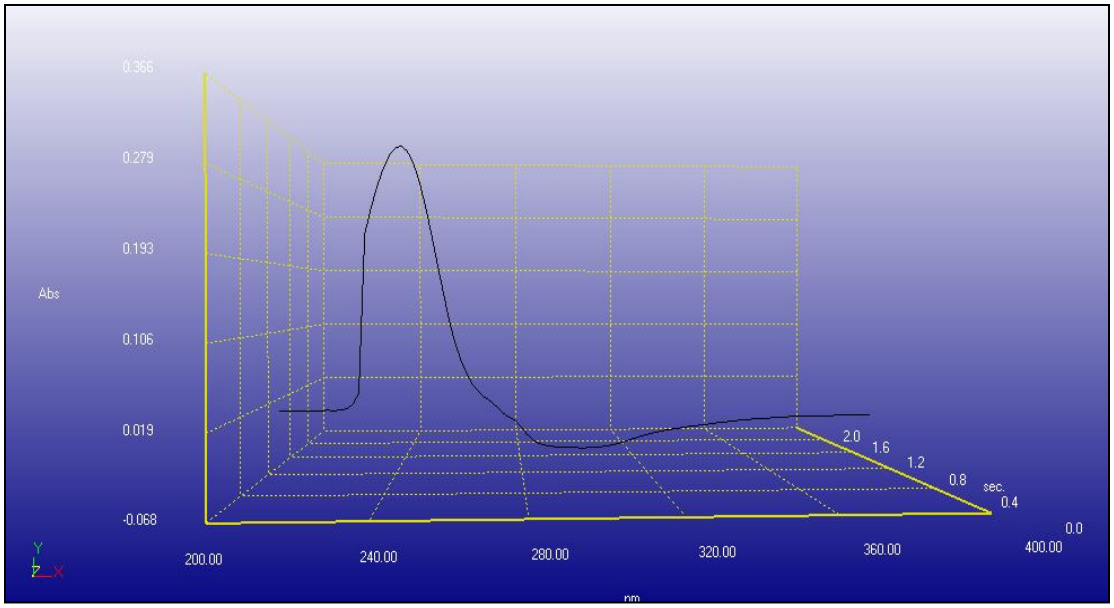

Fig. 4: 3D Spectrum of Benazepril hydrochloride

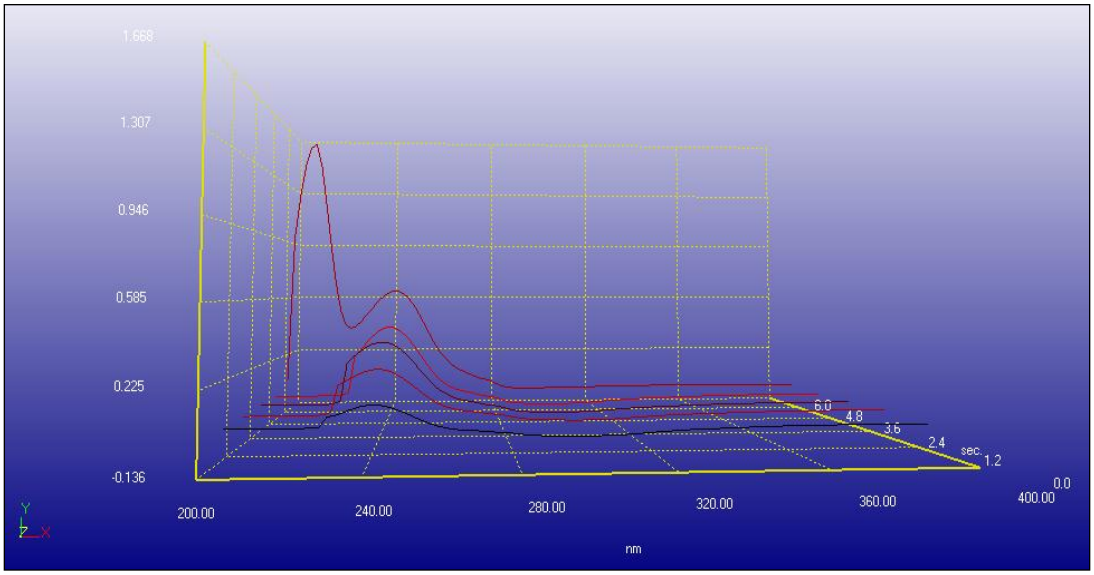

Fig. 5: 3D– spectra of calibration curve of Benazepril hydrochloride

Table 6: Stastical data for linearty

S.No.	Parameter	Remark
1	Linearty range	5-25 µg/ml
2	Regression equation	0.022+ 0.000
3	Correlation co-efficient	0.999

3. EVALUATION OF FORMULATED PATCH

3.1. Thickness

The thickness of the films was measured by using an absolute Digimetic (Mitutoyo) at five different positions. The average readings along with standard deviation are given in Table 7. All the batches of transdermal patch showed thickness variation range from 79.625± 1.111 to 83.613 ± 1.359 µm. Higher thickness in F1 was due to higher ratio of Acryl coat L100: HPMC (5:1). Lower thickness in F5 and F10 were due to lower ratio of Acryl coat L100: HPMC (1:1) and Acryl coat S100: HPMC (1:1) respectively.

3.2. Folding endurance

The folding endurance was measured in triplicate and the results are shown in Table 7.

3.3. Percentage of moisture content

The moisture content was determined by keeping patches in a desiccators containing activated silica. The percentage moisture uptake was calculated as the difference between initial and final weight with respect to final weight. The results of the moisture content studies for different formulations were shown in Table 8 and Fig. 6.

Table: 7: Thickness and Folding endurance of different formulations

S. No.	Formulation code	Thickness (µm)*	Folding endurance*
1.	F1	83.613 ± 1.359	> 235
2.	F2	82.213 ± 1.215	>245
3.	F3	81.113 ± 1.256	>250
4.	F4	80.225 ± 1.219	>245
5.	F5	79.625 ± 1.111	>236
6.	F6	82.351 ± 1.256	>254
7.	F7	83.554 ± 1.147	>248
8.	F8	82.425 ± 1.896	>260
9.	F9	81.331 ± 1.248	>265
10	F10	80.159 ± 1.156	>255

*Values expressed as mean ± S.D, *n* = 3.

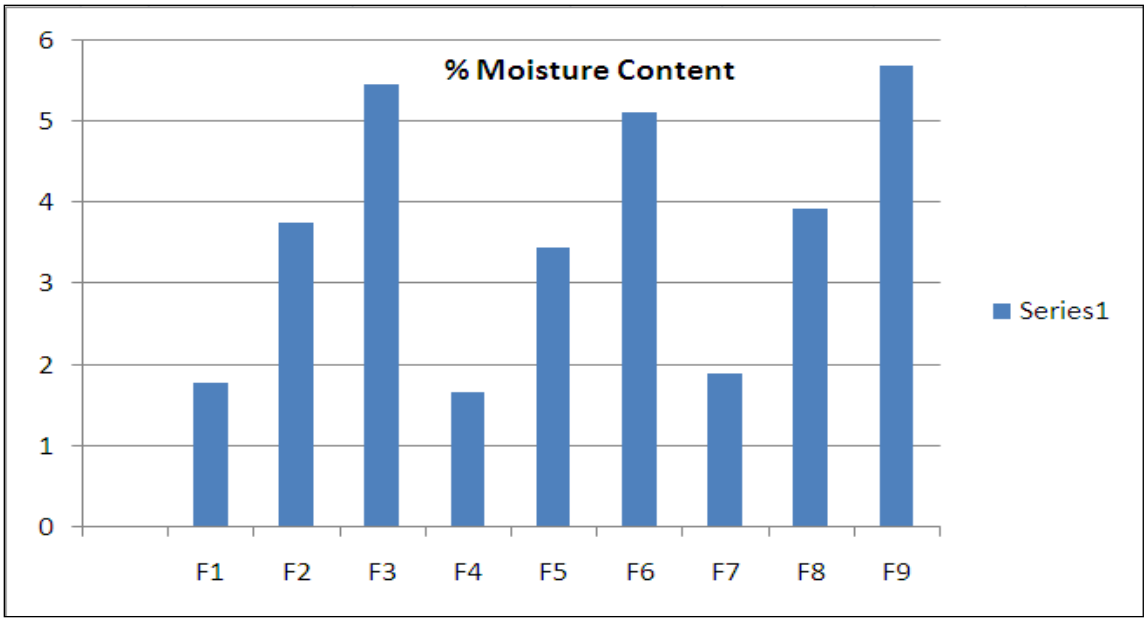

Fig. 6: % Moisture Content of Formulations F1 to F10

The moisture content in the patches ranged from 1.671± 0.012 to 5.690 ± 0.015. Among F1-F5, F1 showed lower moisture content due to higher concentration of Acryl coat L100: HPMC whereas higher concentration of Acryl coat S100: HPMC leads to increased moisture content. The lower moisture content in the formulations helps them to remain stable and become a completely dried and brittle film.

3.4. Percentage of moisture uptake

The percentage moisture uptake was calculated as the difference between final and initial weight with respect to initial weight. The results of moisture uptake studies for different formulations were shown in Table 8 and Fig. 7. % uptake for different formulations ranges from 2.569± 0.22 to 7.895± 0.22. Low moisture uptake protects the material from microbial contamination and bulkiness.

3.5. Water vapor transmission rate

The water vapor transmission rates of different formulations were calculated and the results for different formulations are shown in Table 9. F4 showed lowest water vapor transmission rate of 1.623 ± 0.622 g/cm. day and F3 showed lowest values of 4.122 ± 0.662 g/cm. day.

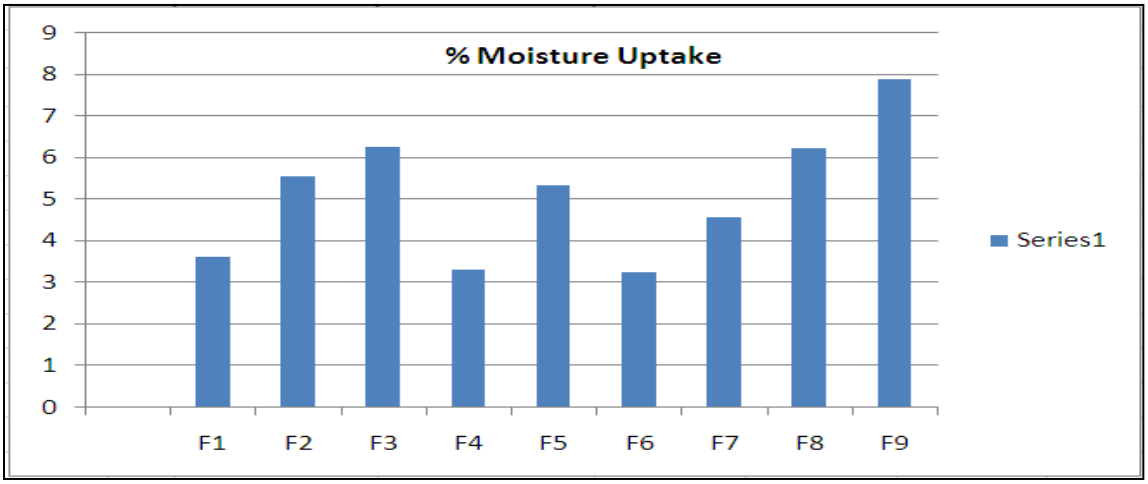

Fig. 7: % Moisture uptake of formulations F1 to F10

Table 8: % Moisture content and moisture uptake of different formulations

S. No.	Formulation code	% Moisture content	% Moisture uptake
1.	F1	1.781 ± 0.011	3.634 ± 0.014
2.	F2	3.766 ± 0.011	5.552 ± 0.013
3.	F3	5.462 ± 0.013	6.253 ± 0.015
4.	F4	1.671 ± 0.012	3.319 ± 0.011
5.	F5	3.448 ± 0.012	5.332 ± 0.013
6.	F6	5.126 ± 0.011	3.251 ± 0.011
7.	F7	1.892 ± 0.015	4.569 ± 0.12
8.	F8	3.925 ± 0.014	6.236 ± 0.10
9.	F9	5.690 ± 0.015	7.895 ± 0.22
10.	F10	3.158 ± 0.015	2.569 ± 0.22

Table 9: Water vapor transmission rate of different formulations

S.No.	Formulation	Water vapor transmission rate (g/cm. day)*
1	F1	1.784 ± 0.597
2	F2	3.611 ± 0.618
3	F3	4.122 ± 0.662
4	F4	1.623 ± 0.622
5	F5	2.519 ± 0.631
6	F6	3.224 ± 0.639
7	F7	1.709 ± 0.612
8	F8	3.801 ± 0.628
9	F9	4.075 ± 0.661
10	F10	2.196 ± 0.688

*Values expressed as mean ± S.D, *n* = 3.

3.6. Drug content analysis

The drug content analysis of different formulations was done according to the procedure given in section 4.6.6. The drug content ranged between 95.857 ± 0.2073 to 97.770 ± 0.1992%. The percentage drug content of all formulations is shown in Table 10. Percentage of drug content was high for all formulations.

3.7. *In Vitro* permeation studies

The *in vitro* permeation studies are predictive of *in vivo* performance of a drug. These studies were performed for different formulations across mice skin using phosphate buffer, pH 7.4 as an *in vitro* study fluid in the receptor compartment of a Franz diffusion cell. The results of these studies are given in Table 11 and shown in Fig.8 (F1-F5).

Formulation F5 with Acryl coat L100: HPMC (1:1) exhibits better drug permeation (89.58%) as compared to its counter-part Acryl coat S 100: HPMC (1:1) with only 60.21% after 10h. Nature of polymer concentration of polymer also affect the drug release. Higher concentration of HPMC (hydrophilic polymer) leads to reduced drug permeation rate. Due to best rate of drug permeation by F5, it was chosen as the optimized formulation and further study was conducted on it.

Release kinetics of optimized formulation F5

Zero and first order release kinetic profile of BH transdermal patches F-5 were presented in Fig. 9 and Fig. 10.

Table 10: Percentage drug content of all the formulations

Sl. No	Formulation code	% Drug content
1	F1	95.857 ± 0.2073
2	F2	96.198 ± 0.2273
3	F3	97.770 ± 0.1992
4	F4	96.373 ± 0.1988
5	F5	96.946 ± 0.2006
6	F6	97.238 ± 0.2230
7	F7	95.913 ± 0.1805
8	F8	96.167 ± 0.2044
9	F9	97.405 ± 0.2162
10	F10	96.798 ± 0.2191

*Values expressed as mean ± S.D, *n* = 3.

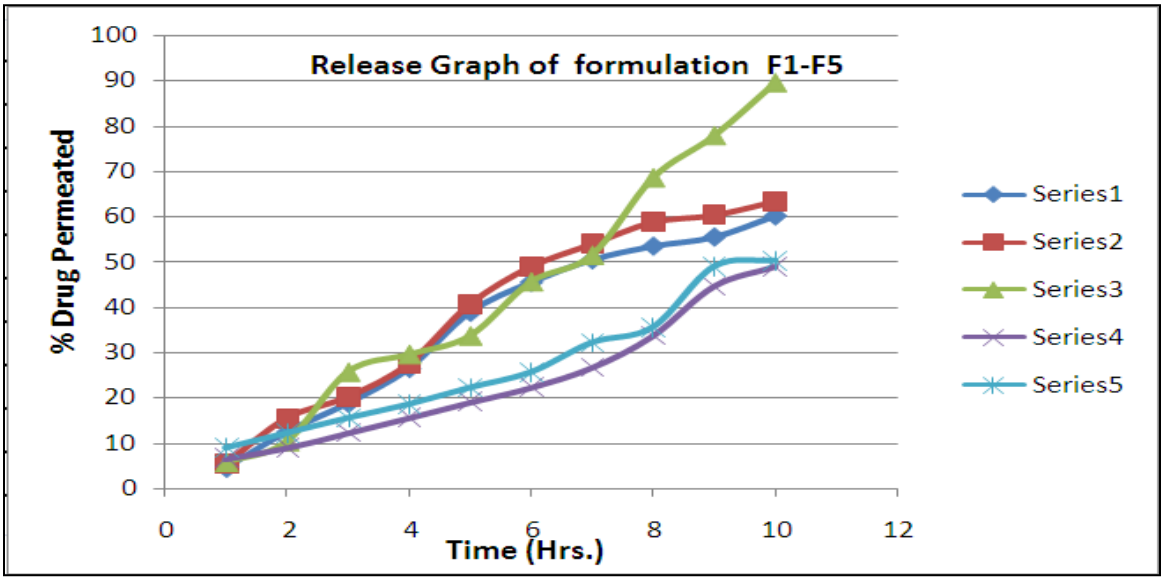

Fig. 8: *In Vitro* % drug permeation of Benazepril hydrochloride in formulations F1-F5

Table 11: *In Vitro* % permeation profile of BH in formulation F1-F10

S. No	Time (h)	% drug permeated									
		F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
1	1	2.56	5.89	4.58	5.56	5.69	6.56	8.98	9.65	12.25	12.25
2	2	5.98	11.58	12.56	15.56	10.25	8.95	12.25	15.56	20.65	20.26
3	3	11.25	15.56	18.89	20.26	25.65	12.23	15.56	18.98	26.65	28.89
4	4	22.36	25.58	26.58	27.56	29.56	15.56	18.59	22.25	33.65	36.65
5	5	31.26	35.89	38.98	40.65	33.65	18.98	22.25	25.65	35.65	39.98
6	6	36.65	40.58	45.58	48.89	45.59	22.25	25.65	32.25	40.25	44.58
7	7	40.15	45.87	50.55	53.88	51.48	26.65	32.15	34.89	45.58	48.87
8	8	44.56	50.25	53.56	58.69	68.59	33.65	35.56	36.65	49.45	50.23
9	9	48.89	52.56	55.58	60.23	77.89	44.56	48.89	49.89	52.15	55.48
10	10	52.26	58.56	60.23	63.25	89.58	48.89	50.25	52.26	55.56	60.21

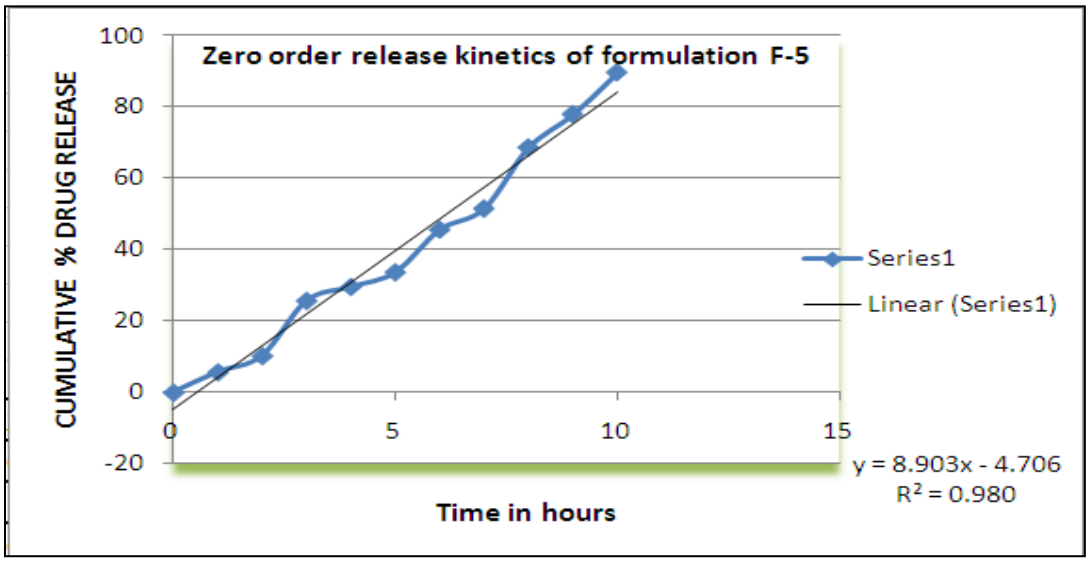

Fig. 9: Zero order release kinetic profile of Benazepril hydrochloride transdermal patches

The cumulative amount of drug permeated per square centimeter of patches through swiss albino mice skin was plotted against time was fitted to zero and first order kinetic model. The regression co-efficient (r2) values for the optimized formulation (F5) was highest in zero order.

Table 12: Kinetic data of BH transdermal patches

Formulation code		Zero order	First order
F-5	r2	0.980	0.814
	slope	8.093	0.159
	Intercept	-4.706	0.585

3.8. SEM analysis

SEM analysis of optimized formulation F5 was shown in Fig. 11 and it concludes uniform distribution of drug in the polymer within the transdermal patches.

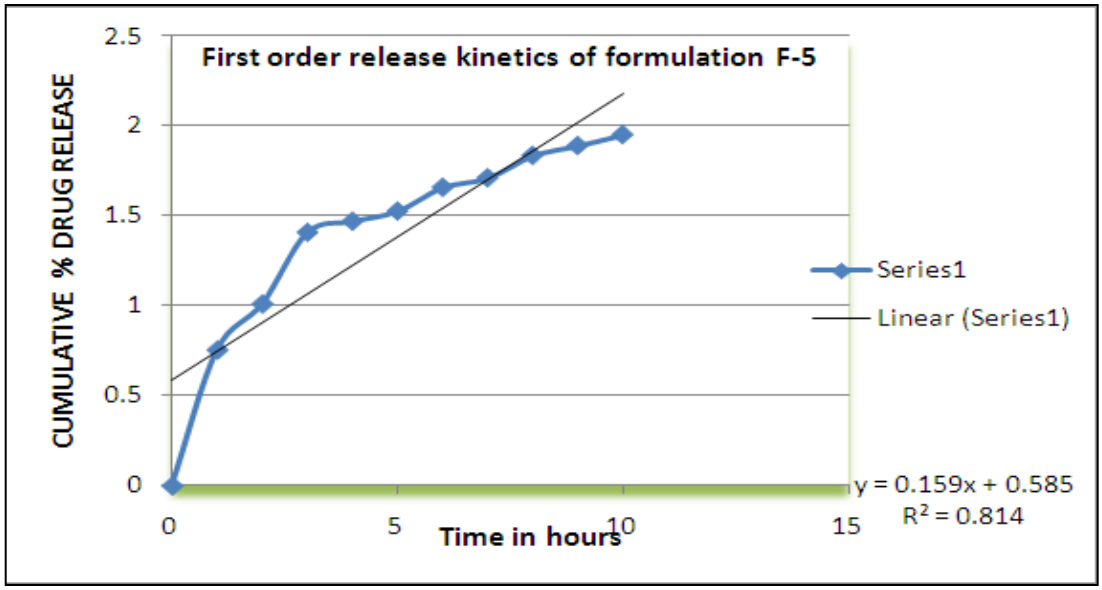

Fig. 10: First order release kinetic profile of Benazepril hydrochloride transdermal patches

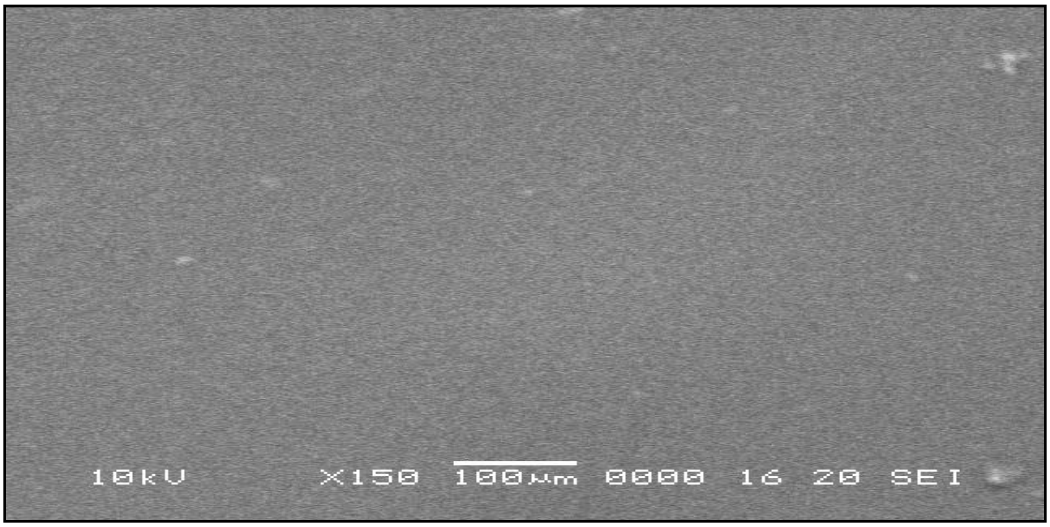

Fig. 11: SEM image of optimized formulation F-5

CONCLUSION

In the present study, an attempt was made to deliver a novel ant diabetic drug, Benazepril hydrochloride through transdermal route in the form of transdermal patches. Transdermal patches of matrix were prepared out of which matrix type of patches was found to be satisfactory. Among the different formulations of matrix type (F1 to F10), the formulation F5 containing Acryl coat S 100 and HPMC was selected as best formulation, after considering its low percentage moisture content (5.462%), percentage moisture uptake (6.253%), water vapor transmission rate (4.122%), better % drug content (97.770%) and maximum 89.58 % drug permeated through the skin at the end of 10 hrs. The drug permeation profile was also found to follow zero order kinetics. The patches were thin, flexible and transparent. The SEM of the formulation F5 showed the formation of pores on the surface after *in vitro* permeation studies. The drug–polymer interaction results suggested no interaction between drug and polymers was observed. The best formulation F5 showed negligible change in % drug content and permeation.

The present study showed that matrix Transdermal patches of Benazepril hydrochloride exhibited better in vitro performance.

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