

Rational Design and Characterization of Transdermal Patch of Irbesartan for Hypertension

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ABSTRACT

Background: Irbesartan is hypertensive drugs approved for high blood pressure and protect the kidneys damage due to diabetes. It is an angiotensin receptor blocker, belongs to BCS class II, exhibit low and variable oral bioavailability due to its poor aqueous solubility. Therefore, it is need to enhancement of dissolution rate and bioavailability. The objective of this study was to develop a transdermal patches system of Irbesartan to reduce the above drawback. **Methods:** Various batch of Irbesartan loaded transdermal patches were prepared by the solvent extraction method employing HPMC and ethyl cellulose as polymer in presence or absence of eudragit. Physicochemical characterization of patches was done by thickness, weight variation, folding endurance, drug content, moisture uptake and loss. The drug interaction was carried out by FTIR spectroscopy. Further, patches were evaluated their *in-vitro* drug release, *ex-vivo* permeation study in Franz diffusion cell. While *in-vivo* skin irritation and toxicity study performed in Wistar rats. **Results:** The final batch was selected on the basis of physicochemical characteristics and proceeds for further studies FTIR result indicated that there was no interaction between drug and polymer. The *in-vitro* release study showed that 93.54% of drugs released at 48 hr and steady-state flux was found to be 0.35 ± 0.23 µg/cm²/h. the developed patch were free from edema and hypersensitivity reaction which is confirm by *in-vivo* study. **Conclusion:** Patches were successfully prepared and their evaluation of excellent quality and uniformity. This can be the potential for therapeutic application due to reduced dosing frequency, improve patient compliance and bioavailability.

Key words: Irbesartan, Transdermal Patch, Polymer, Formulation, Hypertension, Therapeutic.

INTRODUCTION

Hypertensive is a disease characterized by persistent of high blood pressure. Hypertensive is a heart disease associated with a large number of deaths and disabilities worldwide. Hypertension is one of the biggest disease-causing deaths in man. Since it is a chronic disease, it requires long-term treatment. Hypertensive is directly responsible for 57% of all deaths and 24% of heart disease in India.¹

It Irbesartan is an angiotensin II receptor antagonist used in the management of hypertension including treatment of kidney disease in type 2 diabetes mellitus. Irbesartan, is 2-*n*-Butyl -4-spirocyclopentane-1-[(2'-tetrazol-5-yl)biphenyl-4-yl)methyl]-2-

imidazolin-5-one is a potent hypertensive drug.^{2,3} It has a tetrazole system with an acidic system and a biphenyl system, it has no acidic side chain and yet it has a good angiotensin II receptor relationship due to the hydrogen bonding and carbonyl moieties of the amide system. This drug is beneficial especially for geriatric patients when administered by rather than the oral routes. Today about ¾th percent (75%) of the drugs are taken orally but are not found to be as effective. Irbesartan belongs to BCS class II drug having such drawbacks like a very poorly water-soluble drug (< 10 µg/ml), thus making bioavailability to be limited by dissolution rate and its plasma level does

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not increase proportionally with dose thereby leading to potential inter and intra-patient variability.⁴

Therefore, it was the need for another route to overcome these drawbacks and exploit the advantages. The transdermal route was considered the best alternate route for the administration of this drug and placed on the skin to deliver a certain amount of medicine at the bloodstream.⁵ Transdermal drug delivery represents one of the fastest-growing areas of novel drug delivery because it overcomes the difficulty of oral drug especially anti-hypertensive drugs. The transdermal system fits well with a disease that requires chronic treatment.^{6,7}

As the literature review demonstrated that, there is no major study has been dealt on the field of the Irbesartan transdermal patch. Therefore, I developed the Irbesartan loaded transdermal patch for hypertension. It has the probable mechanism of the skin permeation delivery system. In this study transdermal patch was prepared by the solvent extraction method by using ratio of different polymers. Developed patches were characterized their physicochemical characteristics such as thickness, weight variation, folding endurance, percentage drug content, moisture uptake and loss. Further, patches were evaluated their *in-vitro* drug release and *ex-vivo* permeation study in Franz diffusion cell. The *in-vivo* skin irritation and toxicity study performed in Wistar rats.

MATERIALS AND METHODS

Irbesartan was supplied by Yellow Chem Pharma Products, Mumbai. A polymer supplies Eudragit Rs-100, Hydroxy Propyl Methyl Cellulose, Ethyl Cellulose, Plasticizer Dibutyl Phthalate and Permeability Enhancer Dimethyl Sulfoxide was supplied by Central Drug House, Ltd., New Delhi, India. All other chemicals used in this study were analytical grade.

Analytical method development by UV spectrophotometer

The UV spectrophotometer was utilized for the detection and quantification of Irbesartan. For the preparation of the stock solution, 10 mg of the pure drug was accurately weighed and dissolved in 10 ml 0.1 N NaOH and then the volume was made up to 100 ml with 0.1 N NaOH to give standard stock solution 100 µg/mL. From the above stock solution, different concentration (10 µg/mL) was prepared by appropriate dilution to prepare 1-10 µg/mL concentration solution. The sample was filtered and scanned in the range 200-400 nm using a UV spectrophotometer to determine λ_{\max} . The absorbance of the above dilution was determined at 232 nm λ_{\max} on the UV spectrophotometer.

The absorbance values corresponding to each concentration were then statistically evaluated and plotted as a standard graph between absorbance and concentration.⁸⁻¹¹

Development of Transdermal patches

Polymer matrix-infusion type transdermal patches containing the Irbesartan were prepared by the solvent extraction method. The formulation optimization, different batches are represented in Table 1. In this the polymer (hydroxyl propyl methylcellulose, ethyl cellulose, eudragit RS-100) was weighted and dissolved in a ratio of methanol and water to form at constant stirring for 5 to 6 hr. Subsequently, dibutyl phthalate (30% w/v polymeric weight) was added as a plasticizer and dimethyl sulfoxide (20% and 30% w/w weight polymeric) was added as an insulating substance. Finally, Irbesartan (10 mg) was added to the building in a stirring continuum. After a complete mixing solution, allowed to stand for 20 min to ensure the removal of air bubbles. Keep dry at room temperature for 24 hr. The solvent was completely dried for 24 hr when dibutyl phthalate and dimethyl sulfoxide were mixed with the dried matrix. After that the suspension of the films released from the glass petridis.¹¹⁻¹³

Physicochemical characterization of patch

The physicochemical evaluations of transdermal patches are based on the following parameters such as:

The thickness of patch: The thickness of transdermal patches was measured randomly at five different places using a digital vernier calipers and mean values were calculated.¹⁴⁻¹⁶

Weight variation study: This test provides a way to measure the proportions depending on the weight within the batch and batch to batch. Randomly selected patches and calculated the average weight. Individual weight should not deviate from average weight.^{17,18}

Folding endurance: Folding tolerance involves determining the film wrap capacity under the most common wrap conditions. The rolling tolerance is determined by wrapping the film constantly in the same position until it explodes. The number of times the films can be rolled in the same area without cracking is known as wrap tolerance.^{19,20}

Percentage of moisture absorption: Heavy films were stored in desiccators at room temperature for 24 hr. Then extracted and exposed to 84% relative humidity using a saturated solution of Potassium chloride in desiccators until further weight is obtained. % moisture absorption is calculated as given below.²¹

% Moisture absorption = $(\text{Final Weight} - \text{First Weight}) / \text{First Weight} \times 100$

Percentage of moisture loss: Filters with the appropriate weight of each composition are stored in desiccators and have a 98% moisture content (containing calcium chloride) at room temperature and sealed after 48 hr. The experiments were performed in triplicate. The percentage of moisture loss was calculated as the difference between the initial and final weight in relation to the initial weight of the drug bundle in solution.^{22,23}

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

Flatness: The formation of a cut film in a drug loading matrix is an indication of its smoothness. Longitudinal strips were removed from the matrix; the original length of the film was measured and then stored at room temperature for 30 min. The difference in length due to the differences in the flat was measured. Flatness was calculated by measuring the construction of the straps and the zero present of construction was assumed to be equal to 100% flatness.^{24,25}

$$\% \text{ Composition} = \frac{\text{Initial length of individual strands per centimeter} - \text{Final length of individual strands per centimeter}}{\text{Final length of individual strands per centimeter}} \times 100$$

Determination of drug content: Transdermal patch of the specified area was cut into small pieces and deeped into a 100 mL solution of 0.1N NaOH in a mechanical shaker for 20 min to allow the entire drug to explode. The solution was filtered and analysed by UV spectrophotometrically at λ_{max} 232 nm wavelengths to detect drug content in the solution.²⁶

In-vitro drug release studies

In-vitro release was performed in Franz diffusion cell with high acceptor compartment capacity (60 mL). The diffusion cell consists of two compartments, the donor and the receptor compartment. The cellophane membrane (pore size 0.22-0.45 μm) was mounted between the donor and receptor compartment of the diffusion cell. The prepared transdermal patch was placed on the membrane and covered. 7.4 pH buffer solutions were used for the infusion medium and maintained temp at $37 \pm 0.5^\circ\text{C}$. The whole assembly is on the hot plate magnetic stirrer for proper temp as well as movement. 1 mL sample was withdrawn at a predetermined time interval and the same amount is replaced. The sample was further proceeding for the estimation of drug content spectrophotometrically.²⁷⁻²⁹ Each experiment was composed of three bands

to minimize statistical errors that were statistically evaluated.

FTIR Studies

FTIR spectra of Irbesartan, ethylcellulose, HPMC, eudragit RS-100, formulation (batch F3) and physical mixture were recorded by using Thermoscientific FTIR spectroscopy in the range of $4000\text{--}500\text{ cm}^{-1}$. A 10 mg sample was mixed with potassium bromide (200-400 mg) and compressed. The compressed disc was placed in the light path and spectra were obtained. After conducting the exhibition, important themes were identified related to the major working groups.³⁰

Ex-vivo permeation Study

Ex-vivo permeation study was also performed in the Franz diffusion cell in place of the cellophane membrane, the abdominal skin of male Wistar rat was used. Randomly selected Wistar rat (weight 200 to 250 g) was used and hair from the abdominal region was removed carefully by using an electric clipper. After the collection of the abdominal region, the dermal side of the skin was properly cleaned with distilled water to remove any adhering tissues or blood vessels. After the cut into $4.5 \times 4.5\text{ cm}^2$ pieces and hydrated by placing in phosphate buffer saline (PBS, pH = 7.4) overnight before use. Then kept has on Franz diffusion cells. Phosphate buffer pH 7.4 was filled in a receptor compartment in Franz diffusion cell. The prepared formulation was applied over the skin in the donor compartment. The diffusional area of the cells was 3.14 cm^2 . The temp of the assembly was maintained $37 \pm 0.5^\circ\text{C}$ and the stirring rate was maintained at 50 rpm. The sample was withdrawn at predetermined time interval and the same amount is replaced. The sample was further proceeding for the estimation of drug content spectrophotometrically.

Obtained skin permeation data were calculated as the cumulative drug permeation per unit of skin surface (Q_t/S). The cumulative drug permeation (Q_t) was calculated by the following equation:

$$Q_t = V_t C_t + \sum_{i=1}^{t-1} V_s C_i$$

Where,

C_t : Drug concentration of the receiver fluid at each sampling time t ,

C_i : Drug concentration of the nth sample,

V_t and V_s : Volumes of the receiver fluid and sample respectively.

A linear regression analysis was used to determine the steady-state flux and lag time of the drug. The linear

portion of the graph provided the steady-state flux ($\mu\text{g}/\text{cm}^2/\text{h}$) denoted as J_{ss} . The lag-time was obtained by extrapolating the linear portion of the graph to the x-axis. The permeability coefficient (P) was evaluated as $P = J_{ss} / C$

Where, C is the drug concentration in donor compartment.

Obtained data were comparing to flux data with the help of one-way analysis of variance (ANOVA). A *p*-value of 0.05 was considered to be statistically significant.

Skin irritation and toxicity study

The study is approved by the university ethical committee and followed all protocols. Selected the albino Wistar rats and housed in cages with free excess of diet and water. The rats were randomly selected (each group have six animal) and dorsal abdominal skin of the rate was shaved carefully. Transdermal patch was applied to the shaved skin and covered with non-sensitizing micro porous tape. 0.8% formalin aqueous solution was applied as a standard skin irritant. The rats were applied with a new patch each day for up to seven days. The formulations were removed after seven days and check the erythema. Recorded the erythema and compared it with a standard. Erythema was recorded by the Draize scoring method.³¹ According to this method gave a score for erythema. If the score is zero that means no erythema, like that score one for very slightly erythema (light pink), score two for well-defined erythema (pink), score three moderate to severe erythema (light red) and score four for severe erythema (dark red).

RESULTS AND DISCUSSION

Analytical method development by UV spectrophotometer

The calibration sample were prepared from stock solution (1, 2, 3, 4, 5, 6, 7, 8, 9, 10 $\mu\text{g}/\text{mL}$). The absorbance of the sample was determined at 232 nm by using Shimadzu 1800 UV spectrophotometer. The linear line is observed with regressions coefficient 0.9997 (Figure 1).

Physicochemical characterization of patch

All the batches of the transdermal patch showed thickness variation range from 0.126 ± 0.007 to 0.164 ± 0.001 mm as shown in Table 2. High thickness of batch F3 and F5 was found, it may be due to low solubility of ethyl cellulose in solvent render the uneven distribution of the polymer layer. The weigh variation of patch showed very negligible variation observed.

The folding endurance values of all the prepared patches were found to be satisfactory which indicates that the patches prepared by polymer mixture HPMC and ethyl cellulose in a concentration of 3:1 were having optimum flexibility and were not brittle whereas the batch F1 has shown less flexibility.

The maximum moisture content obtained in the patches ranged from 2.04 ± 0.308 to $4.23 \pm 1.62\%$. The moisture content in the formulations was found to be increased by an increase in the polymer amount. The environment also influences the moisture content. Similarly, the percentage of moisture loss has abstained in range of 1.45 ± 0.230 to $2.25 \pm 0.933\%$. Batch F3 showed very less amount of moisture loss, which exhibits better stability of patch. All formulations were acceptable about Irbesartan content. Formulation batch F3 found the maximum entrapment efficiency.

In-vitro drug release of formulation

Drug release studied based on time-dependent percentage drug release. Drug released from

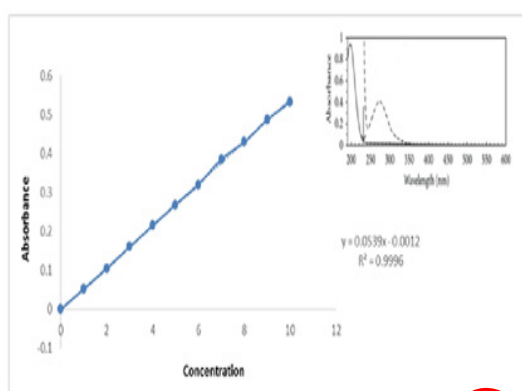
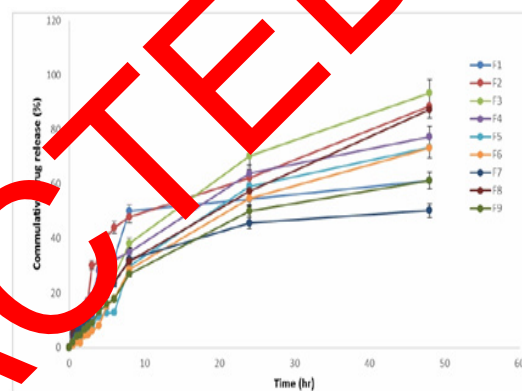
Table 1: Formulation optimization: different ration of polymer and other excipients.

Batch	Drug (mg)	Polymer ration	DBT (ml)	Polymer (mg)			Solvent (Methanol: Chloroform)
				HPMC	EC	Eudragit RS 100	
F1	100	2:1:0	0.129	300	150	0	3:1
F2	100	2:1:0	0.129	300	150	0	3:1
F3	100	2:1:0	0.129	300	150	0	3:1
F4	100	5:1:0	0.129	375	75	0	3:1
F6	100	5:1:0	0.129	375	75	0	3:1
F7	100	5:1:0	0.129	375	75	0	3:1
F5	100	5:0:1	0.129	375	0	75	3:1
F8	100	5:0:1	0.129	375	0	75	3:1
F9	100	5:0:1	0.129	375	0	75	3:1

Table 2: Physicochemical properties of different batches.

Batches/S.N	F1	F2	F3	F4	F5	F6	F7	F8	F9
Thickness (mm)	0.126±0.007	0.151±0.009	0.152±0.003	0.129±0.005	0.164±0.001	0.151±0.004	0.160±0.006	0.149±0.004	0.128±0.004
Weight variation (g)	0.056±0.003	0.052±0.001	0.057±0.002	0.053±0.001	0.053±0.009	0.058±0.006	0.046±0.010	0.053±0.011	0.050±0.013
% moisture uptake	4.23±1.62	2.05±0.740	2.04±0.308	2.896±1.598	3.52±0.957	2.56±0.320	2.86±1.05	3.18±0.700	3.45±0.873
% moisture loss	2.45 ±0.821	1.84 ±0.915	1.45±0.230	1.45±0.566	2.15±0.965	1.65±0.093	2.45±0.377	2.25±0.508	2.25±0.933
Folding endurance	196 ±9.00	204±15.00	244±21.00	224±11.00	231±8.00	218±15.00	215±16.00	238±8.00	215±16
Percentage drug content	78.72 ±2.00	95.25±0.377	97.16±2.30	84.67±2.70	88.16±1.90	88.38±1.70	78.61±1.40	93.74±0.38	81.99±1.10

All the values are mean ± SD, n=3, S.D = standard deviation.

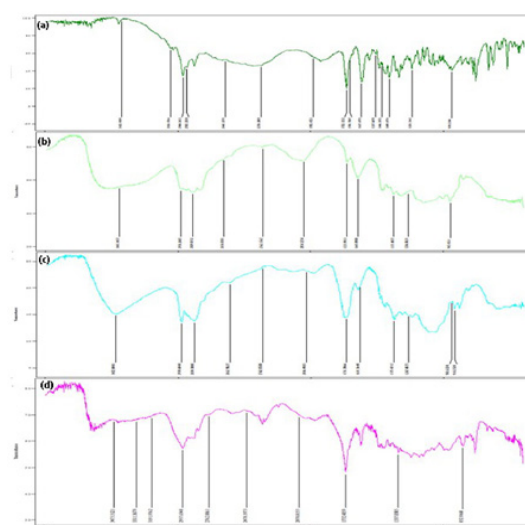
**Figure 1: Calibration curve of Irbesartan in 0.1N NaOH.****Figure 2: Cumulative percentage drug release of different batches of transdermal patch.**

transdermal matrix patches was conducted in Franz diffusion cell using a cellophane membrane. The batch F7 showed a 50% drug release at 48 hr while F1 and F9 have shown release of about around 61%. This is maybe the presence of more polymers in the formulation. The order of drug release was found to be $F3 > F2 > F8 > F4 > F5 > F6 > F9 > F7$ (Figure 2). For further study batch F3 is selected and release data were put in zero order, first-order and Higuchi model equation. The correlation coefficient values were found to be 0.986, 0.901 and 0.992 for zero, first and Higuchi models. Hence, drug release from the patch follows a diffusion rate-controlled mechanism.

According to the basis of physicochemical characterization, drug contents and release study one batch (F3) was concluded as an optimized formulation and proceeded for further study.

FTIR study

FTIR studies were performed to know the interaction between different excipients and drug which was used for the formulation of the transdermal dermal patch

**Figure 3: FTIR spectra of (a) ethyl cellulose, (b) HPMC, (c) physical mixture and (d) formulation.**

(Figure 3). The FTIR spectrum of Ethyl cellulose exhibits following characteristics peaks such as at, 3472.5 cm^{-1} for N-H stretching, 2974 cm^{-1} for C-H aliphatic group, 1631 cm^{-1} for C=C bend, stretching,

1375 cm^{-1} for C-H Asymmetrical stretching mode, 1267 cm^{-1} for CH₃ methylene groups, 918 cm^{-1} for isopropyl groups. The FTIR spectrum of HPMC exhibits at 3443 cm^{-1} for N-H stretching group, 2976 cm^{-1} for C-H aliphatic groups, 1371 cm^{-1} for C-H asymmetric stretching mode. The spectrum batch F3 exhibits peaks at 3395 cm^{-1} for N-H stretching, 2957 cm^{-1} for C-H aliphatic group, 1577 cm^{-1} for C=C aromatic bend and stretching, 1386 cm^{-1} for C-H asymmetrical stretching, 1147, 1238 cm^{-1} for CH₂ Methylene twisting, wagging Groups, 913 cm^{-1} for Alkenes respectively. While in the physical mixture group showed the same group found in the formulation group, i.e. Superimpose to each other. It indicates that there is no interaction between the drug and the excipients.

Ex-vivo permeation Study

Selected batch F3 proceeds for the permeation study and maximum permeation was observed around 81.32%. The steady-state flux value was found to be $0.35 \pm 3.23 \mu\text{g}/\text{cm}^2/\text{hr}$ with a permeation coefficient of 8.05 ($\times 10^3 \text{cm}/\text{hr}$). Whereas the control group found to be $10.3 \pm 0.36 \mu\text{g}/\text{cm}^2/\text{hr}$ steady states flux with 2.05 ($\times 10^3 \text{cm}/\text{hr}$) a permeation coefficient.

Skin irritation and toxicity study (Hypersensitivity reaction)

Transdermal patch always applied to the epidermis layer of skin. It is necessary for such formulation to have biocompatible and free for irritation or sensitivity hypersensitivity reaction. To evaluate the potential of patches to causes skin irritation tests were carried out on the rat's skin. The rats were observed after seven days for the growth of signs of erythema or redness. The score of erythema was read and recorded by the Draize scoring method. If the score is zero that means no erythema, like that score one for very slightly erythema (light pink), score two for well-defined erythema (dark pink), score three for moderate to severe erythema (light red) and score four for severe erythema (dark red). None of the formulated patches were shown to exhibit edema in comparison to standard group in seven days. These results suggest that patches are suitable for further human use due to non-allergic and non-irritant nature.

DISCUSSION

The skin is a most common and specific route to deliver active drug molecule that are meant to act in the tissue. Those active drug molecules that have to permeate the tissue can be absorbed into the systemic circulation and produce action systemically or locally. The presented works have been made to develop a transdermal drug

delivery system of Irbesartan for enhancement of aqueous solubility as well as bioavailability.

Before optimization the Irbesartan qualitative analysis was performed by UV spectrophotometric method. The analytical method was selected to evaluated the drug concentration in the formulation for this purpose, the UV spectrophotometric method was selected to the determination of λ_{max} for drug which was found to be 232 nm and from this a calibration curve was plotted by taking different concentration of solutions which can be used as a reference for the release studies for Irbesartan. The transdermal patch was prepared by the solvent extraction method employing controlled release grade of HPMC and ethyl cellulose in the presence or absence of eudragit, in existence of permeability enhancer DMSO (Table 1). The optimization purposes, different batch of formulation were prepared. The addition of plasticizer was found to be essential to improve mechanical properties of patches and easily remove from aluminum foil surface without rupture. Prepared transdermal patches of Irbesartan were evaluated for their physicochemical evaluation parameters such as thickness, weight variation, present moisture content, present moisture loss, folding endurance.

Prepared patches were further characterized for their percent drug content and *in-vitro* drug release through semipermeable membrane. The % Drug content of formulation F1-F9 was worried to 78.72 ± 2.00 to 97.16 ± 2.30 . All formulation indicated that, the drug were uniformly distributed through the patches and evidenced by the low value of standard deviation. *In vitro* drug permeation studies were carried out for the different formulations using Franz diffusion the cumulative % drug releases along with its standard deviation were found to be in range of $61.39\% \pm 1.55$ to $93.54\% \pm 0.92$ at 48 hr. The formulation F3 ratio 2:1:0 (HPMC: EC: Eudragit RS-100) with DMSO as permeation enhancer was considered as best formulation, since it showed maximum *in-vitro* drug release as $93.54\% \pm 0.92$. The relationship can be established as between the various formulation batches thus, by varying amount of polymer in film, percent release can be varied. Drug-polymer affinity can be major factor that control release of drug from formulation. The release of drug from the batch can be recognized to the leaching of the soluble component, which leads to the formation of pores and thus a decrease in the mean diffusion path length of drug molecules to release into the dissolution medium, result in higher dissolution rates. The ingredients such as HPMC act as antinucleating an agent that retards the crystallization of a drug. Therefore, play an important role in improving the solubility of a drug in the matrix

by sustaining the drug in an amorphous form so that it undergoes rapid solubilisation by penetration of the dissolution medium. The criteria for the selection of batch were physicochemical properties (smooth, uniform, substantive, flexible, weight variation, present moisture content and moisture loss, folding endurance), % drug content and *in-vitro* drug release through semipermeable membrane.

Further, FTIR studies were performed to know the interaction between different excipients and drug which was used for the formulation of transdermal drug delivery system. From the FTIR spectra, it was clear that there was no change in peaks position of Irbesartan, when mixed with the polymer. Thus there was no interaction between Irbesartan and polymers in formulation. The permeation of drug from the transdermal patch could be controlled by presence of appropriate selected polymers and their blends and right choice of permeation enhancer. It is well known that using blends of the polymers one could achieve desired steady state along with controlled/sustained drug release from the patches. According to the literature, diffusion is the main mechanism by which drug release and permeation from the transdermal patch. It is governed by two steps: in the first step depends on the rate of hydration of polymer which involves changes in the entanglement of individual drug molecules at the matrix surface. In second step involves the movement of the drug molecule from the surface to the bulk of the fluid via diffusion membrane.

The *ex-vivo* permeation of patches was evaluated abdominal skin of male Wistar rat. The results of drug permeation from the patch revealed that drug was released from the formulation and permeated through the abdominal skin membrane; hence they can possibly permeate through the membrane. The *in-vivo* skin irritation and toxicity study was performed by eliminating the risks of hazard for molecules of transdermal drug delivery system. None of the formulated patches were free from edema in seven days that is suitable for further human use due to non-allergic and non-irritant nature. Therefore, transdermal patch of Irbesartan is effective delivery of a drug throughout the products intended shelf-life or delivery period and have generally recognised-as safe status.

CONCLUSION

The transdermal patch of Irbesartan has been developed in different ratios of polymer-like HPMC and ethyl cellulose. The patch was revealed good promising results for all the estimated parameters. Based

on physicochemical characterization, drug contents and *in-vitro* release study F3 batch was concluded as an optimized formulation. The formulation showed better *in-vitro* release as well as high *ex-vivo* permeation in the skin. The formulation exhibits toxicity and edema free when applied in rats. This can be the potential for therapeutic application due to reduced dosing frequency, improve patient compliance and bioavailability.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

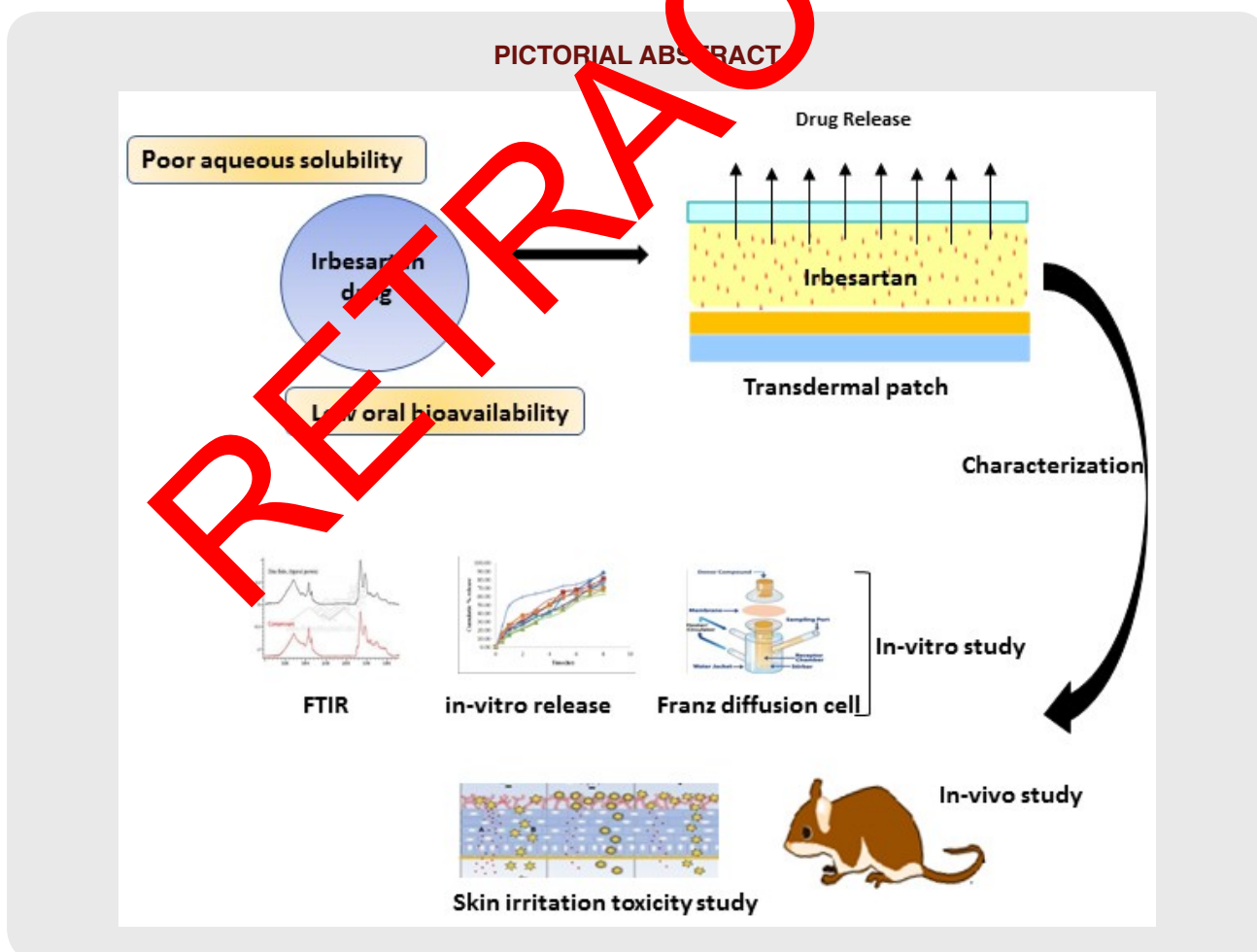
ABBREVIATIONS

DMSO: Dimethyl sulfoxide; **EC:** Ethyl Cellulose; **HPMC:** Hydroxyl Propyl Methyl Cellulose; **FTIR:** Fourier Transform Infrared-spectroscopy; **UV:** Ultraviolet-visible.

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SUMMARY

- Irbesartan is hypertensive drugs, have an angiotensin receptor blocker, belongs to BCS class II, which showed low solubility and variable oral bioavailability. Therefore, develop a transdermal patches system of Irbesartan to enhance the dissolution rate and bioavailability.
- Irbesartan transdermal patches were prepared by the solvent extraction method employing HPMC and ethyl cellulose as polymer.
- Prepared patches were proceed for their physicochemical properties, drug polymer interaction, drug release, *ex-vivo* permeation study, and *in-vivo* skin irritation/toxicity study in Wistar rats.
- The batch was showed desired physicochemical properties, no interaction, better release, with high flux. While *in-vivo* study confirms that, the patch was free from edema and hypersensitivity reaction.
- This prepared transdermal patch of Irbesartan can be the potential for therapeutic application due to reduced dosing frequency, improve patient compliance and bioavailability.

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