Section A-Research paper
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Formulation and Evaluation of Transdermal Patches of Azilsartan

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Abstract: With oral administration, Azilsartan is poorly absorbed; peak plasma concentrations occur 1 to 3 hours after a dose. The liver significantly metabolises the bioavailability, which is roughly 60 %. About 11 hours pass between half-lives. Azilsartan is an excellent option for the design and development of transdermal treatment systems due to its low therapeutic dose and significant liver biotransformation. An alternative dosage form for the current oral, parenteral medication delivery system was being developed as part of the current investigation. Azilsartan transdermal patches were made utilising a particular process and a combination of HPMC and EC polymers in various ratios. Several evaluation criteria, including thickness, folding endurance, weight uniformity, content uniformity, swelling index, percentage moisture content, moisture uptake, surface pH and in vitro release studies, PK study, and permeation study, were applied to all the patches that had been developed. Regarding integrity, flexibility, drug dispersion, and other quality control criteria, all patches displayed satisfactory features. In order to identify the drug release mechanism, the data were plotted. The medication release experiment of 24 hours was prolonged. The penetration was made better using DMSO, which untangled the lipid layer. Improved medication penetration is achieved by the formulation with a high concentration of HPMC (A1). The A2 and A6 helped maintain a steady pace of discharge. A sustain release polymeric transdermal patch was developed to deliver Azilsartan over the skin barrier gradually. This shows that Azilsartan transdermal application maintains the drug's claimed regulated release for a long time.

Keywords: Azilsartan, Transdermal, Patch, Antihypertensive drug etc.

Introduction

Transdermal patches are created to treat a variety of disorders and are delivered through the widely recognised transdermal drug delivery system (TDDS) [1]. The idea of treating sick situations systemically by administering medications through the skin is becoming more and more popular due to its many benefits. Limiting hepatic first pass metabolism, improving therapeutic effectiveness, extending the duration of action of powerful medications with short plasma half-lives, and maintaining a constant plasma level of the drug are only a few of the significant benefits of transdermal drug delivery. Yet only medications with low dosages, low melting points, low molecular weights, and a solubility of more than 1 mg/mL in both water and mineral oil can be delivered via transdermal means [2].

Transdermal drug delivery systems are designed to minimise drug retention and metabolism in the skin while increasing the amount of drug that enters the bloodstream through the skin [3-5]. These medical advantages reflect TDDS's enhanced marketing potential [6]. The intercellular micro route accounts for the majority of drug molecule skin penetration; as a result, the significance of permeation or penetration enhancers in TDDS is crucial since they reversibly diminish the stratum corneum's barrier resistance without causing harm to healthy cells [7]. The first transdermal patch was created by the California-based Alza Corp. in 1981 for the treatment of motion sickness using the medication scopolamine (Transderm-Scop), and was later followed by Transderm-nitro for the treatment of angina pectoris. As a result of its ongoing success, 35 TDDS patches are currently available on the market for conditions including hypertension, angina pectoris, motion sickness, female menopause, and male hypogonadism [8]. Transdermal delivery's market share increased every year from $12.7 billion in 2005 to $21.5 billion in 2010, $31.5 billion in 2015, and continues to rise.

During the gastrointestinal absorption phase, the prodrug Azilsartan medoxomil quickly hydrolyses to Azilsartan, the active metabolite. It dissolves in acetic acid, methanol, and dimethyl sulfoxide readily but is essentially insoluble in water. This substance can be used to treat mild to moderate cases of essential hypertension as it has a pKa of 6.1 and a log P value of 5.7t, making it a selective AT1 subtype angiotensin II receptor blocker (ARB) [9,10].

Just a small number of pharmacological compounds are supplied transdermally due to the stratum corneum's formidable barrier function, despite the transdermal route's numerous benefits. The use of chemical penetration enhancers (PE) such solvents, surfactants, fatty acids, and terpenes, as well as physical procedures like iontophoresis, electroporation, sonophoresis, and microneedles, are the two main methods for increasing transdermal

permeation rate [11]. The goal of this study was to create transdermal patches for Azilsartan and assess how the polymer affected the drug's release.

Material and Methods

Material

Anant Pharmaceutical Pvt. Ltd. in India provided the Azilsartan API. The following substances were used: Alcohol/CHCl3, Dimethyl Sulfoxide (DMSO), Propylene Glycol (DBP/PG), Cellulose Acetate Phthalate (CAP), Di-Butyl Phthalate, Hydroxypropyl Methylcellulose (HPMC), and Ethyl Cellulose.

Methods

Preformulation study

Identification of drug

Melting point analysis, infrared spectroscopy, and ultraviolet spectroscopy all helped identify Azilsartan.

Melting point determination

Take a small amount of the medicine in a capillary tube that is sealed at one end to control the drug's melting point. The melting point device was used to place the capillary tube, and the temperature at which the drug melted was recorded. This operation was repeated three times, and the mean value was documented.

Determination of λ max and plotting of calibration curve of Azilsartan in methanol

A precisely weighed 10.0 mg of Azilsartan was dissolved in 10 ml of methanol to provide a 1000 g/ml concentration of the medication (stock solution), and from the stock solution, Azilsartan was obtained at concentrations of 10, 15, 20, 25, and 35 g/ml. All dilutions were contrasted with methanol as a blank throughout the 400–200 nm scans. The drug's spectrum was examined in order to confirm the maximum value, and a calibration curve was created with absorbance versus concentration.

Drug and polymer compatibility study

Fourier Transform Infrared Spectroscopy (FTIR)

This investigation was done to determine whether the polymers PVP, PVA, HPMC, and ethyl cellulose were compatible with the medication Azilsartan. Also, they aid in the assessment of

the suitability of polymers used in the creation of transdermal patches. A FTIR spectrometer (IR Affinity 1Model, Japan) was used to intentionally create an FTIR spectrum. Azilsartan with HPMC was one of the physical mixtures that was made individually with KBr, dried in a hot air oven for about an hour, then stayed in desiccators before being scanned for spectra between 4000 and 500 cm-1.

Differential Scanning Calorimetry (DSC)

Before being calibrated, the differential scanning calorimeter was subjected to the powdered medication. A sample was sealed up tight in an aluminium betel and subjected to nitrogen gas at a flow rate of 50 mL/min. The thermograms were acquired at a scanning temperature range of 50-250°C at a heating rate of 10 °C/min. Each run began with the correction of the criterion. DSC thermograms showed Azilsartan as the temperature.

Preparation of transdermal patches

Using the mercury substrate technique and several polymer grades, Azilsartan-containing transdermal patches were produced. The table shows how much of each of the three polymers hydroxypropyl methyl cellulose, cellulose acetate phthalate, and ethyl cellulose was required. The polymers are dissolved by adding 10 ml of ethanol or chloroform, and the liquid is then left alone for a short period of time to allow the polymers to swell. Then, when the polymers had completely dissolved in the solvent combination, Azilsartan was added in the proper quantity and well mixed into the polymeric solution. After the required quantity of dibutyl phthalate or propylene glycol has been added, the liquid is vortexed. For solvent evaporation, the cleaned mercury-containing petridish was set aside. The rate of solvent evaporation is controlled by turning a glass funnel upside down over the petridish. The following day, the dried films were removed and stored in a desiccator.

Table 1: Formulation table for Azilsartan

Ingredients	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	**Q6**	**Q7**	**Q8**	**Q9**	**Q10**	**Q11**	**Q12**
Azilsartan in mg	100	100	100	100	100	100	100	100	100	100	100	100
HPMC in mg	500	-	-	200	200	-	500	-	-	200	200	-

CAP in mg	-	500	-	300	-	200	-	500	-	300	-	200
EC in mg	-	-	500	-	300	300	-	-	500	-	300	300
DBP/PG (w/v)	40 % PG	60 % DBP	40 % DBP	50 % DBP	40 % DBP	40 % DBP	40 % PG	60 % DBP	40 % DBP	50 % DBP	40 % DBP	40 % DBP
Alcohol / CHCl3 in ml	10	10	10	10	10	10	10	10	10	10	10	10
DMSO	20 %	20 %	20 %	20 %	20 %	20 %	40 %	40 %	40 %	40 %	40 %	40 %

Evaluation of transdermal patches

Physical Appearance

Each transdermal patch was meticulously examined for colour, flexibility, homogeneity, and smoothness.

Thickness

The patches' thickness was measured with a screw gauge at five different, randomly selected spots on the films (micrometer). Such a determination was made for each formulation.

Weight Uniformity

Weighing each patch independently allowed us to calculate the average weight of three films.

Folding endurance

A strip must be consistently cut to a certain width and folded repeatedly until it breaks. The value of endurance was measured by how many folds the film could withstand simultaneously without rupturing [12].

Determination of Drug content

The patch's one square centimetre was removed, and it was properly weighed. Each sample was dissolved in 100 cc of 7.4 phosphate buffer solution and then subjected to a 24-hour

magnetic stir. The absorbance of the solution is measured using UV-VIS spectrophotometers at certain wavelengths. The total amount of Azilsartan in the patch was determined [13].

Scanning electron microscopic studies

The films were mounted in the SEM equipment using double-sided adhesive tape. The coated films were investigated in a SEM (JEOL/EO, JSM-6390, Kyoto, Japan) at room temperature and with the appropriate magnification. The acceleration voltage was paired with the secondary electron image as a detector to produce images of the formulation used to determine the surface morphology of the patches [13].

X-Ray diffraction studies

The sample's spectra were recorded using a Rigaku Miniflex II X-ray diffractometer with Cu-NF filtered CuK radiation. Quartz served as an internal reference for calibration. The computer and digital graphic assembly were connected to the powder x-ray diffractometer, which used a Cu-NF 25KV/20 mA tube as a source of CuK radiation in the 0 to 50 oC temperature range [14].

Differential scanning calorimetric analysis

The thermograms were produced after the samples were heated using a micro calorimeter (DuPont-9900, USA) from 0 to 300 oC at a heating rate of 10 oC/min in an environment of argon or nitrogen.

Water vapour transmission

These investigations used equal-diameter vials as their permeation cell. One gramme of calcium chloride was put into vials, the cells were washed, dried, and the films were firmly adhered to the brim with adhesive. The vials were then weighed. The carefully weighed vials are kept in desiccators that contain saturated potassium chloride solution (200 ml). Every day for up to 7 days, the vials were taken out of storage and weighed. The increased weights were used to determine the water vapour transit rate [15].

Permeation Studies

Using a thermostatically controlled Franz diffusion cell setup, the permeation studies were carried out. With the dermis facing the donor compartment, freshly excised rat epidermis was placed to the receptor compartment. Samples were taken from the sampling port on a regular basis, and the equivalent amount of fresh buffer was also replaced to maintain sink conditions. Phosphate buffer with a pH of 7.4 was put into the receptor compartment. The temperature was held at 37.2 °C, and the stirring speed was 100 rpm. Diffusion investigations

lasting 24 hours were carried out. Spectrophotometry was used to analyse the samples at 252 nm absorption maxima [16].

Skin Irritation study

Healthy rabbits are used in a skin sensitivity test (average weight 1.2 to 1.5 kg). The rabbit's 50 cm2 dorsal area, which is covered with hair, can be cleaned by shaving it. Applying the prepared mixes to your skin is an option. The patch must be removed after 24 hours, and the skin's oedema and irritation must be assessed [16].

Efficacy in Rats against hypertension

The MUROMACHI MK2000ST was used to monitor the baseline blood pressure (BP) of rats utilizing a non-invasive tail cuff and digital BP display system. The blood pressure was initially measured and determined to be normal. Thereafter, for two weeks, Physostigmine 15 mg/kg intravenously was administered to induce hypertension. Hypertension developed after 14 days, and a mean blood pressure of 150 mmHg was selected. Four groups (n=5) were made for the rats. Groups 1 and 2 received no treatment (control), whereas Groups 3 and 4 were treated with transdermal patches containing the drug Azilsartan in Formulation A5 and Formulation A6, respectively. All day long, rats' blood pressure was monitored (1, 2, 4,6,10, 24 Hrs) [17].

Pharmacokinetic evaluation of patches on animals

Wistar Albino adult rats were used in the bioavailability investigation, and any abnormalities in the rats' superficial skin were looked for. The dorsal side was shaved, and rats were only selected if their weight was between 230 and 250 g. Rats were monitored before receiving the transdermal patches to guard against any unwanted consequences of shaving. Rats were placed on a strict fasting regimen during this time. Three groups had been prepared. The dosage of Azilsartan (5 mg/kg) was administered orally to Group I, Group II, and Group III, respectively. Blood was drawn at several time points, including 2, 4, 8, and 24 hours. After centrifuging, plasma samples were maintained in vials at -700C until the analysis was finished. The drug's plasma levels were assessed using reverse phase HPLC. A chromolith column was used with a flow rate of 1.5 ml/min and a mobile phase of Methanol: Acetonitrile: Phosphate buffer pH 3.0 (45:25:30 v/v) (column length: 100 x 4.6 mm, 2 m). The injection volume was 10 L, and the retention time was 5.5 min [18].

Stability studies

The formulation stability experiments were finished according ICH specifications. Aspects of the samples' physical characteristics, such as colour and elasticity, were carefully examined [18].

Result and Discussion

Preformulation study

API characterization

Table 2: Organoleptic properties of Azilsartan

Sr. No.	Name of property	Specification
1.	Colour	White
2.	Odour	Unpleasant
3.	Nature	Amorphous

Identification of pure drug

a) Melting Point

Table 3: Melting point of Azilsartan

Sr.no.	Melting point	Reference range	Average melting point
1	195℃		
2	193℃	193-195 ℃	193.33℃
3	192℃		

Melting point of Azilsartan was initiate to be 193.33℃, that is in compass as given in literature (193-195 ℃). Consequently, the drug can be expressed as pure.

b) UV Spectroscopy

i) Determination of λ max

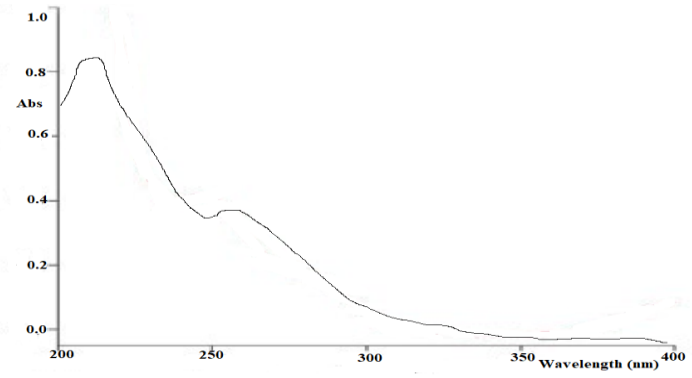

Fig.1: UV Spectra of pure Azilsartan in methanol

Absorption maximum was found to be at 252 nm. Therefore, 252 nm was designate as λ max for additional studies.

ii) Calibration curve of Azilsartan in methanol

Table 4: Different concentration & absorbance of Azilsartan

Sr.no.	Concentration (µg/ml)	Absorbance
1	0	0
2	10	0.194
3	15	0.301
4	20	0.389
5	25	0.463
6	30	0.581
7	35	0.649

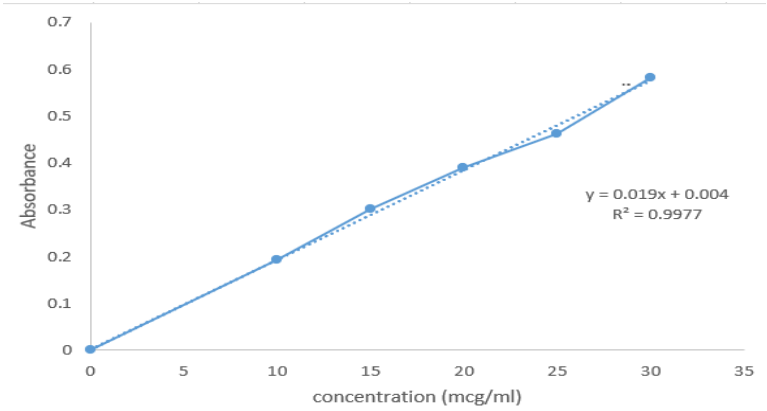

Fig.2: Calibration curve of Azilsartan in methanol

Table 5: Parameters of calibration curve

Sr.No.	Parameter	Finding
1	Wavelength detection	252 nm
2	Correlation coefficient	Y= 0.019x - 0.004
3	Regression equation	R^2 = 0.9977

Solubility study

Saturation solubility study

The raw material for Azilsartan solubility in water and different pH buffer (0.1 N HCl pH 1.2, Acetate buffer pH 4, Phosphate buffer pH 6.8 and 7.4). Due to the organic acids' pH maximum effect, Azilsartan had a solubility profile with its greatest solubility at phosphate buffer pH 7.4. Azilsartan was found to dissolve at rates of 14.23%, 18.43%, 23.76%, 27.65%, and 33.12%. Comparing the solubility of the phosphate buffer solution to different buffers, pH 7.4 had the highest solubility.

Table 6: Solubility study of Azilsartan

Sr.no.	Different buffers	% Solubility
1	Water	14.23 %
2	0.1 N HCl (pH 1.2)	18.43 %
3	Acetate buffer (pH 4)	23.76 %
4	Phosphate buffer solution (pH 6.8)	27.65 %
5	Phosphate buffer solution (pH 7.4)	33.12 %

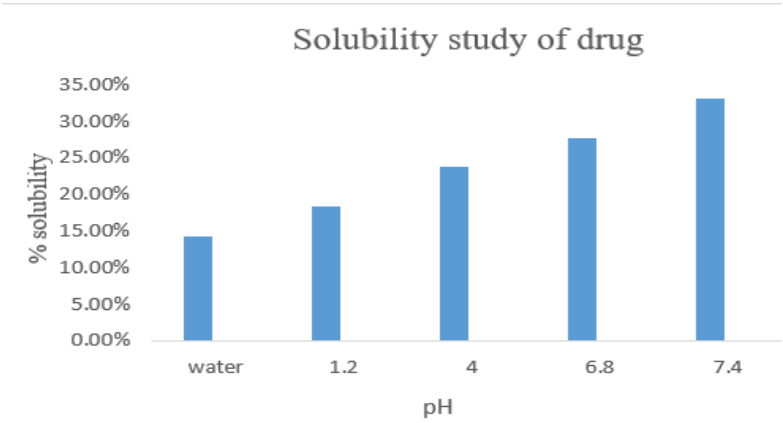

Fig. 3: Solubility study of Azilsartan in water and different buffer

Drug -excipient interaction study

a. Fourier-transform infrared spectroscopy (FTIR)

FTIR spectrum of Azilsartan was manifest in following Fig. revealed characteristic peaks representing the presence of functional groups claim by its chemical structure. From this we can consider that the Azilsartan was of pure quality.

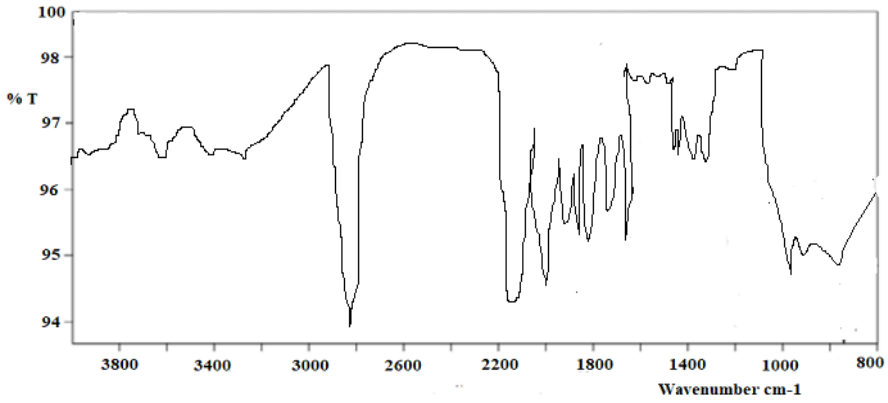

Fig. 4: FT-IR spectra of pure drug Azilsartan

Following interpretation of FT-IR Spectrum of drug, it was concluded that the attributes peaks resemblance to the functional category present in the molecular structure of Azilsartan were found within the reference range and accomodate its recognition.

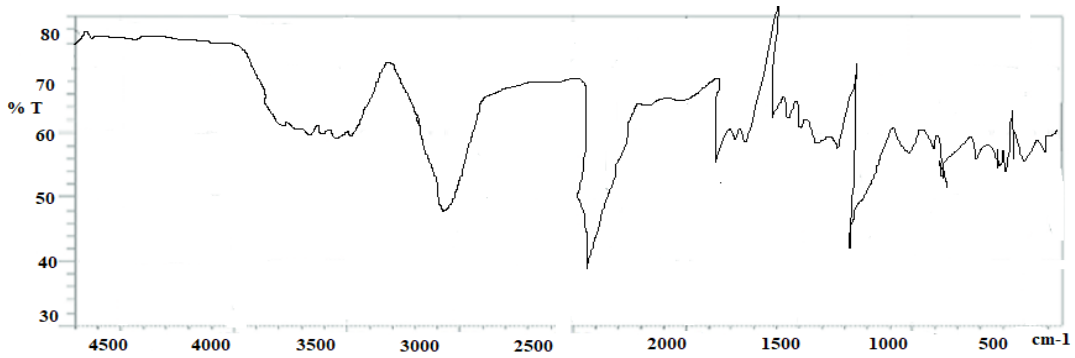

Fig. 5: FT-IR spectra of HPMC

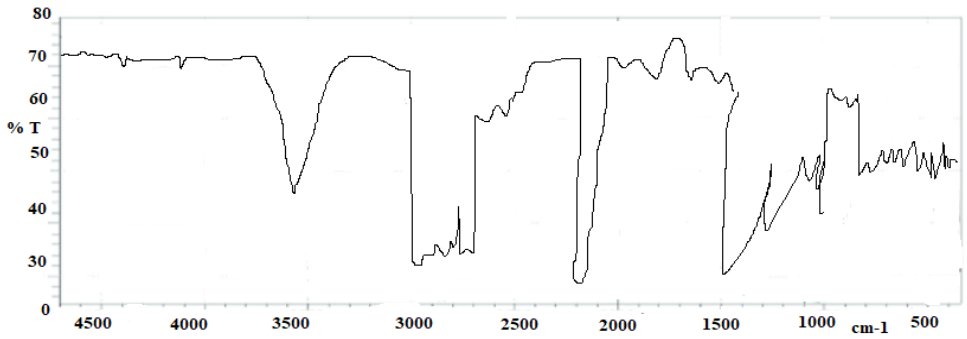

Fig. 6: FT-IR spectra of Ethyl cellulose

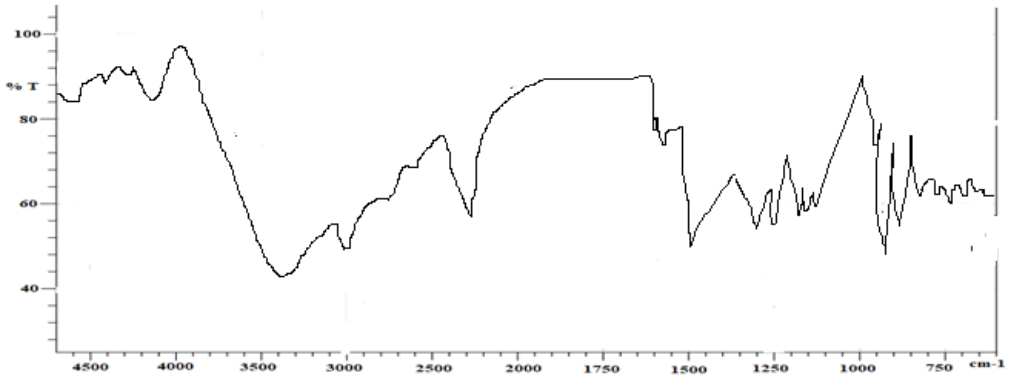

Fig. 7: FTIR spectra of physical mixture (Drug +HPMC+EC)

The peaks of pure medicine and selected polymer combinations are identical, with only small variations in cm-1. This implies that there is no interaction between medications and polymers.

The produced formulations of Azilsartan patches remain abridged according to their physiochemical characteristics. were transparent or translucent, thin, elastic, flexible, and smooth. The produced formulations' drug content homogeneity is distributed as follows: A11>A6>A12>A5>A8>A7>A2>A1>A3>A9>A4>A8, and A10>A2>A1. The drug content values show that Azilsartan is evenly distributed across the formulations.

Table 7: Physicochemical properties of Azilsartan patches

Formulation	Physical appearance	Weight	Thickness	Drug content	Folding endurance
A1	++	0.64	0.147	96.53	> 295
A2	++	0.77	0.220	97.34	>227
A3	++	0.79	0.230	95.75	> 17
A4	++	0.78	0.185	93.86	>252
A5	++	0.82	0.310	98.06	>272
A6	++	0.75	0.236	98.56	>242
A7	++	0.70	0.162	97.35	>297
A8	++	0.79	0.231	97.85	>227
A9	++	0.85	0.254	95.48	>17

A10	++	0.86	0.195	93.74	>252
A11	++	0.86	0.266	98.66	>272
A12	++	0.80	0.248	98.64	>242

The surface characteristics of the created formulations were investigated using scanning electron microscopy (patches). SEM photomicrographs show that membranes A4, A5, and A6 all have uniform, flat surfaces, however the surface of A6 formulation is denser and rougher than that of A4 and A5.

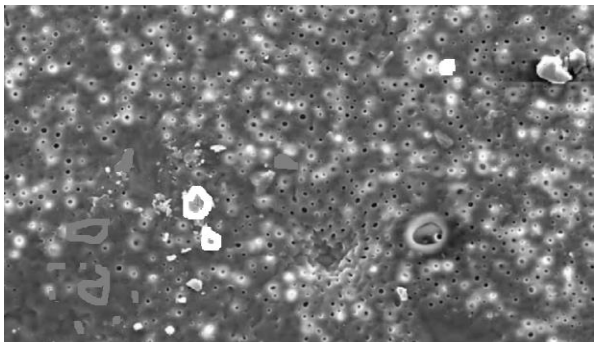

Fig. 8: SEM image of A4 patch

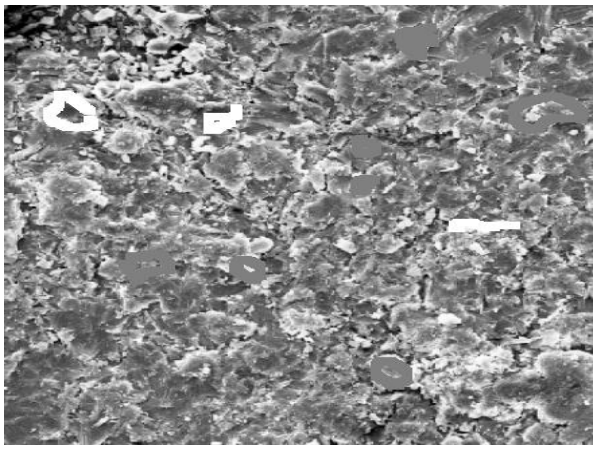

Fig. 9: SEM image of A6 patch

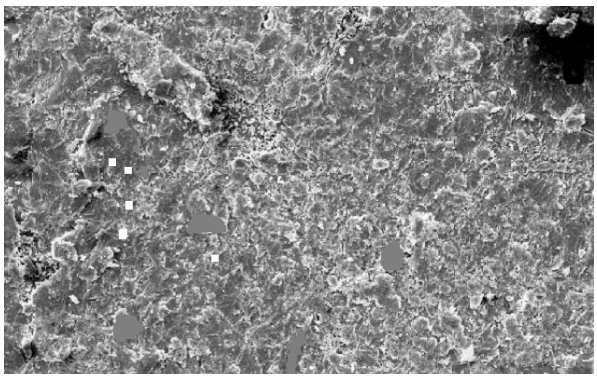

Fig. 10: SEM image of A5 patch

Differential scanning calorimetry

Azilsartan melting endotherm in its purest form was 198°C. The DSC test of A5 exhibited a broad endotherm because residual moisture in polymers causes this. The DSC thermogram of Azilsartan A5 exhibits endothermic peaks that are quite near to the temperature of the pure drug. It can be concluded from this that there is no interaction between the medication and the polymers.

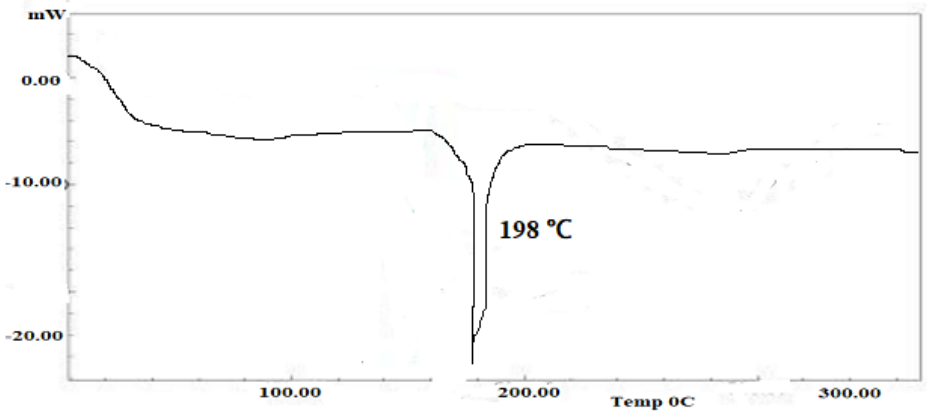

Fig.11: DSC thermogram of Azilsartan

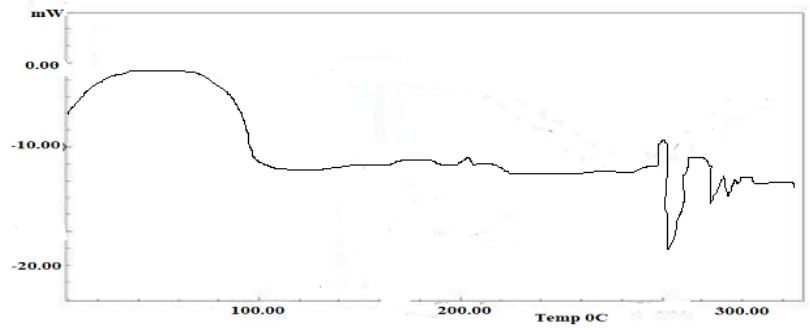

Fig. 12: DSC thermogram of dummy patch A5

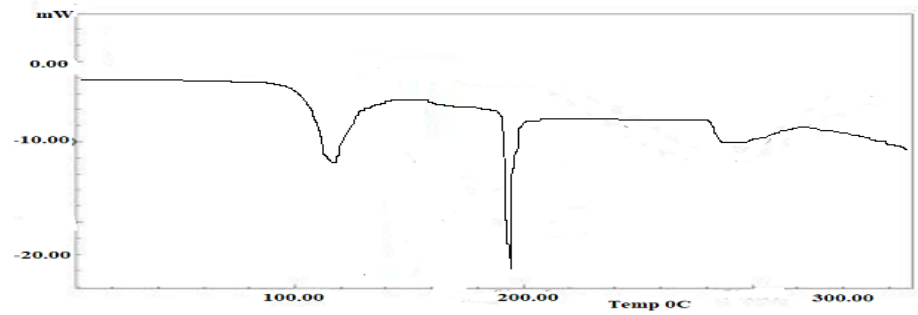

Fig. 13: DSC thermogram of drug loaded patch of A5

In contrast to the A5 dummy patch, which does not show any peaks, and the A5 patch containing the drug, which shows peaks between the ranges of 15 and 28, Azilsartan X-ray diffractograms show prominent peaks between the ranges of 5 and 25. This shows that the medication's modest crystalline character is what gives rise to the formulation's choice.

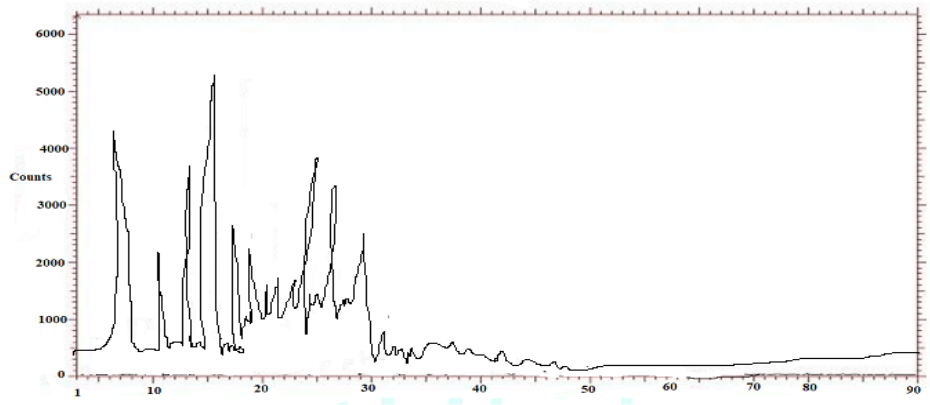

Fig. 14: XRD diffraction of Azilsartan

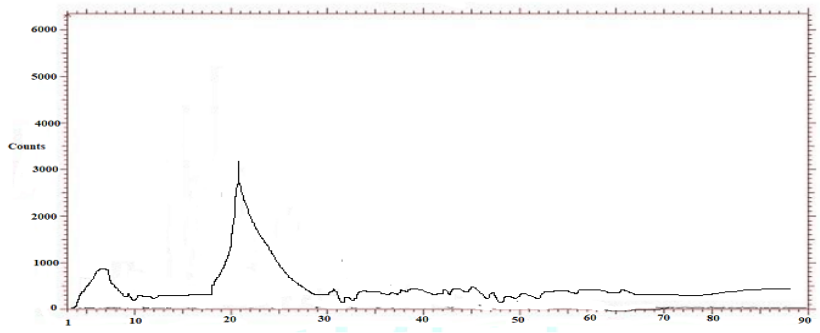

Fig. 15: XRD diffraction of Azilsartan Patch without drug

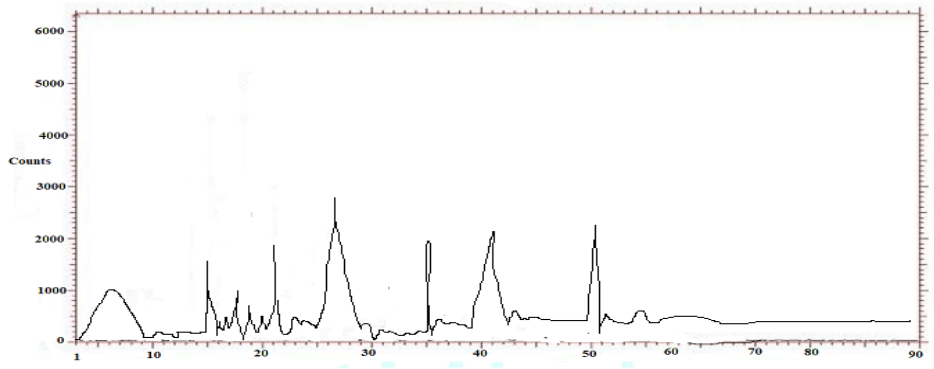

Fig. 16: XRD diffraction of Formulation A5

The water vapor transmission (WVT) through the matrix patches that regulate the rate of transmission is what determines the permeability qualities. The created matrix type of transdermal patches all have water vapor permeable surfaces. The WVT rates for the first, second, third, fourth, fifth, sixth, seventh, eighth, ninth, tenth, eleventh, and twelveth quarters were, respectively, 0.084, 0.046, 0.015, 0.035, 0.031, 0.096, 0.067, 0.018, 0.024, 0.026, 0.019, and 0.060.

The results of various patches placed on the skin over the abdominal muscles of rats that had just exercised are listed. In order to determine the steady-state flow, the cumulative amount of medication absorbed per unit of skin surface area was plotted against time, and the slope of the linear section of the plot was calculated (JSS). The permeability coefficient (Kp) was then calculated using the following equation:

$$\mathbf{Kp = JSS / CV}$$

Where CV is the total concentration of the drug in the donor compartment.

Through in-vitro drug release experiments, the percentage of drug permeations was calculated for each formulation. A1, A2, A3, A4, A5, A6, A7, A8, A9, A10, A11, and A12 had the following respective values at the conclusion of the 24th hour: 97.71, 96.56, 82.45, 90.44, 83.87, 94.11, 70.25, 73.48, 64.76, 74.77, and 60.45. While using 20% DMSO, permeability increases as HPMC concentration increases, however when using 40% DMSO, permeation rates increase as CAP concentration rises. Drug formulations containing 20% DMSO penetrate the drug more than those containing 40% DMSO, according to the drug permeation experiment.

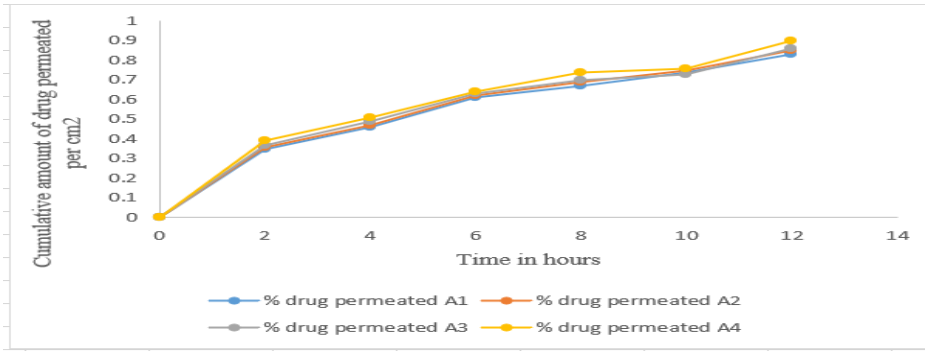

Fig. 17: In-vitro permeation of Azilsartan of all formulated patches through the rat skin of formulation A1 to A4

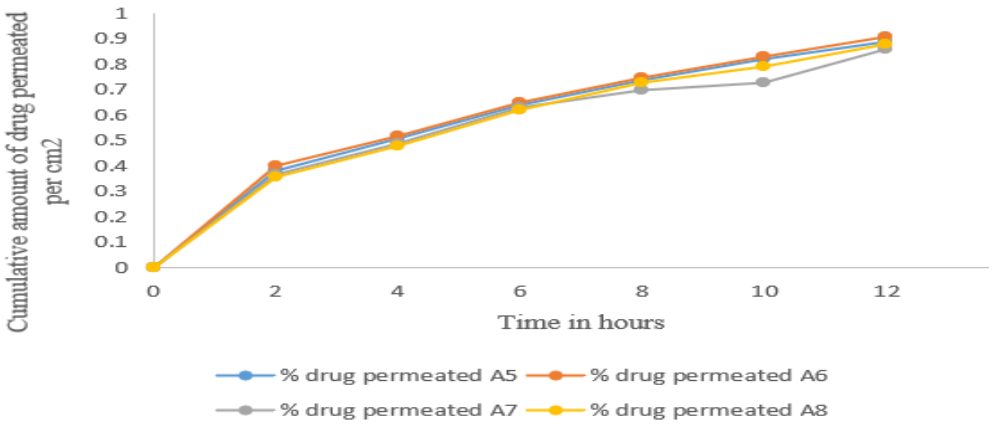

Fig. 18: In-vitro permeation of Azilsartan of all formulated patches through the rat skin of formulation A5 to A8.

When compared to the control patch, A6 exhibits no signs of erthyema or odema during the initial skin irritation experiment employing the selected formulation on albino rabbits. This demonstrates that these compositions are suitable for topical use on skin.

Table 8: Skin irritation test of selected Azilsartan patch on rabbit

Formulation	Erythema	Edema
A6	--	--

-- Nil

+ Mild

++ Severe

+++ Very severe

The prepared formulations are stable in nature. There is no effectiveness in color, plasticity and drug content.

Transdermal patches efficacy in Rats against hypertension

In rats, dexamethasone administration increased blood pressure, as seen in Table 10. During treatment, a drug called Azilsartan was given orally, greatly lowering blood pressure. However, after two hours, the effect peaked, and BP increased over the following 24 hours. It was found that there was no difference between the initial and 24-hour blood pressure values. Systolic and diastolic blood pressure measurements are shown in Tables 9

and 10. On the other hand, after transdermal patch therapy, BP gradually decreases (formulation A5 and A6). The BP dropped significantly at six hours. Within the first hour, the BP dramatically dropped, and the effects lasted for 24 hours. For formulation A6, the BP decrease was greatest at 6 hours. Taking this into account, it was found that transdermal Azilsartan patches produced a more prolonged and continuous drug release than oral administration. Orally administered Azilsartan started working fast but then started to wear off, causing blood pressure to start to rise again. It is therefore very clear that specifically created Azilsartan patches gradually release the medication over a predetermined length of time, resulting in the control of high blood pressure for a significant amount of time within a 24-hour period. Hence, problems with oral distribution, such as low bioavailability, are avoided via transdermal patches (Formulation A6). Systolic and diastolic blood pressure measurements are shown in Tables 9 and 10.

Table 9: Antihypertensive effect of transdermal route and oral route for Azilsartan (Reduction of systolic BP)

Group	**Treatment**	**Systolic mean BP (mmHg)**						
		Initial	**1 Hr**	**2 Hr**	**4 Hr**	**6 Hr**	**10 Hr**	**24 Hr**
I	Control	175.34	175.96	174.26	172.86	171.48	176.84	175.75
II	Oral	172.87	127.17	98.87	117.26	129.37	137.28	170.85
III	A5	174.38	122.58	115.24	107.98	100.46	104.74	107.46
IV	A6	14.23	117.76	111.54	98.75	95.76	97.89	101.39

Table 10: Antihypertensive effect of transdermal route and oral route for Azilsartan (Reduction of Diastolic BP)

Group	**Treatment**	**Diastolic mean BP (mmHg)**						
		Initial	**1 Hr**	**2 Hr**	**4 Hr**	**6 Hr**	**10 Hr**	**24 Hr**
I	Control	94.74	95.77	94.65	96.13	95.85	93.74	93.69
II	Oral	92.83	88.39	82.11	91.65	92.66	93.16	92.12
III	A5	93.25	90.87	85.57	83.16	82.18	82.68	82.75
IV	A6	94.85	83.12	84.47	81.87	80.47	81.15	81.84

Pharmacokinetic effect on transdermal patches

The patches' pharmacokinetic effects as determined by blood plasma concentration. When compared to transdermal patches, oral Azilsartan medication yielded results that were noticeably different. The highest concentrations for formulations A5 and A6 were discovered to be 6.24 0.76 and 7.54 0.23 g/ml, respectively, whereas the highest concentration for oral Azilsartan was found to be 6.06 0.11 g/ml during the maximum time period of 2 hours. It was discovered that the elimination half-lives of formulations A5 and A6 were prolonged; this suggests that the drug remained in the body for a longer period of time before being entirely eliminated. Lower values of the elimination rate constant signify sustained action release. When compared to the oral delivery of Azilsartan, the AUC for Formulation A5 and A6 was shown to be greater. Table 11 shows that A5 and A6 have the maximum bioavailability when compared to oral bioavailability.

Table 11: Pharmacokinetic parameters of drug after oral Azilsartan and transdermal patch of Azilsartan

Parameters	**Oral**	**A5**	**A6**
C max (ug/ml)	5.23 ± 1.43	5.75 ± 0.37	6.24 ± 0.18
T max (h)	2 Hrs	12 Hrs	12 Hrs
Ke (h-1)	0.234 ± 0.0005	0.035 ± 0.029	0.028 ± 0.05
T ½ (h)	5.34 ± 1.85	17.69 ± 1.52	18.45 ± 1.79
AUC (0-24) (ugh/ml)	43.75 ± 2.35	69.24 ± 1.65	77.48 ± 2.13
AUC (0-∞) (ugh/ml)	44.16 ±2.47	156.67 ± 1.48	167.56 ± 0.79
F %	-	164.587	182.476

Conclusion

The transdermal drug delivery system for Azilsartan that was created using various polymers, including cellulose acetate phthalate (CAP), di-butyl phthalate, propylene glycol (DBP/PG), hydroxypropyl methylcellulose (HPMC), and ethyl cellulose, had positive results for all of the parameters that were tested. Based on the outcomes of different evaluation criteria, including the lowest film thickness, film weight and% elongation, higher folding endurance, and in vitro drug release. Azilsartan was released from the formulation and passed through

the rat skin, proving that it could pass through human skin as well. This was demonstrated by the results of drug permeation from transdermal patches of Azilsartan through the abdomen skin of rats.

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