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TRANSDERMAL PATCH OF AN ANTIHYPERTENSIVE DRUG: ITS DEVELOPMENT AND EVALUATION

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ABSTRACT

The purpose of this research was to develop a polymer matrix diffusion controlled transdermal drug delivery system containing drug Telmisartan with different ratio of hydrophilic (HPMC) and lipophilic (EC, Eudragit RS 100) polymeric system by solvent casting technique on aluminum foil by using 30% w/v Dibutyl Phthalate of the polymeric weight, incorporated as plasticizer and 20% w/v, 30% w/v Dimethyl Sulfoxide(polymeric weight) was used to be permeation enhancer for transdermal drug release. Total Nine formulation developed by using same drug and different polymeric ratio. All transdermal patches were physicochemical evaluated with thickness, weight variation, % moisture uptake, % moisture loss, folding endurance, flatness, drug content and % drug release. All prepared transdermal patches indicate good physical stability. The invitro permeation study performed by diffusion cells. The maximum invitro % drug release was observed up to 48 hrs with formulation F8 containing HPMC: EC: Eudragit RS 100 in (5:0:1) ratio.

KEYWORDS: Polymers (HPMC: EC: Eudragit RS 100), Permeability enhancer (DMSO), Plasticizer (DBT), Telmisartan.

INTRODUCTION

A transdermal patch is a medicated adhesive patch that is placed on the skin to deliver a specific dose of medication through the skin and into the blood stream.[1]

An benefits of a transdermal patch over other types of medication delivery such as oral, topical, intravenous, intramuscular, etc. is that the patch provides a controlled release of the medication into the patient, usually through either a porous membrane covering a reservoir of

medication or through body heat melting thin layers of medication embedded in the adhesive.[2]

Transdermal drug delivery system, the delivery of drugs through the skin has been always a challenging area for researchers, due to barrier properties exhibit by the outermost layer of skin stratum cornum. Specially in last twenty years, the transdermal drug delivery system has become a more focusing technology that offers significant clinical benefits over other dosage forms, because transdermal drug delivery offers controlled as well as state blood concentration.[3]

TDDS for the treatments of hypertension

Developing controlled drug delivery has become increases the importance in the pharmaceutical industry. Today about ¾ th % (75%) of drug are taken orally but it are not found be as effective as desired. To improve such character transdermal drug delivery system was emerged as Novel drug delivery system. Transdermal drug delivery represents one of the most rapidly advancing areas of novel drug delivery because it overcomes the difficulties of oral antihypertensive drugs.

TDDS have many advantage over conventional antihypertensive drug delivery such as non-invasive, ease of use, withdrawn (increases side effect) , avoid first pass metabolism, best patient compliance, no need of hospitalizations, avoid gastric irritation, reducing dosing frequency of drug. Hence TDDS was selected for the treatment of hypertension.

Hypertensive is a disease characterized by persistently high blood pressure. Hypertension is one of the largest deaths causing disease for the human being. Since it is a chronic disease so it necessitates long term treatment. Hypertensive a cardiovascular disease account for a large proportional of all death and disability worldwide. Hypertensive is directly responsible for 57% of all strokes death and 24% of coronary heart disease in India. Transdermal system is ideally suited for disease that demand chronic treatment. In this project TDDS are mainly used for the delivery of antihypertensive drug from transdermal patches.[4]

Telmisartan is a angiotensin II receptor antagonist, Telmisartan interferes with the binding of angiotensin II to the angiotensin II AT_1 receptor by binding reversibly and selectively to the receptor in vascular smooth muscle and adrenal gland. As angiotensin II is a vasoconstrictor,

which also stimulates the synthesis of and release of aldosterone, blockage of its result in decrease vascular resistance hence B.P falls.[5]

MATERIALS and METHODS

Telmisartan IP was obtained as a gift sample from Unichem Pharmaceutical Laboratory, Baddi, Himanchal Pradesh. Polymer such as Eudragit Rs-100 was also obtained as a gift sample from Evonic India Pvt, Ltd, Research Centre, Mumbai and other excipients such as Hydroxyl Propyl Methyl Cellulose, Ethyl Cellulose, Plasticizer Dibutyl Phthalate and Permeability Enhancer Dimethyl Sulfoxide were available in department.

Preformulation studies

The Preformulation studies of drug were conducted as per IP.

FTIR Studies of drug and excipients

FTIR spectra was recorded for Telmisartan and prepared transdermal patches using Thermoscintific FTIR in the region of 4000-500 cm^{-1}. 10 mg sample were mixed with potassium bromide (200-400 mg) and compressed disc were placed in the light path and spectra was obtained. After running the spectra, significant peaks relating to major functional groups were identified. Spectra of subsequent sample of the same compound were comparing with original.[6]

Melting point of the drug

Melting point of the drug (Telmisartan) was determined by capillary tube method. In this method, small amount of the drug was filled in the capillary and one end of the capillary was packed. The capillary tube was placed in liquid filled Thiele tubes over gas burner. The temperature was increased then and note down the temp. When drug was start to melt. Repeat these procedures at least three times and take average of them. The melting point of Telmisartan drug is 262-263^{0}C.[7, 8, 9]

Partition Coefficient

For determination of partition coefficient of drug, equal ratio of chloroform and water, (10ml each) was taking. In this mixture excess amount of drug was added and shaked properly in separating funnel for mixing the drug with both phases and leave the mixture of solution for 24 hr for proper separation into two phases such as chloroform and water. After 24 hrs chloroform and water phases separated individually in beaker. Sonicate the obtained filtrate

for better clearance of the solution for 15 minute at 80 Hz. Perform the dilution and check the absorbance at 295nm and find out the concentration of drug in each phases. Repeat the same procedure in triplicate for better accuracy.[10, 11]

Analytical method adoption by UV spectrophotometer

For the analysis of Telmisartan concentration in formulation, the UV spectrophotometer was used and for method adopting following steps were performed.

Preparation of 0.1N NaOH (100 ml)

0.4 mg sodium hydroxide was weighted and transferred in 100 ml volumetric flask and volume was maked up to 100 ml with water.[12]

Preparation of stock solution

For the preparation of stock solution 10 mg of the pure drug was accurately weighed and dissolved in 10 ml 0.1 N NaOH and then volume was made up to 100 ml with 0.1 N NaOH to give standard stock solution 100 µg/ml. This solution works as stock solution.[13, 14]

Determination of λ max of Telmisartan

Stock solution of Telmisartan (100 µg/ml) was prepared in 0.1 NaOH. From stock solution the sample of concentration 10 µg/ml prepared by appropriate dilution. The sample were filtered and scanned in the range 200-400 nm using UV spectrophotometer to determine λ max.[15, 12]

Preparation of calibration sample

Calibration sample was prepared from stock solution (100 µg/ ml). From stock solution 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1.0 ml solution was withdrawn from stock solution and volume was make up to with 0.1 N NaOH to got serial dilution (1,2,3,4,5,6,7,8,9 and 10 µg/ml).[13,14]

Preparation of calibration curve for Telmisartan

To prepare calibration curve serial dilution of Telmisartan in concentration range 1 µg/ml to 10 µg/ml were prepared in 0.1NaOH and absorbance of these dilution were determined on UV spectrophotometer at λ max 295 nm using NaOH as blank. The absorbance values corresponding to each concentration were than statistically evaluated and plotted as a standard graph between absorbance on Y-axis and concentration on X –axis.[13, 14]

Formulation of Transdermal patches

Polymer Matrix-diffusion type transdermal patches containing Telmisartan drug was prepared by solvent casting method. This required proportion of polymers as per formulation table (hydroxyl propyl methyl cellulose, ethyl cellulose, eudragit RS-100 were weight in requisite ratio as per formulation table design and dispersed in 15 ml of casting solvent that is methanol 15 ml and 5 ml of chloroform by continuous stirring for 5 to 6 hrs. Then dibutyl phthalate (30% w/v of polymeric weight) was incorporated as a plasticizer and dimethyl sulfoxide (20% and 30% w/w of polymeric weight) was incorporated as a penetration enhancer in formulation. At last Telmisartan (100 mg) was added into the formulation with continuous stirring .After complete mixing solution was allow to stand for 20 minute to ensure the removal of air bubbles. Then resulting solution was poured on aluminum foil placed on glass Petridis and dried at room temperature for 24 hrs. The rate of evaporation was controlled by inverting a funnel over the Petridis. The solvent completely dried in 24 hrs where dibutyl phthalate and dimethyl sulfoxide remained in drug polymer matrix. After drying the films were peeled off from the glass Petridis. The patches were then stored in a desiccator containing calcium chloride.[15, 16, 17]

Table -1Formulation chart

F.C	Drug (mg)	Polymeric ratio HPMC: EC: E RS 100	DBT (ml)	POLYMER			DMSO (ml)	SOLVENT Methanol, chloroform (ml)
				HPMC (mg)	EC (mg)	Eudragit RS 100 (mg)		
F1	100	2:1:0	0.129	300	150	0	0	3:1
F2	100	2:1:0	0.129	300	150	0	0.081	3:1
F3	100	2:1:0	0.129	300	150	0	0.122	3:1
F4	100	5:1:0	0.129	375	75	0	0	3:1
F6	100	5:1:0	0.129	375	75	0	0.081	3:1
F7	100	5.1:0	0.129	375	75	0	0.122	3:1
F5	100	5:0:1	0.129	375	0	75	0	3:1
F8	100	5:0:1	0.129	375	0	75	0.081	3:1
F9	100	5:0:1	0.129	375	0	75	0.122	3:1

Evaluation of prepared TDDS

The physicochemical evaluations of transdermal patches are based on following parameter.

Uniformity of 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.[10, 18, 19]

Weight variation study

Weight variation was studied individually. Weighing 5 randomly selected patches and calculating the average weight. The individual weight should not deviate from the average weight. This test provides a means for measuring uniformity in terms of the weight within a batch as well as batch to batch.[20, 21]

Folding endurance

Folding endurance involves determining the folding capacity of the films subjected to frequent extreme conditions of folding. Folding endurance is determined by repeatedly folding the film at the same place until it break. The number of times the films could be folded at the same place without breaking is known as folding endurance.[22, 23]

Percentage moisture uptake

Weighed films are kept in desiccators at room temperature for 24 h. These are then taken out and exposed to 84% relative humidity using saturated solution of Potassium chloride in desiccators until a constant weight is achieved. % moisture uptake is calculated as given below.[24]

$$\% \text{ Moisture uptake} = \frac{\text{final weight} - \text{inital weight}}{\text{inital weight}} \text{x}100$$

Percentage moisture loss

Accurately weighed films of each formulation were kept in desiccators and exposed to an atmosphere of 98% relative humidity (containing anhydrous calcium chloride) at room temperature and weighed after 48 hrs. The test was carried out in triplicate. The percentage of moisture loss was calculated as the difference between initial and final weight with respect to initial weight for obtained the standard curve of drug in solution. [25, 26]

$$\% \text{ Moisture loss} = \frac{\text{inital weigght} - \text{final weight}}{\text{final weight}} \text{x}100$$

Drug content determination

Transdermal patch of specified area was cut into small pieces and taken into a 100 ml 0.1N NaOH solution on mechanical shaker for 20 minute so as to allow the whole drug to dissolve. 1 ml withdrawn from stock solution and volume was maked up to 10 ml by 0.1N NaOH

solution. The solution was filtered and analyzed spectrophotometrically at λ max at 295nm wavelength for obtained the concentration of drug in solution.[27]

Flatness

The construction of film strip cut from a drug loaded matrix film is an indicator of its flatness. Longitudinal strips were cut out from the prepared medicated matrix film, the initial length of film was measured, and then kept at room temperature for 30 minute. The variations in the length due to non uniformity in flatness were measured. Flatness was calculated by measuring construction of strips and zero percentage of construction was considered to be equal to 100% flatness.[28, 29]

$$\% \text{ construction} = \frac{\text{initial lenght of each strips in cm} - \text{final lenght of each strips in cm}}{\text{final lenght of each strips in cm}} \times 100$$

In vitro drug release studies

The in vitro release was carried out the semipermeable membrane using open ended cylinder. The cylinder consists of two chambers, the donor and the receptor compartment. The donor compartment was opened at the top and was exposed to atmosphere. The temperature was maintained at 37^0C and receptor compartment was provided with sampling port. The diffusion medium used was 7.4 pH buffer solutions. The drug containing patch was kept in the donor compartment and it was separated from the receptor compartments by semi permeable membrane. The semipermeable membrane was previously soaked for 24 hrs in 7.4 pH buffer solution. The receptor compartment containing 100 ml of 7.4 pH buffer solution in a beaker was maintaining temperature at 37±2°C and stirred at 100 rpm with magnetic beads operated by magnetic stirrer.1 ml solution withdrawn from receptor comportment and volume maked up to 10 ml with 0.1N NaOH solution. A sample of 1 ml was withdrawn at predetermined time intervals and replaced with fresh 0.1N NaOH solution due to maintaining sink condition. The concentration of drug was determined by spectrophotometrically at 295 nm.[30, 31, 32]

As per formulation table nine formulations (from F1-F9) of Telmisartan TDDS was developed and evaluated to optimize the formulations among these. Each formulation was developed in three batches to minimize the manual mistakes which were statically evaluated.

RESULTS AND DISCUSSION

Preformulation Studies

FTIR studies

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

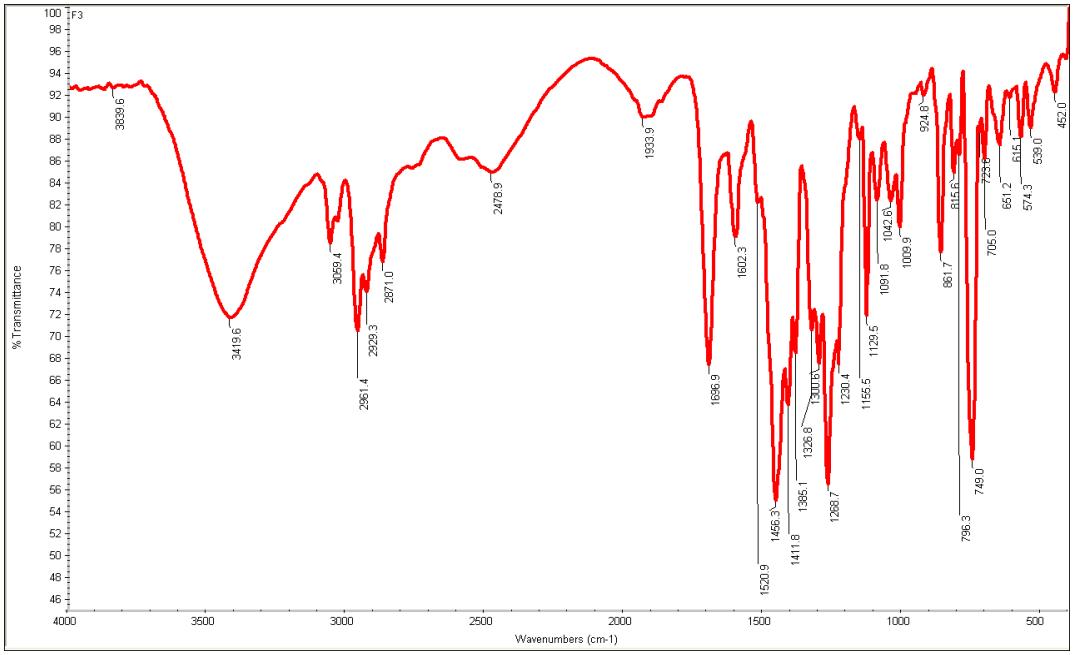

Figure -1 FTIR Spectra of Telmisartan

The FTIR spectrum of Telmisartan exhibits following characteristics peaks at, 3419.6 Cm^{-} for N-H Stretching , 3059 Cm^{-} for Aromatic C-H Stretching, 2961.4 Cm^{-} for Aliphatic C-H Stretching,1696.9 Cm^{-} for Carbonyl Groups , 1602cm^{-} for Aromatic C=C Bends and Stretching , 1520 Cm^{-} for C=C In Plan Ring Stretching, 1456.3 Cm^{-} for Aromatic C=C Groups, 1385.1 Cm^{-} for C-H Asymmetrical Stretching,1268.7 Cm^{-} for Carbolic Acid Functional Groups, 924.8 Cm^{-} for Alkenes, 919-922 Cm^{-} for Isopropyl Groups, 932-926 Cm^{-} for t-Butyl Groups, 900-675 Cm^{-} for Out Of Plane C-H Bending Vibration, 720 Cm^{-} for Rock Methylene Groups.

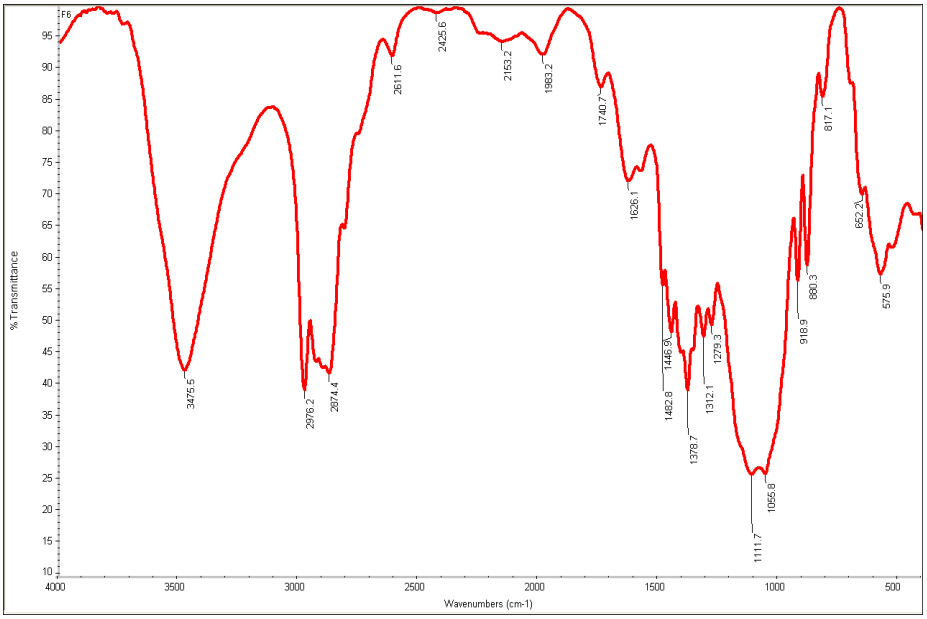

Figure -2 FTIR Spectra of EC

The FTIR spectrum of Ethyl cellulose exhibits following characteristics peaks at,3475.5cm^{-1} for N-N stretching, 2976.2 cm^{-1} for C-H aliphatic group, 1626.1 cm^{-1} for C=C bend, stretching, 1378.7 cm^{-1} for C-H Asymmetrical stretching mode, 1279.3 cm^{-1} for CH_3 methylene groups, 918.9 cm^{-1} for isopropyl groups

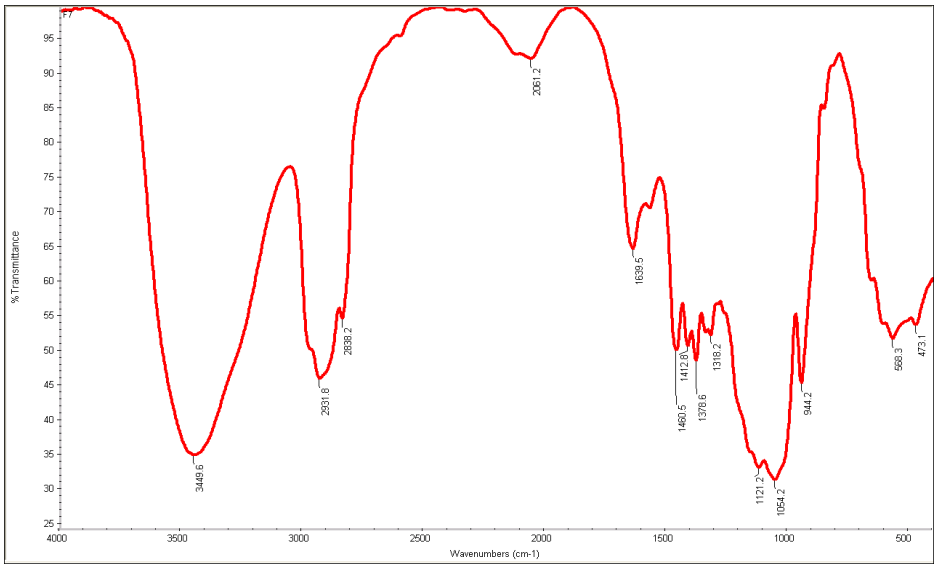

Figure-3 FTIR Spectra of HPMC

The FTIR spectrum of HPMC exhibits following characteristics peaks at 3449.6 cm^{-1} for N-H stretching group, 2931.8 cm^{-1} for C-H aliphatic groups, 1378.6 cm^{-1} for C-H asymmetric stretching mode.

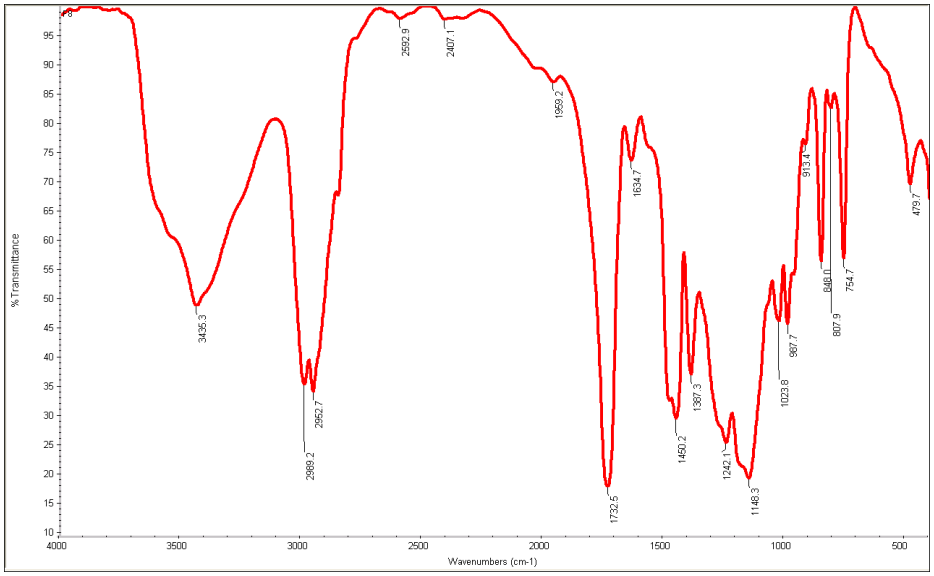

Figure- 4 FTIR Spectra of Eudragit RS-100

The FTIR spectrum of Eudragit RS-100 exhibits following characteristics peaks at 1387.3 cm^{-1} for C-C asymmetrical stretching.

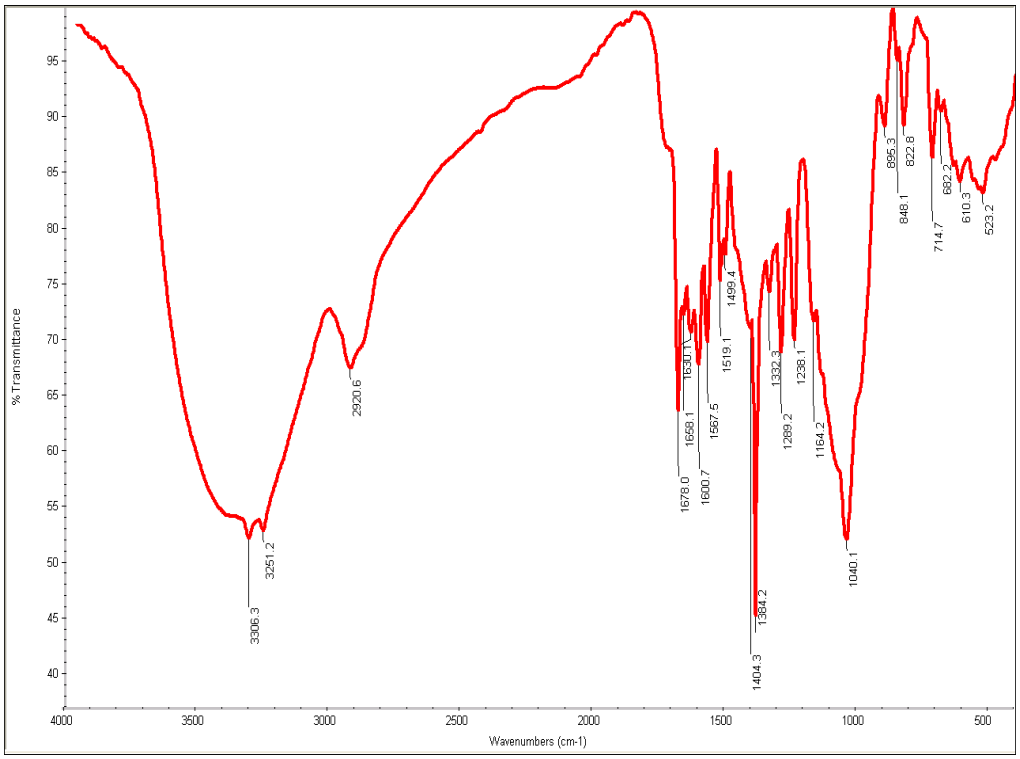

Figure- 5 FTIR Spectra of F9 formulation

The FTIR spectrum of batch F9 (HPMC:EC:Eudragit RS100 ratio 5:0:1) of transdermal patch there are following characteristics peaks at 3306.3 cm^{-1} for N-H stretching, 2920.6 cm^{-1}

for C-H stretching, 1600.7 cm^{-1} for C=C aromatic bending, stretching, 1332.3 cm^{-1} for methylene groups.

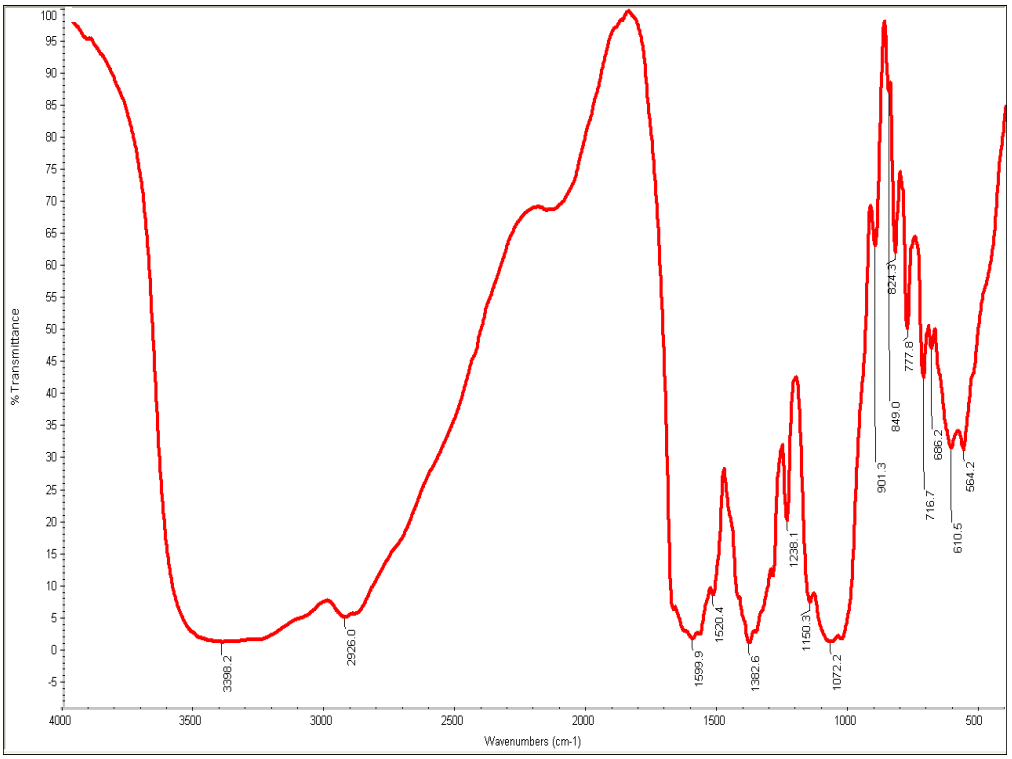

Figure -6 FTIR Spectra of F1 formulation

The FTIR spectrum batch F1(HPMC: EC: Eudragit RS100 ratio 2:1:0) exhibits following characteristics peaks at 3398.2 cm^{-1} for N-H stretching, 2926.0 cm^{-1} for C-H aliphatic group,1599.9 cm^{-1} for C=C aromatic bend and stretching, 1382.6 cm^{-1} for C-H asymmetrical stretching, 1150.3, 1238.1 cm^{-1} for CH_2 Methylene twisting, wagging Groups, 901.3 cm^{-1} for Alkenes, 716.7 cm^{-1} form ethylene rock in phase.

Melting point

Melting point of the drug was found to be 262^0 C, and the normal range 261-263^0C.

Partition coefficient

Partition coefficient of the drug was found to be 6.62 (log $P_{O/W}$), and the normal range log $P_{o/w}$ is 6.68.

Determination of λ max of Telmisartan

From stock solution 10 µg/ml solutions of Telmisartan was prepared in 0.1 N NaOH. The solution were scanned at the wavelength range of 200-400 nm. The λ max for Telmisartan in 0.1NaOH was found to be 295nm.

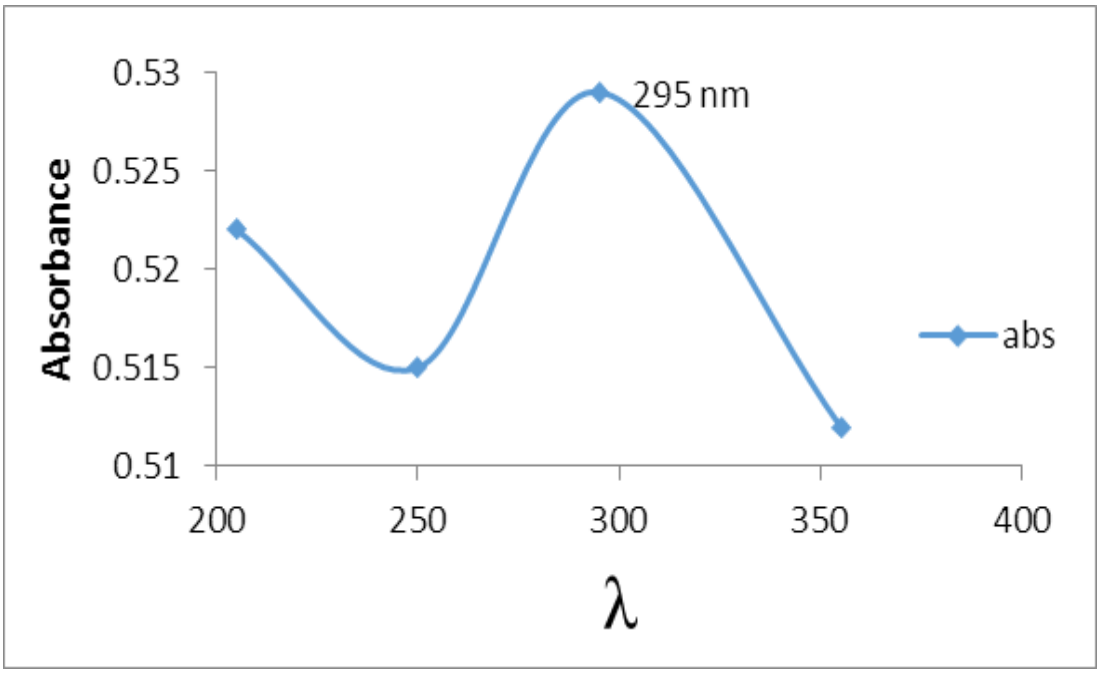

Figure-7 Spectra of Telmisartan in 0.1 N NaOH

Calibration curve of Telmisartan in 0.1 N NaOH

For the preparation of Calibration curve, the calibration sample were prepared from stock solution (1, 2, 3, 4,5 ,5, 6, 7, 8 ,9, 10 µg/ml). The absorbance of sample was determined at 295 nm by using Shimadzu 1601 UV spectrophotometer. The absorbance's on different concentration are as following,

Table - 2 Absorbance of Telmisartan in 0.1 N NaOH at 295 nm

Concentration (µg/ml)	Regressed Values of Absorbance
0	0
1	0.051
2	0.105
3	0.159
4	0.213
5	0.267
6	0.321
7	0.375
8	0.429
9	0.483
10	0.537

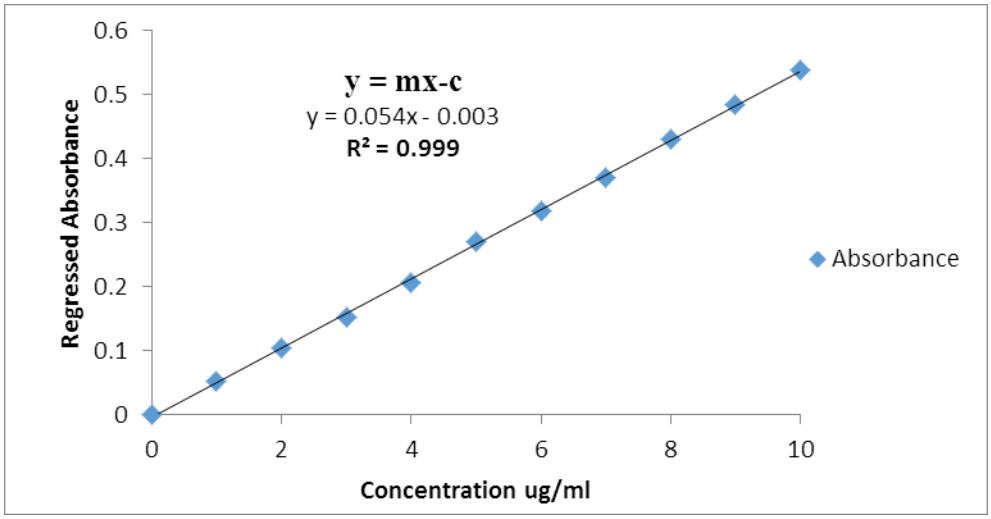

Figure -8 Calibration curve of Telmisartan in 0.1N NaOH

Physicochemical Evaluation of TDDS

Table - 3 The results of all 9-batches of transdermal patches

F.C / S.N	F1	F2	F3	F4	F5	F6	F7	F8	F9
Thickness (mm)	0.118 ±0.007	0.117 ±0.009	0.152 ±0.003	0.121 ±0.005	0.156 ±0.001	0.152 ±0.004	0.159 ±0.006	0.156 ±0.004	0.146 ±0.004
Weight variation (g)	0.055 ±0.003	0.051 ±0.001	0.056 ±0.002	0.052 ±0.001	0.052 ±0.009	0.057 ±0.006	0.045 ±0.010	0.051 ±0.011	0.049 ±0.013
% moisture uptake	4.19 ±1.62	2.15 ±0.740	2.09 ±0.308	2.96 ±1.598	3.50 ±0.957	2.61 ±0.320	2.45 ±1.05	3.28 ±0.700	3.25 ±0.873
% moisture loss	2.53 ±0.821	1.86 ±0.915	1.33 ±0.230	1.38 ±0.566	2.67 ±0.965	1.49 ±0.093	2.12 ±0.377	2.90 ±0.508	2.91 ±0.933
Folding endurance	195 ±9.00	205 ±15.00	225 ±21.00	219 ±11.00	229 ±8.00	221 ±15.00	209 ±16.00	248 ±8.00	231 ±16
% drug content	79.72 ±2.00	96.25 ±0.377	95.16 ±2.30	87.67 ±2.70	88.16 ±1.90	84.38 ±1.70	78.61 ±1.40	98.74 ±0.38	82.99 ±1.10

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

Percentage drug release of formulation

Drug released from transdermal patches simply by diffusion. The transdermal patches of Telmisartan were prepared as per described formulation table and showed drug release as following, nine-batches of Telmisartan transdermal patches were also evaluated on the basis of time dependent percentage drug release and interpritate which one of the patches showed better release of drug in out of nine-batches of the transdermal patches containing different ratio of drug and polymers.

Table - 4 Cumulative % drug release

Cumulative Percentage (%) Drug Release									
Time in hrs.	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
0.5	3.91 ±0.94	1.34 ±0.44	1.18 ±0.31	6.73 ±0.57	2.13 ±0.58	0.78 ±0.00	5.13 ±0.61	6.21 ±0.44	1.87 ±0.41
1.0	5.30 ±1.38	5.61 ±0.67	2.72 ±0.62	7.25 ±0.68	2.87 ±0.68	1.31 ±0.22	6.37 ±1.25	9.5 ±0.68	3.55 ±0.42
1.5	6.56 ±1.60	10.67 ±0.79	5.52 ±0.44	8.09 ±0.68	3.41 ±0.50	1.77 ±4.10	7.46 ±0.81	10.80 ±0.45	4.64 ±0.76
2.0	8.44 ±1.07	15.54 ±0.58	8.148 ±0.53	13.55 ±0.98	4.48 ±0.50	4.14 ±0.59	9.23 ±0.85	12.31 ±0.57	6.49 ±0.65
2.5	9.12 ±1.87	17.04 ±0.81	11.97 ±0.54	16.76 ±0.98	6.02 ±0.51	4.42 ±0.69	10.02 ±0.74	13.39 ±0.57	7.94 ±1.64
3.0	10.41 ±2.10	23.03 ±1.30	12.93 ±0.75	18.99 ±1.02	7.83 ±0.51	6.37 ±0.80	12.34 ±0.57	16.35 ±0.80	9.06 ±0.56
4.0	11.41 ±1.67	31.09 ±0.97	14.65 ±0.66	28.07 ±1.13	11.34 ±0.61	8.91 ±0.71	16.72 ±0.80	17.52 ±0.70	13.04 ±0.66
5.0	23.27 ±1.69	40.13 ±0.84	19.10 ±0.66	29.37 ±1.11	12.34 ±0.61	15.11 ±0.42	19.10 ±1.12	23.61 ±0.93	15.33 ±0.71
6.0	33.73 ±1.47	45.00 ±1.0	25.11 ±0.66	32.03 ±1.09	12.42 ±0.81	18.06 ±0.72	23.55 ±1.23	24.28 ±0.94	17.84 ±0.69
8.0	51.08 ±2.17	47.00 ±0.97	36.26 ±1.09	34.90 ±1.02	29.30 ±0.73	28.79 ±0.73	32.42 ±1.05	31.61 ±0.61	27.05 ±0.47
24	56.55 ±2.19	61.39 ±0.76	70.22 ±0.69	63.2 ±1.00	56.09 ±0.54	54.79 ±0.50	44.82 ±0.78	56.38 ±0.86	49.07 ±0.59
27	58.45 ±1.19	70.29 ±0.98	80.77 ±0.69	65.23 ±1.11	62.86 ±0.55	57.41 ±0.54	49.11 ±1.01	60.33 ±0.53	51.84 ±0.80
30	59.92 ±1.56	74.55 ±0.76	82.04 ±.93	68.23 ±1.03	68.33 ±0.66	61.29 ±0.74	49.99 ±1.12	77.17 ±0.63	55.54 ±0.71
48	62.45 ±1.55	94.55 ±1.89	83.94 ±0.92	77.35 ±1.23	74.44 ±0.75	72.35 ±0.74	51.00 ±1.01	97.29 ±1.32	61.92 ±0.72

All the values are mean ± SD, n=3.

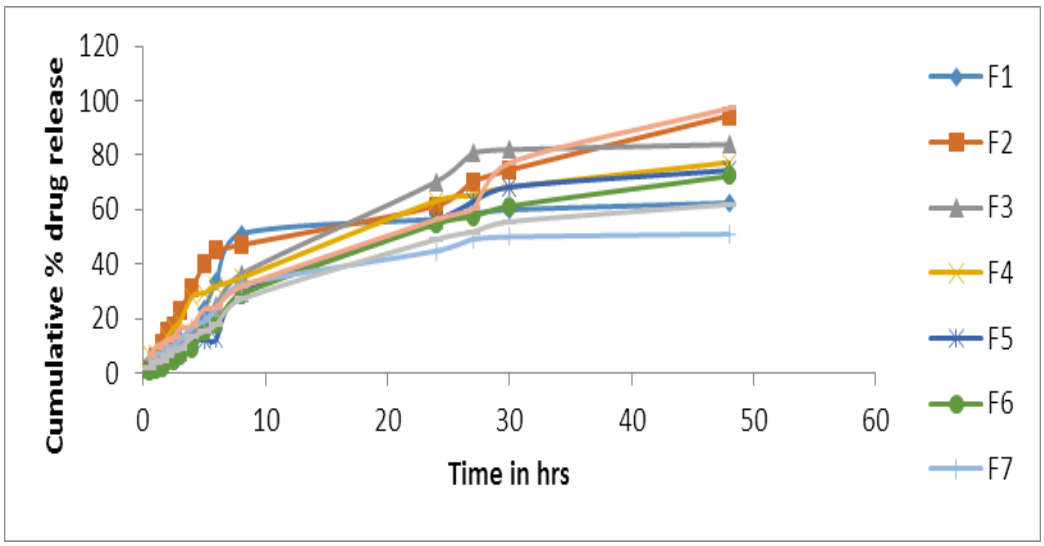

Figure -8 Cumulative % drug release of patch F1 to F9

DISCUSSION

Firstly the Preformulation studied was performed on Telmisartan and drug was found to be up to mark as per IP.

The analytical method was selected to evaluated the drug concentration in the formulation for this purpose, the UV spectrophometric method was selected to the determination of λ max for drug which was found to be 295 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 Telmisartan in transdermal drug delivery system.

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 IR spectra, it was clear that there was no change in peaks position of Telmisartan, when mixed with the polymer. Thus there was no interaction between Telmisartan and polymers the formulation.

Transdermal patches were successfully prepared by polymer matrix diffusion-controlled transdermal drug delivery system.

In this project nine batches of transdermal patches of Telmisartan were prepared by mixing of plasticizer (DBT), Drug (Telmisartan) and different ratio of polymers (HPMC, EC, Eudragit RS-100), permeability enhancer (DMSO) as per formulation table.

The addition of plasticizer was found to be essential to improve mechanical properties of patches and easily remove from aluminum foil surface without rapture.

The physical appearances of the various formulations in term of their uniformity, transparency, smoothness, flexibility, stickiness, homogenicity, opaque properties were recorded.

Prepared transdermal patches of Telmisartan were evaluated for their physicochemical evaluation the parameters selected were thickness, weight variation, % moisture content, % moisture loss, folding endurance, % drug content and invitro drug release through semipermeable membrane.

The thicknesses of patches F1-F9 were varied such as 0.118, 0.117, 0.152, 0.121, 0.156, 0.152, 0.159, 0.156 and 0.146 mm with standard deviation ranges F1-F9 as 0.007, 0.009,

0.003, 0.005, 0.001, 0.004, 0.006, 0.004, and 0.004. The value in the film thickness measurements ensured uniformity of the patches prepared by solvent evaporation method.

The weight variation of patches F1-F9 were obtained ranges as 0.055, 0.051, 0.056, 0.052, 0.052, 0.057, 0.045, 0.051 and 0.049 g having the standard deviation of formulation F1-F9 ranges 0.003, 0.001, 0.002, 0.001, 0.009, 0.006, 0.010, 0.011, 0.013 which indicating that different batches with in patch weights generally similar.

The % moisture uptakes of patches F1-F9 were found to 4.19, 2.15, 2.09, 2.96, 3.50, 2.61, 2.45, 3.28, 3.25 with the standard deviation ranges F1-F9 as 1.62, 0.74, 0.308, 1.59, 0.957, 0.320, 1.05, 0.700 and 0.873.

The moisture content indicates that the increase the concentration of hydrophilic polymer that is HPMC was directly proposnal to increases the moisture content of the patches.

The % moisture loss of patches F1-F9 were found to be as 2.53, 1.86, 1.33, 1.38, 2.67, 1.49, 2.12, 2.90, 2.91with the standard deviation 00.821, 0.915, 0.230, 0.566, 0.965, 0.093, 0.377, 0.508, 0.933.

Folding endurance of all the patches F1-F9 were found to be in the ranges 195, 205, 225, 219, 229, 221, 209, 248, 231 folds until breaked the patches and the standard deviation were found to be as 9.00, 15.00, 21.00, 11.00, 8.00, 15.00, 16.00, 8.00, 16.00.

All the patches were 100% flat in each formulation.

The % Drug concent of formulation F1-F9 were found to be 79.72, 96.25, 95.16, 87.67, 88.16, 84.38, 78.61, 98.74, 82.99 having the standard deviation of patches F1-F9 as 2.00, 0.377, 2.30, 2.70, 1.90, 1.70, 1.40, 0.38, and 1.10. All the formulation indication that the drug was uniformly distributed through the patches and evidenced by the low value of standard deviation.

Cumulative % drug release was evaluated after physicochemical evaluation along with release studies was conducted on the different batches.

The cumulative % drug release along with its standard deviation for F1, F2, F3, F4, F5, F6, F7, F8, F9 were found to be 62.45% ±1.55, 94.55% ± 1.89, 83.94% ± 0.92, 77.35% ±1.23, 74.44% ± 0.75, 72.35% ± 0.74, 51.00% ±1.01, 97.29% ± 1.32, 61.92% ± 0.72 at 48 hrs.

The formulation F8 ratio 5:0:1 (HPMC: EC: Eudragit RS-100) with DMSO as permeation enhancer was considered as best formulation, since it showed maximum invitro drug release as 97.29% ± 1.32 at 48 hrs.

The drug release from all the patches are ordered as F8> F2> F3> F4> F5> F6> F1> F9 > F7.Unlike the formulation F1, F2, F3, F4, F5, F6, F7, F8, F9, the F8 achieved a high cumulative amount of drug permeation at the end of 48 hrs. Based on physiochemical experiments, F8 was chosen for further studied.

In above all formulation F8 was found to showed maximum release of drug at 48 hrs. F8 contains 97.29 % release at 48 hrs. Among formulation F1-F9, F8 was found to be most suitable candidate for further studies due to its better invitro release pattern.

CONCLUSION

After the studies of invitro release F8 formulation was found to be best formulation because it's released 97.29 % drug at 48 hrs. F8 formulation contained drug, DMSO, DBT and polymers HPMC: EC: Eudragit RS-100 having polymeric ratio 5:0:1. Further in-vivo studies can be conducted to get better results with this formulation.

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