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The Development, Evaluation and *In Vitro* Release Study of the Terbinafine Transdermal Patch

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Abstract

Transdermal drug delivery is an alternative route for systemic drug delivery, which minimizes the absorption and increase the bioavailability. Orally Terbinafine undergoes extensive metabolism and frequent high doses are required to maintain the therapeutic level as a result, dose development toxic effect. The purpose of this research work was to formulation and evaluation of transdermal drug delivery system of Terbinafine using various polymers such as HPMC E25, Eudragit-RS100 and PVP K25 with different proportions by solvent evaporation technique. The Fourier transform infrared study revealed no physical or chemical interactions between Terbinafine and excipients. The prepared formulations were evaluated for different physicochemical characteristics such as thickness, folding endurance, drug content, percentage moisture absorption, and percentage moisture loss. The diffusion studies were performed by using modified Franz diffusion cells. The result of dissolution studies shows that formulation, SA12 showed maximum release of 92.56% in 06 h, whereas SA22 showed minimum release of 45.89% in 06 h. Based on the drug release and physicochemical values obtained the formulation SA 12 is considered as an optimized formulation, which shows higher percentage of drug release.

Keywords: Terbinafine; Eudragit-RS 100; PVP K25; Transdermal patch; Solvent evaporation technique

Introduction

The potential of intact skin as the route of drug administration has been known for years; the inspiration for using skin for the delivery of drug is obtained from ancient times [1]. Utilization of skin as a route for delivering drugs as has been an alternative to conventional methods including injections and tablets. Advantages of transdermal drug delivery include the avoidance of pain, hepatic first-pass metabolism, sustain drug release, easy use and withdrawal in case of side effects. However, the major limitation for transdermal drug delivery system (TDDS) is that the skin has the outmost layer of the epidermis; the stratum corneum (SC) provides an outstanding barrier towards the absorption of substances [2]. Oral delivery of complex molecules such as peptides and proteins has been hampered by the degradation in the gastrointestinal tract. As a result, various types of particulate systems such as biodegradable microspheres and liposomes have been proposed as potential delivery vehicles to protect these drugs in the gastrointestinal tract. Unfortunately, these particulates generally display low oral absorption efficiencies [3]. Millions of unsafe injections are delivered in developing countries, and the transmission of certain blood borne pathogens via this route is thought to be a major public health problem [4]. Several technological advances developed to overcome this challenge. These advances can be broadly divided into two categories; physical and chemical methods. Physical methods employed for increasing transport of molecules across the skin uses mechanical, electrical, magnetic or thermal energy source to promote transport of macromolecules by disrupting the skin membrane. Examples of physical approaches include the use of micro needle array, ballistic liquid jet, high velocity particles, ultrasound, electric current, abrasion, ablation, lasers, pressure waves, radiofrequency thermal ablation, magnetophoresis of diamagnetic solutes and thermophoresis [5].

To overcome the barrier properties of the skin for drugs is an incorporation of suitable vehicles. Substances that promote the penetration of topically applied drugs through stratum corneum and epidermis are commonly referred to as skin permeation enhancers, accelerants, adjuvant, or sorption promoters [6]. Dimethylsulfoxide (DMSO) is widely studied penetration enhancers in many areas of pharmaceutical sciences as a "universal solvent". DMSO denatures the intercellular structural protein of the stratum corneum [7]. Over the last 2-3 decades, the skin has become an important route for the delivery of drugs for topical, regional, or systemic action. The skin has evolved as a physical and biochemical protective barrier, prevents the loss of water from the body, and guards against entry into the body of external toxic chemicals and infectious agents. The stratum corneum, which is the outermost layer of the skin and comprised of keratin-rich cells embedded in multiple lipid bilayers, has been considered the rate-limiting structure governing percutaneous absorption of many kinds of permeants [8].

Terbinafine is a well-established antifungal agent, widely used in fungal infections, its chemically [(2E)-6, 6-dimethylhept-2-en-4-yn-1-yl] (methyl) (naphthalen-1-ylmethyl) amine. Upon oral administration of Terbinafine tablets as a result of first-pass metabolism is approximately 40%. A single oral dose of 250 mg Terbinafine results in peak plasma concentration (C_{max}) of 0.83 µg/ml within 2 h of administration. The absorption half-life is 0.8 h and the distribution half-life is 4.6 h. This originates the need of an alternative route of administration, which can bypass the hepatic first-pass metabolism. Transdermal route is an alternative choice of route of administration for such drugs. Efforts offer added advantages, such as maintenance

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of constant and prolonged drug level, reduced frequency of dosing, minimization of inter and intra patient variability, self administration and easy termination of medication, leading to patient compliance by using different polymers ratio and penetration enhancers in optimized quantity [9].

Materials and Methods

Terbinafine was received as a gift sample from Shreya Life Sciences (Aurangabad, India). Poly Vinyl Pyrrolidone K25 (PVP K25) and Eudragit RS-100 were generous gift from Evonik India Pvt. Ltd. (Mumbai, India). Dimethyl sulfoxide (DMSO) and di-n-butyl-phthalate (DBP) were procured from Loba Chemie, Mumbai. Other materials used in the study ethanol, chloroform, methanol, dichloromethane were of analytical grade. Double-distilled water was used throughout the study.

Partition coefficient determination

The partition coefficient studies were performed by using n-octanol as non-aqueous phase and water as an aqueous phase. The two phases were mixed in equal quantities and kept for saturation with each other in separating the funnel. After mixing the system remain undisturbed for half an hour. About 10 mg of drug added to this solution and was occasionally shaken in separating the funnel. After shaken the resulting solution was kept a site for 24 hr. After 24 hr, two phases were separated in a separating funnel. The aqueous phase was filtered. Suitably diluted and amount of Terbinafine in an aqueous phase was determined by measuring absorbance at 223.5 nm using ultraviolet (UV) spectrophotometer. The partition coefficient of Terbinafine was calculated from the ratio between the concentration of Terbinafine in organic and aqueous phases from the below mentioned formula [10].

$$\text{Partition coefficient} = \frac{\text{Concentration of drug in non-aqueous phase}}{\text{Concentration of drug in aqueous phase}}$$

Fourier transforms infrared (FT-IR)

FT-IR technique was used to study the physical and chemical interaction between drug and excipients. The FT-IR study revealed no physical or chemical interactions between drug and polymer [11,12].

Differential scanning calorimetry (DSC)

DSC analysis is a thermo analytical tequnique used to identify the difference in the amount of heat required to increase the temperature of a sample and reference as a function of temperature. DSC, thermo analysis gives characteristic and comparable results for the pure drug and the prepared formulation as patch [13].

Preparation of terbinafine transdermal patches

The transdermal patches containing Terbinafine were prepared by solvent evaporation technique in glass ring; contain mixture of polymer I (HPMC E5) and polymer II (PVPK 25 OR Eudragit RS-100) were dissolved in 3 ml solvent Methanol: Chloroform, (1:1) by using magnetic stirrer; then the 72 mg plasticizer polyethylene glycol 400, 24 mg penetration enhancer dimethyl sulfoxide and finally added 6 mg Terbinafine in the above polymeric solution and stirred for 15 minutes. Final volume of above solutions was placed on the aluminium foil wrapped and placed in Petri dish to facilitate the evaporation of solvent at a controlled rate over the drying period of 12 hr by using inverted funnel. The dried films were removed; cut into specified area and kept in desiccators until used (Table 1) [14].

Evaluation of patches

Physical appearance: All the prepared patches were visually inspected for color, clarity, flexibility and smoothness [15].

Thickness of the patch: The thickness of the drug loaded patch was measured in different points by using a digital micrometer and determines the average thickness and standard deviation for the same to ensure the thickness of the prepared patch, (Table 2) [16].

Weight uniformity: The prepared patches were dried at 60°C for 4 hr before testing. A specified area 3 × 3 cm of the patch was cut in different parts of the patch and weigh in digital balance. The average weight and standard deviation values are to be calculated from the individual weight, (Table 2) [16].

Folding endurance: A strip of a specific 2 × 2 cm area was cut evenly and repeatedly folded at the same place till it broke. The number of times the film could be folded at the same place without breaking gave the value of the folding endurance, (Table 2) [17].

Percentage moisture absorption

The weighed films were kept in desiccators at room temperature for 24 hr containing a saturated solution of potassium chloride in order to maintain 84% RH. After 24 hr the films are to be reweighed and determine the percentage moisture uptake from the below mentioned formula, (Table 3) [17].

Percentage Moisture Uptake=Final Weight-Initial Weight/Initial Weight × 100

Batch	Polymer I (mg)	Polymer II*(mg)	Batch	Polymer I(mg)	Polymer II**(mg)	Polymer II* (mg)
SA1	200	10	SA25	160	10	-
SA2	200	20	SA26	160	20	-
SA3	200	30	SA27	160	30	-
SA4	200	40	SA28	160	40	-
SA5	180	10	SA29	140	10	-
SA6	180	20	SA30	140	20	-
SA7	180	30	SA31	140	30	-
SA8	180	40	SA32	140	40	-
SA9	160	10	SA33	200	10	10
SA10	160	20	SA34	200	20	20
SA11	160	30	SA35	200	30	30
SA12	160	40	SA36	200	40	40
SA13	140	10	SA37	180	10	10
SA14	140	20	SA38	180	20	20
SA15	140	30	SA39	180	30	30
SA16	140	40	SA40	180	40	40
SA17	200	10**	SA41	160	10	10
SA18	200	20**	SA42	160	20	20
SA19	200	30**	SA43	160	30	30
SA20	200	40**	SA44	160	40	40
SA21	180	10**	SA45	140	10	10
SA22	180	20**	SA46	140	20	20
SA23	180	30**	SA47	140	30	30
SA24	180	40**	SA48	140	40	40

*PVP K25; **EudragitRS-100

Table 1: Formulation of Terbinafine transdermal patches SA1-SA48.

Batch	T	WU	FE	Batch	T	WU	FE
SA1	0.161 ± 0.0103	0.305	98	SA25	0.152 ± 0.0028	0.210	105
SA2	0.160 ± 0.0241	0.295	96	SA26	0.151 ± 0.0025	0.230	70
SA3	0.158 ± 0.0165	0.310	97	SA27	0.151 ± 0.0025	0.265	98
SA4	0.152 ± 0.0132	0.275	95	SA28	0.156 ± 0.0110	0.235	97
SA5	0.156 ± 0.0110	0.265	55	SA29	0.153 ± 0.0143	0.260	70
SA6	0.157 ± 0.0095	0.250	67	SA30	0.152 ± 0.0086	0.281	89
SA7	0.161 ± 0.0047	0.283	70	SA31	0.150 ± 0.0080	0.295	92
SA8	0.155 ± 0.0075	0.273	78	SA32	0.156 ± 0.0110	0.278	78
SA9	0.156 ± 0.0062	0.230	96	SA33	0.151 ± 0.0131	0.305	98
SA10	0.158 ± 0.0085	0.240	95	SA34	0.152 ± 0.0050	0.320	99
SA11	0.161 ± 0.0050	0.280	97	SA35	0.155 ± 0.0057	0.310	97
SA12	0.160 ± 0.0057	0.250	99	SA36	0.151 ± 0.0062	0.311	98
SA13*	-	-	-	SA37	0.152 ± 0.0057	0.330	95
SA14*	-	-	-	SA38	0.152 ± 0.0050	0.340	97
SA15*	-	-	-	SA39	0.152 ± 0.0050	0.310	98
SA16*	-	-	-	SA40	0.151 ± 0.0062	0.320	95
SA17	0.156 ± 0.0086	0.265	98	SA41	0.156 ± 0.0075	0.270	98
SA18	0.157 ± 0.0050	0.280	99	SA42	0.155 ± 0.0057	0.266	97
SA19	0.152 ± 0.0050	0.290	98	SA43	0.152 ± 0.0086	0.360	95
SA20	0.152 ± 0.0050	0.278	99	SA44	0.153 ± 0.0075	0.298	97
SA21	0.150 ± 0.0080	0.252	99	SA45	0.155 ± 0.0057	0.278	87
SA22	0.150 ± 0.0147	0.315	99	SA46	0.157 ± 0.0121	0.260	79
SA23	0.152 ± 0.0095	0.283	98	SA47	0.151 ± 0.0050	0.256	92
SA24	0.152 ± 0.0050	0.283	84	SA48	0.152 ± 0.0050	0.265	96

T: Thickness** (mm); WU: Wt. Uniformity (mg); FE: Folding Endurance; *Patch is not formed; **SD mean (n=6)

Table 2: Thickness, Weight Uniformity and Folding Endurance of Terbinafine transdermal patches SA1-SA24.

Batch	MA %	ML %	WVTR	Batch	MA %	ML %	WVTR
SA1	04.73	03.51	0.0388	SA25	12.63	07.31	0.0277
SA2	06.72	04.45	0.0277	SA26	10.73	10.43	0.0290
SA3	02.20	01.85	0.0390	SA27	09.61	06.98	0.0277
SA4	07.12	02.12	0.0277	SA28	12.75	10.44	0.0277
SA5	04.49	03.40	0.0297	SA29	12.30	11.53	0.0280
SA6	05.68	03.75	0.0240	SA30	10.32	05.69	0.0518
SA7	08.03	06.46	0.0277	SA31	10.16	05.08	0.0555
SA8	09.90	06.10	0.0277	SA32	10.34	03.44	0.0462
SA9	05.24	03.88	0.0925	SA33	10.00	08.19	0.0462
SA10	06.25	04.50	0.0211	SA34	08.75	05.06	0.0314
SA11	07.67	05.96	0.0365	SA35	09.20	04.61	0.0462
SA12	05.60	03.24	0.0370	SA36	10.95	08.57	0.0462
SA13*	-	-	-	SA37	10.57	03.66	0.0460
SA14*	-	-	-	SA38	08.82	07.30	0.0450
SA15*	-	-	-	SA39	11.47	01.63	0.0668
SA16*	-	-	-	SA40	12.11	02.95	0.0555
SA17	09.43	02.64	0.0277	SA41	08.00	07.40	0.0462
SA18	08.07	05.35	0.0240	SA42	10.90	01.50	0.0450
SA19	12.06	03.44	0.0370	SA43	10.55	04.16	0.0370
SA20	10.93	05.08	0.0278	SA44	11.11	02.81	0.0277
SA21	11.11	03.17	0.0324	SA45	10.32	08.16	0.0462
SA22	06.82	04.76	0.0185	SA46	09.37	06.12	0.0648
SA23	09.18	01.06	0.0370	SA47	10.78	07.24	0.0370
SA24	08.88	04.61	0.0370	SA48	12.45	09.45	0.0462

MA: Moisture Absorption; ML: Moisture Loss; WVTR: Water Vapor Transmission Rate; *Patch is not formed

Table 3: Percent Moisture Absorption, Percent Moisture Loss and Water Vapour. Transmission Rate of Terbinafine transdermal patch SA1-SA48.

Percentage moisture content/loss

The prepared films were weighed individually and kept in desiccators containing fused calcium chloride at room temperature for 24 hr. After 24 hr the films were reweighed and determined the percentage moisture content from the below mentioned formula, (Table 3) [18].

Percentage Moisture Content=Initial Weight-Final Weight/Final Weight × 100

Water vapor permeability/Transmission rate

Glass vials of 5 ml capacity were washed thoroughly and dried to a constant weight in an oven. About 1 g of fused calcium chloride was taken in the vials and the polymer films were fixed over the brim with the help of an adhesive tape. Then the vials were weighed and stored in a humidity chamber at 85% RH condition for a period of 24 hrs. The vials were removed and weighed at various time intervals like 3, 6, 12, 18 and 24 hrs to note down the weight gain, (Table 3) [19].

Drug content

A specified area of size 2 × 2 cm transdermal patch SA1-SA48 was dissolved in a phosphate buffer 7.4 up to 10 ml. Then the solution was filtered through a whatman filter paper and the drug content were analyzed with the spectroscopic method (Table 4) [20].

In vitro drug diffusion study

In vitro skin permeation studies were performed by using a Franz diffusion cell with a receptor compartment capacity of 20 ml. The rat skin was mounted between the donor and receptor compartment of the diffusion cell, the formulated patches were cut into size of 2 cm^2 and placed over the drug release membrane and the receptor compartment of the diffusion cell was filled with phosphate buffer pH 7.4. The whole assembly was fixed on a magnetic stirrer, and the solution in the receptor compartment was constantly and continuously stirred using magnetic beads at 100 rpm, the temperature was maintained at 37 ± 0.5^0C. The samples of 1 ml were withdrawn at time interval of 1, 2, 3, 4, 5 and 6 hr analyzed for drug content UV-Visible spectrophotometrically at 223.5 nm. The receptor phase was replenished with an equal volume of phosphate buffer at each time of sample withdrawal. The cumulative amounts of drug permeated per square centimeter of patches were plotted against time (Table 5 and Figure 1) [21].

Results and Discussion

Physical appearance

The transdermal patches were transparent, smooth, uniform and flexible.

Thickness

The thicknesses of the prepared transdermal patches were observed in the range of 0.150 ± 0.0080 mm to 0.161 ± 0.0103 mm, (Table 2).

Weight uniformity

Weight uniformity of the prepared transdermal patches was observed in the range of 0.210 to 0.360 mg, (Table 2).

Folding endurance

Folding endurance of the prepared transdermal patches was observed in the range of 55 to 105, (Table 2).

Batch	DC (%)	Batch	DC (%)	Batch	DC (%)
SA1	80.22	SA17	84.00	SA33	76.27
SA2	80.22	SA18	70.00	SA34	85.00
SA3	85.62	SA19	76.21	SA35	91.77
SA4	87.16	SA20	75.36	SA36	85.77
SA5	81.63	SA21	86.20	SA37	76.44
SA6	89.93	SA22	88.81	SA38	79.92
SA7	86.53	SA23	75.21	SA39	74.22
SA8	82.14	SA24	84.36	SA40	89.95
SA9	89.55	SA25	70.66	SA41	90.15
SA10	88.77	SA26	79.76	SA42	88.66
SA11	80.51	SA27	85.96	SA43	87.50
SA12	92.89	SA28	72.58	SA44	84.74
SA13*	-	SA29	84.24	SA45	71.50
SA14*	-	SA30	87.54	SA46	76.34
SA15*	-	SA31	86.95	SA47	78.67
SA16*	-	SA32	86.95	SA48	82.56

DC: Drug Content; *Patch is not formed

Table 4: Drug content (%) of Terbinafine transdermal patches SA1-SA48.

Time (h)	SA1	SA2	SA3	SA4	SA5	SA6	SA7	SA8	SA9	SA10
1	15.30	11.84	14.29	25.72	26.27	20.12	19.53	15.23	16.56	16.45
2	38.40	19.62	27.85	35.23	36.27	39.45	30.13	24.15	27.67	32.27
3	55.15	33.57	32.19	54.49	45.49	56.04	36.15	36.64	39.87	36.46
4	59.17	48.15	49.42	61.94	52.86	67.51	39.51	45.90	48.56	42.46
5	61.50	60.13	64.73	68.11	59.69	71.81	49.50	56.77	54.64	48.24
6	65.70	64.70	68.34	**87.45**	67.04	**80.75**	61.14	62.34	64.15	55.92
Time (h)	**SA11**	**SA12**	**SA13**	**SA14**	**SA15**	**SA16**	**SA17**	**SA18**	**SA19**	**SA20**
1	22.16	19.45	23.12	22.64	18.34	15.79	23.18	16.09	24.17	17.87
2	45.96	38.35	42.45	35.12	34.16	38.74	42.51	25.28	42.08	36.48
3	55.56	56.67	52.55	51.20	55.67	43.03	46.92	37.45	56.76	48.81
4	61.25	67.78	65.70	66.19	66.17	46.62	50.49	46.74	68.43	57.97
5	69.78	81.94	78.61	77.23	78.52	54.62	55.04	51.33	77.03	64.97
6	87.35	**92.56**	**85.99**	89.00	88.89	62.61	64.87	59.17	**88.30**	70.43
Time (h)	**SA21**	**SA22**	**SA23**	**SA24**	**SA25**	**SA26**	**SA27**	**SA28**	**SA29**	**SA30**
1	21.06	7.91	19.16	24.45	22.56	18.14	19.16	20.58	16.65	13.34
2	34.12	10.55	35.55	49.93	41.96	20.27	29.87	31.87	29.69	23.75
3	40.98	14.59	40.26	54.90	55.25	26.03	36.71	36.66	37.73	36.41
4	55.69	19.48	44.58	60.24	60.25	32.30	42.86	44.34	44.85	48.86
5	65.39	25.88	48.12	64.93	70.73	38.78	47.15	47.12	50.65	54.97
6	**72.46**	45.89	65.57	71.27	**76.29**	46.65	54.65	53.93	61.54	65.33
Time (h)	**SA31**	**SA32**	**SA33**	**SA34**	**SA35**	**SA36**	**SA37**	**SA38**	**SA39**	**SA40**
1	23.54	13.06	20.16	14.65	17.51	16.65	18.25	21.31	19.67	17.65
2	46.29	18.56	34.83	21.47	27.48	25.25	34.79	41.10	35.21	34.24
3	65.10	36.65	49.60	31.58	32.02	38.18	44.36	52.36	45.61	43.16
4	77.51	42.86	57.60	36.56	39.89	48.54	50.09	58.13	52.49	47.60
5	82.73	47.32	63.75	40.34	43.83	54.23	53.97	64.75	60.70	56.29
6	**88.52**	58.99	**69.64**	49.57	57.57	63.81	64.09	72.46	**74.19**	68.15
Time (h)	**SA41**	**SA42**	**SA43**	**SA44**	---	---	---	---	---	---
1	17.14	19.15	15.17	19.89	---	---	---	---	---	---
2	25.19	28.46	22.87	29.71	---	---	---	---	---	---
3	38.39	35.47	38.70	34.12	---	---	---	---	---	---
4	41.25	41.34	46.87	42.60	---	---	---	---	---	---
5	49.56	51.78	52.67	54.71	---	---	---	---	---	---
6	**67.78**	64.89	65.79	66.49	---	---	---	---	---	---

The percentage drug release in 6 h was found to be highest 92.56% for formulation SA12 carrying HPMC E5 and PVP K25 and minimum 45.89% for formulation SA22 carrying HPMC E5 and Eudragit RS-100.

Table 5: Percentage cumulative drug release of formulation SA1-SA10.

Percent moisture absorption

The percent moisture absorption of the prepared transdermal patches was found to be between 2.20 to 12.75, (Table 3).

Percentage moisture content/loss

The percent moisture losses of the prepared transdermal patches were found to be between 1.06 to 11.53, (Table 3).

Water vapor permeability/Transmission rate (WVTR)

The water vapour transmission rate of the prepared transdermal patches was found to be between 0.0185 to 0.0925 (Table 3).

Differential scanning calorimetry

Differential scanning calorimetry enables the quantitative detection of all processes in which energy is required or produced (i.e., endothermic or exothermic phase transformations). The thermo grams of Terbinafine (TH1), HPMC E5 (H1), PVP K25 (PV1), physical mixture of Terbinafine, HPMC E5, PVP K25 (D1+P1), patch formulation (SA12-FP) are presented in Figure 2. The Terbinafine showed a melting peak at 206.99°C. Peak of Terbinafine at 206.77°C was present at the same position i.e., near to 206°C in the physical mixture of drug with both HPMC E5 and PVP K25 patch formulation excipients. This confirmed the physicochemical stability of drug with the formulation excipients used in the study.

FT-IR

Drug - excipients interactions play a vital role with respect to release of drug from the formulation amongst others. FT-IR techniques have been used here to study the physical and chemical interaction between drug and excipients used. Infrared (IR) spectra of Terbinafine (E), physical mixture of Terbinafine, HPMC E5 AND PVP K25 (B), HPMC E5 (C), PVP K25 (D) and Terbinafine (E) are shown in Figure 3. Infrared absorption spectroscopy (IR) of Terbinafine showed sharp band at 2968, 1413 and 1361 cm^{-1} due to stretching vibration bands of C-H, C=C and C-N respectively. From the figure it was observed that there were no changes in these main peaks in FT-IR spectra of mixture of drug and polymers, which show there were no physical interactions because of some bond formation between drug and polymers.

Drug content

The drug content in all formulations SA1-SA48 was found to be ranging from 70.00% to 92.89%. That indicates that the drug was dispersed uniformly throughout the patches. The drug content of each formulation SA1-SA48 was evaluated (Table 4).

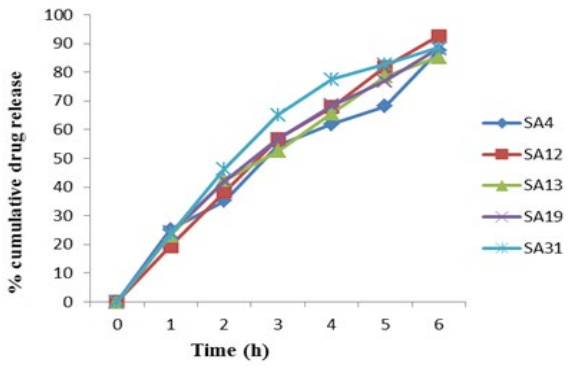

Figure 1: Percentage cumulative drug release of optimized batches SA4, SA12, SA13, SA19 and SA31.

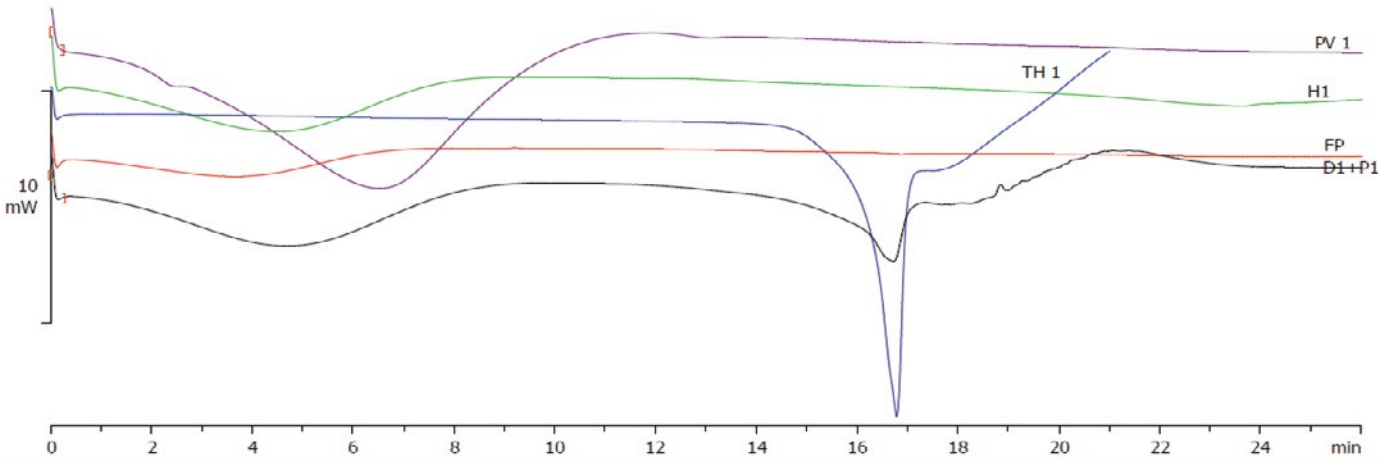

Figure 2: Overlay DSC thermo gram of Terbinafine-TH1, HPMC-H1, PVP K25-PV1, physical mixture-D1+P1 and Formulation SA12-FP.

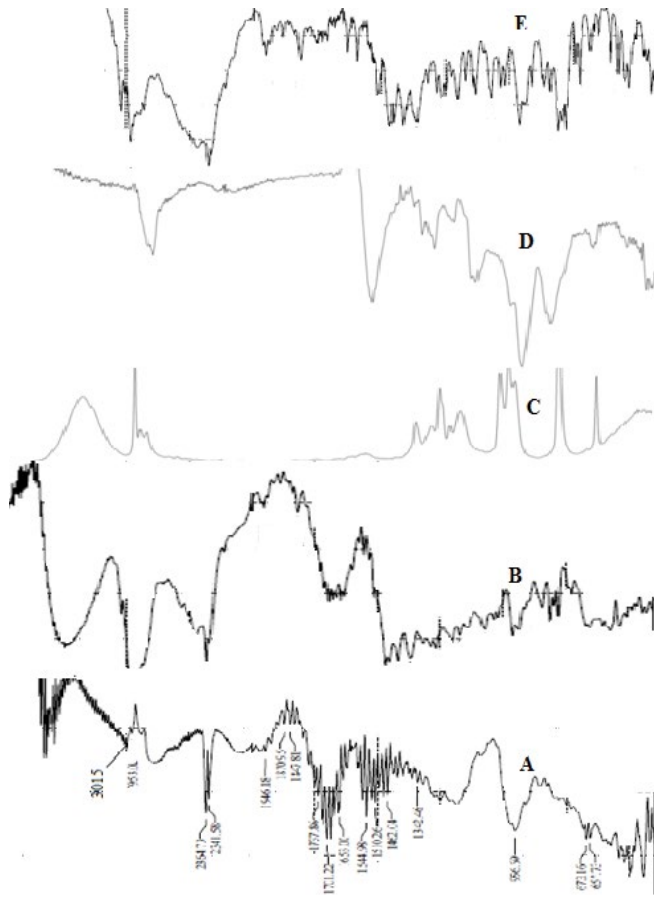

Figure 3: Formulation SA12 (A), physical mixture of Terbinafine, HPMC E5 and PVP K25 (B), HPMC E5 (C), PVP K25 (D) and Terbinafine (E).

In vitro drug diffusion study

From the obtained data; concluded that the optimized batches SA4, SA12, SA13, SA19 and SA31 are selected on the basis of their drug content and percentage drug release. The optimized batches shows suitable physical and mechanical properties like thickness, weight uniformity, folding endurance, percentage moisture loss, percentage moisture absorption, water vapour transmission rate and drug content. The optimized batches SA4, SA12, SA13, SA19 and SA31 shows better percentage cumulative drug release as compared to other batches. The percentage drug release in 6 h was found to be highest 92.56% for formulation SA12 carrying HPMC E5 and PVP K25 and minimum 45.89% for formulation SA22 carrying HPMC and eudragit RS-100 (Table 5 and Figure 1).

Conclusion

Transdermal patch showed good controlled release properties. The results of the present study demonstrated that Terbinafine can be considered for Transdermal patch containing HPMC E5 and Eudragit-RS100 as polymers, DMSO as permeation enhancer and plasticizer polyethylene glycol 400 for controlled release of the drug over a period of 06 h for the management of fungal infection. The Transdermal drug delivery system holds a promising future in effective Transdermal delivery of bioactive agents and opportunities for clinicians to experiment with various drugs to study their systemic and local effects.

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