ISSN: 0975-766X
CODEN: IJPTFI
Available Online through *Research Article*
www.ijptonline.com

FORMULATION AND EVALUATION OF TRANSDERMAL PATCHES OF GLIMEPIRIDE

Anupama Kumari*
Department of pharmaceutics, Lord Shiva College of Pharmacy Sirsa, Haryana.
Email: robinshrm7@gmail.com

Received on: 04-03-2019 *Accepted on: 30-03-2020*

Abstract

A transdermal patch is medicated adhesive patch that is placed on the skin to deliver a specific dose of medication through the skin. The main objective of formulating the transdermal delivery system of glimepiride was to prolong the drug release time, to reduce its frequency of administration. Ten formulations of glimepiride were prepared by incorporating 64 mg of drug in each patch and by varying the concentration of polymers *i.e.* Hydroxy Propyl Methyl Cellulose (HPMC E15LV), Poly Vinyl Alcohol (PVA) and Poly Vinyl Pyrrolidone (PVPK30).

In formulation Poly Ethylene Glycol (PEG400) was incorporated as plasticizer and diethylsulphoxide (DMSO) was used as penetration enhancer. These transdermal patches were prepared by solvent casting technique. Different evaluation parameters *i.e.* thickness of films, weight variation, drug content determination, folding endurance, % moisture uptake, % moisture loss, water vapour transmission rate, swelling index, etc. were used for the evaluation of drug free and drug loaded films. The *in- vitro* dissolution studies were carried out in phosphate buffer saline pH 7.4 using Franz diffusion cell. The egg membrane was used as a semi permeable membrane for this dissolution study. Finally it has been observed that F5 exhibits Fickians release. Based on the drug release and physicochemical values obtained from the formulation F5 is considered as an optimized formulation which shows higher percentage of drug release (87.708±0.32%) at 24 hours. The formulation F5 then subjected to skin irritation study to determine its potential for skin irritation on application. It didn't show any erythema on the mice.

Keywords: PEG400, PVPK30, PVA, Transdermal patches, Franz diffusion cell, solvent casting technique.

Introduction

The main objective of transdermal drug delivery system is to deliver drugs into systemic circulation through skin at predetermined rate with minimal inter and intrapatient variation.[1] The major advantages provided by transdermal drug delivery are following: improved bioavailability, longer duration of action resulting in a reduction in dosing frequency, more uniform plasma levels, reduced side effects. Transdermal patches have been useful for reducing first-pass drug-degradation effects.[2]

The first transdermal patch, Transderm SCOP was approved for the prevention of nausea and vomiting associated with travelling by FDA in 1979. Most transdermal patches are designed to release the active ingredient at a zero-order rate for a period of several hours to days after application to the skin.[3] In transdermal patches drug penetrate into various layers of skin and permeation across the skin into systemic circulation.[4]

The penetration power of drug through skin can be enhanced by some chemicals such as dimethylsulphoxide , azones, pyrrolidones, urea and fatty acids. In general, once drug molecules cross the stratum corneal barrier, then passage into deeper dermal layers and systemic uptake occurs relatively quickly and easily.[5] Glimepiride is an oral medium to long acting antidiabetic drug from the sulphonylurea class. It is a second generation drug of sulfonylurea which is used in type 2 diabetes. It provoke a brisk release of insulin from beta cells of pancreas by blocking the ATP- sensitive k+ channels, resulting in depolarization and Ca^{2+} influx. It causes reduction in hepatic glucose production and increase in peripheral insulin sensitivity.[6]

Experimental

Materials: Pure glimepiride was procured from Aristo Private Limited, Andheri Mumbai. Potassium dihydrogen orthophosphate, Di-Sodium hydrogen phosphate, chloroform and HCl were obtained from M/s Rankem laboratories, New Delhi. DMSO, PVA, HPMC E 15LV, PVP K30 and PEG400 were obtained from M/s Leo chem., Banglore. Sodium chloride, Methanol, n-octanol, Whatman filter paper and sodium hydroxide were obtained from M/s Bharat instruments and chemicals, Hisar. All reagents used in this study were of analytical grade.

Methods

Prepration of drug free films[7,8]

The drug free films of different polymers were prepared by solvent casting technique employing mercury as a substrate. Overall ten batches were formulated using different ratios of HPMC E15LV, PVA and PVPK30.Casting solution was prepared by dissolving weighed quantities of polymer PVPK30 and PVA (total weight of polymers were kept 500 mg), HPMC E15LV and PVPK30 (total weight of polymers were kept 500 mg) and plasticizer (36% w/w of polymers) in an appropriate solvent system using magnetic stirrer continuously stirring for 3 hour in such a manner that evaporation of solvent was minimum. For the formulation of drug free films, mercury was used as the backing membrane and spread uniformly on a glass petridish which was kept on a table with smooth horizontal surface. A glass bangle as a mould was placed in the petridish over mercury surface and about 10 ml of the solution was poured on the mercury (26.40 cm^2). The rate of evaporation was controlled by inverting the funnel over the mould. After 24 h, the dried patches were cut into 2 cm diameter, wrapped in aluminum foil and stored over fused calcium chloride in desiccators at room temperature for further use.

Fig.1 Drug free films prepared by solvent casting method.

Table-1: Composition of drug free films.

Batch Code	Polymeric ratio		Plasticizer PEG400 % Polymer Wt.	Casting Solvent Chloroform: Methanol (1:1)	Casting solvent water (ml)
	HPMCE15 LV: PVPK30	PVA: PVPK30			
F1	1:1	__	36	10	__
F2	1:2	__	36	10	__

F3	1:3	__	36	10	__
F4	3:2	__	36	10	__
F5	2:3	__	36	10	__
F6	__	1:1	36	__	10
F7	__	1:2	36	__	10
F8	__	1:3	36	__	10
F9	__	3:2	36	__	10
F10	__	2:3	36	__	10

Total polymeric weight**:** 500 mg

Density of PEG400 =1.13 therefore, Amount used 0.159 ml

Determination of partition coefficient[9,18]

Partition coefficient of glimepiride was determined by taking 10 ml of n-octanol which was saturated with aqueous phase (7.4 PBS) by stirring with magnetic stirrer and kept undisturbed for half an hour. After that 10 mg of drug was added to this solution and was shaken on mechanical stirrer. Two layers were separated through separating funnel and filtered through Whatman paper 0.45 μm. Using U.V. spectrophotometer at wavelength 228 nm, partition coefficient of glimepiride was determined. The experiment was performed in triplicate and average partition coefficient was

The partition coefficient of drug ($K_{o/w}$) was calculated by formula given below:

$$K_{O/W} = \frac{\text{Concentration of drug in n-octanol}}{\text{Concentration of drug in PBS (Ph 7.4)}}$$

Table-2: Partition coefficient of glimepiride.

S. No	Partition coefficient	Mean
1	0.82±0.001	0.82±0.001
2	0.80±0.002	
3	0.82±0.001	

Drug compatibility studies[7]

The pure glimepiride and a mixture of it with the polymers, PVA, HPMC E15LV and PVPK30 were mixed separately with IR grade KBr and corresponding pellets were prepared by applying pressure in hydraulic

press. The pellets were scanned over a wave number range of 4000-400 cm^{-1}. The glimepiride along with the physical mixture of HPMC E15LV and PVPK30 was kept at different environmental conditions to observe the physical compatibility of the drug with excipients. A comparison of the initial sample, control sample and samples kept at different environmental conditions for physical changes were observed with respect to colour, odour, lump formation etc. The result obtained from physical compatibility studies were confirmed by FTIR studies Fig.2 (a, b) compares FTIR spectra of pure drug and its mixture with HPMCK E15LV and PVPK30.

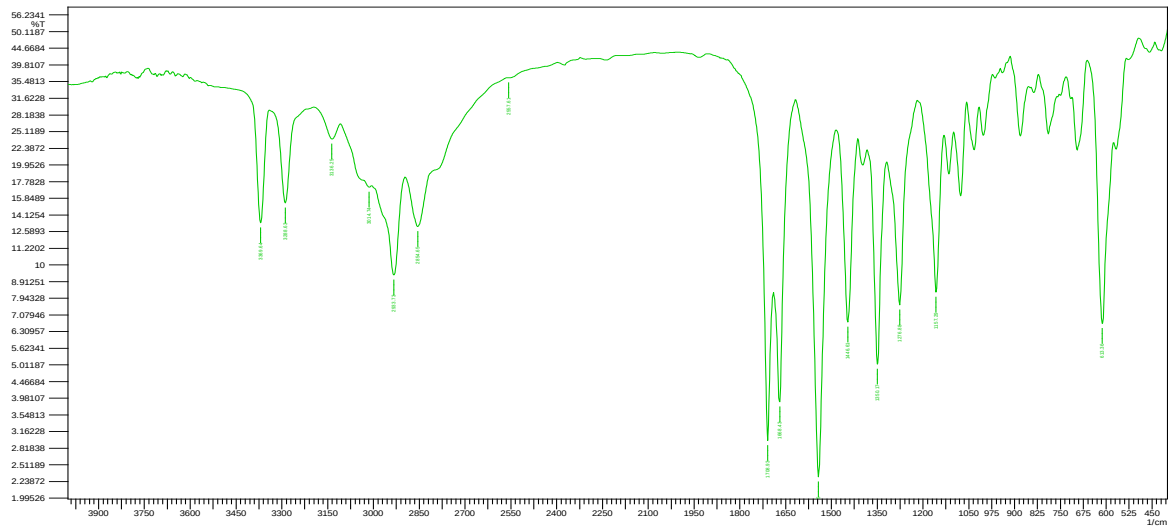

Fig. 2 (a) FTIR spectrum of pure glimepiride.

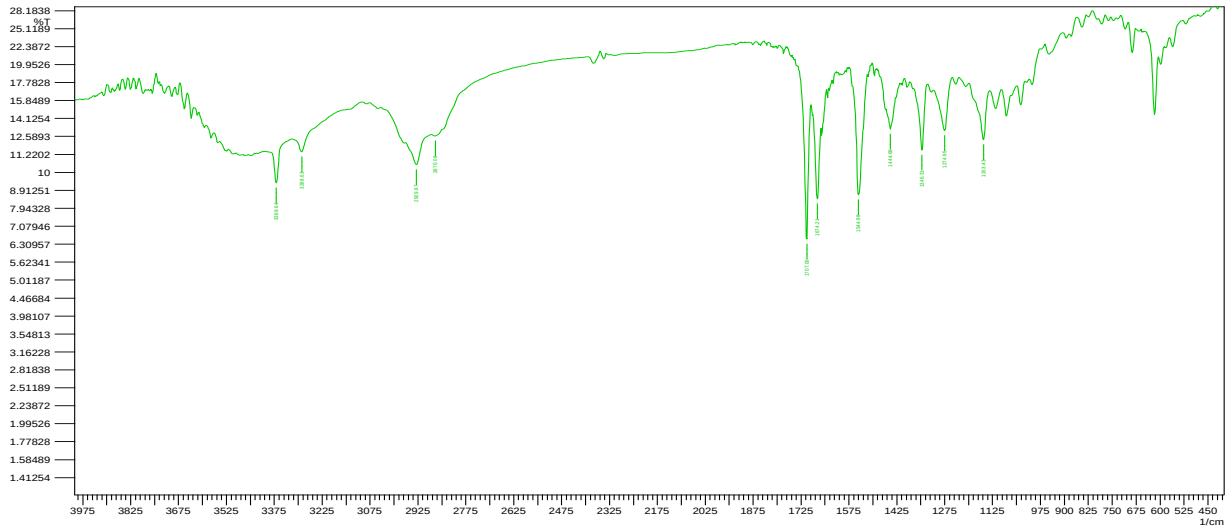

Fig. 2 (b) FT-IR spectrum of physical mixture of glimepiride, HPMC E15LV and PVPK30.

On comparing of above two spectra it is evident that all the peaks of glimepiride were present in the sample (drug + excipients) kept under compatibility studies therefore it can be concluded that there was no physical and chemical changes occurred indicating that excipients are compatible with glimepiride.

Preparation of drug loaded films[7,10]

The monolithic films of different polymers along with drug were prepared by the same procedure as used for preparation of drug free films.

Calculation of the amount of drug for circular cast film

Internal diameter of bangle (mould) = 5.8cm.

Internal surface area of bangle (πr^2) = (3.14 x 2.9 x 2.9) = 26.40 cm^2

Diameter of transdermal film = 2 cm

Area of transdermal film (πr^2) = 3.14 x 1 x 1 = 3.14 cm^2

Therefore, number of transdermal films cut out from one circular cast film

= 26.40 / 3.14 = 8 films

Amount of drug loaded in one film = 8 mg

Hence drug loaded in one circular cast film = 8 x 8 = 64 mg

Therefore 64 mg of glimepiride is needed for one circular cast film.

Table-3: Composition of transdermal patches of glimepiride.

Batch Code	Polymeric ratio		Drug (mg)	Penetration Enhancer (DMSO) % Polymer wt.	Plasticizer PEG400 % Polymer wt.	Casting Solvent Chloroform: Methanol (1:1)	Casting Solvent Water (ml)
	HPMC E15LV: PVPK30	PVA: PVPK30					
F1	1:1	__	64	12	36	10	__
F2	1:2	__	64	12	36	10	__
F3	1:3	__	64	12	36	10	__
F4	3:2	__	64	12	36	10	__
F5	2:3	__	64	12	36	10	__
F6	__	1:1	64	12	36	__	10
F7	__	1:2	64	12	36	__	10
F8	__	1:3	64	12	36	__	10
F9	__	3:2	64	12	36	__	10
F10	__	2:3	64	12	36	__	10

Polymeric weight**:** 500 mg

Density of PEG 400 is 1.13 g/ml therefore amount used 0.159 ml

Density of DMSO is 1.1004 g/ml therefore amount used0.0545 ml

Results and Discussion

Evaluation of transdermal patches [11,12,13]

Thickness

The thickness of transdermal patches was measured at three different places by using a micrometer and the mean values were calculated.

Weight variation

Uniformity of weight was determined by weighing five matrices of each formulation. After each film unit was weighed individually on a digital balance, the average weight of film was taken as the weight of the film.

Folding endurance

This test was carried out to check the efficiency of the plasticizer and the strength of the prepared patches. Folding endurance of the film was determined repeatedly by folding a small strip (2 cm × 2 cm) at the same place till it breaks. The number of times the film can be folded at the same place without breaking gives the value of folding endurance.

Percentage moisture absorption

The films were weighed accurately and placed in the desiccator containing 100 ml of saturated solution of aluminum chloride, which maintains 84% RH. After 3 days, the films were taken out and weighed. The percentage moisture absorption was calculated.

$$\text{Moisture absorption}(\%) = \frac{\text{Final wt.-Intial wt.}}{\text{Initial wt.}} \times 100$$

Percentage moisture loss

The films were weighed accurately and kept in a desiccator containing anhydrous calcium chloride. After 3 days, the films were taken out and weighed. The moisture loss was calculated.

$$\text{Moisture loss}(\%) = \frac{\text{Initial wt. – Final wt.}}{\text{Final wt.}} \times 100$$

Water vapor transmission rate

The water vapor transmission is defined as the quantity of moisture transmitted through per unit area of a patch in unit time. Glass vials of equal diameter were used as transmission cells. These transmission cells were washed thoroughly and dried to a constant weight in an oven. About 1 g of fused anhydrous calcium chloride as a desiccant was placed in the cells and the polymeric films were fixed over the brim with the help of an adhesive tape. The preweighed cells were stored in a closed desiccator containing saturated solution of potassium chloride to maintain 84% RH. The cells were taken out and weighed after 24 h of storage. Water vapor transmission (Q) usually expressed as number of grams of moisture gain per 24 h per square centimeter, was calculated.

$$Q = \frac{WL}{S}$$

Where,

W is g of water transmitted / 24 h, L is patch thickness in cm, S is surface area in cm^2

Swellability

The films (3.14 cm^2) were weighed and placed in a petridish containing 10 ml of double distilled water and was allowed to imbibe. Increase in weight of the patch was determined at preset time intervals, until a constant weight was observed. The degree of swelling (S) was calculated.

$$S\% = \frac{W_t - W_o}{W_o} \times 100$$

S% is percent swelling, W_t is the weight of patch at time t and W_o is the weight of patch at time zero.

Table-4: Different evaluation parameters of drug loaded transdermal patches;

Formulation code	**Thickness (mm)**	**Weight variation (mg)**	**Folding endurance**	**% Moisture absorption**	**% Moisture loss**	**Water vapour transmission rate (gm/cm.24 h)**	**Swellability index (%)**
F1	0.202±0.002	50.24±0.25	260±1.70	2.58±0.064	4.68±0.03	5.26 ±0.34	32.16±0.25
F2	0.206±0.0	51.18±0.	265±4.50	2.52±0.125	5.42±0.04	4.38 ±0.28	34.24±0.

	04	50					34
F3	0.210±0.005	52.10±0.45	270±2.61	3.02±0.234	6.38±0.01	5.14 ±0.14	35.19±0.16
F4	0.215±0.002	53.12±0.30	282±3.45	5.39±0.381	8.12±0.05	8.53±0.34	33.47±0.31
F5	0.218±0.003	55.90±0.54	300±5.03	4.42±0.252	6.67±0.01	6.32±0.24	35.14±0.34
F6	0.310±0.012	56.29±0.38	240±2.72	2.54±0.134	3.10±0.15	5.15±0.32	36.01±0.21
F7	0.312±0.014	57.22±0.52	230±4.12	3.24±0.256	4.25±0.25	3.64±0.38	38.34±0.34
F8	0.314±0.015	56.32±0.41	230±3.26	4.01±0.311	5.03±0.36	4.32±0.21	40.12±0.15
F9	0.318±0.012	55.26±0.32	250±5.12	5.02±0.215	6.50±0.17	3.19±0.42	38.29±0.24
F10	0.320±0.013	48.17±0.25	246±6.47	4.69±0.259	5.01±0.23	2.21±0.30	39.43±0.39

In-vitro permeation studies [14]

The *in-vitro* release profile is an important tool that predicts in advance how a drug will behave *in-vivo*. *In-vitro* studies were performed using a Franz diffusion cell (Fig. 3) with a receptor compartment capacity of 22 ml.

Fig.3: Permeation studies using Franz diffusion cell.

The receptor compartment was filled with phosphate buffer saline pH 7.4 and egg membrane was mounted between the donor and receptor compartment of the diffusion cell. The prepared transdermal film was placed on egg membrane.

The whole assembly was kept on a magnetic stirrer and the solution was stirred continuously at 600 rpm using a magnetic bead at 37±1°C. The 2 ml of sample was withdrawn at different time interval and replaced with equal volume of diffusion medium. Sample was analyzed spectrophotometrically at 228 nm for the determination of glimepiride.

Table-4: *In-vitro* release data of transdermal patches of glimepiride developed using PVA and PVPK30.

Time (h)	Cumulative percentage drug release									
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**
0	0	0	0	0	0	0	0	0	0	0
0.25	4.168± 0.18	2.618± 0.61	2.616± 0.65	3.327± 0.01	8.918± 0.03	5.118± 0.25	2.186± 0.46	4.181± 0.21	6.815± 0.11	3.150± 0.80
0.5	9.845± 0.08	7.011± 0.41	5.255± 0.51	6.215± 0.03	17.101 ±0.27	11.251 ±0.15	4.525± 0.40	8.165± 0.16	11.279 ±0.06	5.436± 0.60
1	16.504 ±0.01	13.217 ±0.49	8.732± 0.46	10.156 ±0.15	22.221 ±1.73	17.316 ±0.19	9.731± 0.39	17.215 ±0.19	15.051 ±0.35	10.208 ±0.59
2	28.435 ±0.07	20.181 .50	15.016 ±0.91	17.418 ±0.43	33.561 ±0.20	23.290 ±0.20	15.271 ±0.50	25.321 ±0.01	18.161 ±0.34	15.190 ±0.43
3	36.708 7±0.17	25.218 ±0.25	22.457 ±0.16	23.309 ±0.32	40.270 ±1.60	30.416 ±0.30	22.502 ±0.15	33.432 ±0.18	23.910 ±0.71	21.315 ±0.12
4	42.184 ±0.12	37.315 ±0.10	27.918 ±0.59	29.516 ±0.41	46.281 ±0.95	36.581 ±0.55	27.431 ±0.51	41.683 ±0.29	29.450 ±0.51	25.201 ±0.22
5	46.205 ±0.08	42.510 ±0.45	32.910 ±0.39	31.327 ±0.54	51.226 ±0.12	43.181 ±0.42	31.352 ±0.67	46.571 ±0.41	35.511 ±0.24	30.109 ±0.40
6	49.181 ±0.28	48.419 ±0.30	37.127 ±0.81	35.625 ±0.44	56.128 ±0.18	50.259 ±0.53	35.325 ±0.45	49.432 ±0.58	51.501 ±0.81	39.215 ±0.35
7	52.191	50.270	41.518	40.781	65.182	53.321	40.156	53.211	60.104	42.319

	±0.81	±0.25	±0.71	±0.68	±0.21	±0.32	±0.30	±0.44	±0.50	±0.32
8	56.646 ±0.66	52.310 ±0.30	44.201 ±0.55	45.511 ±0.51	70.167 ±0.32	58.459 ±0.59	42.615 ±0.36	58.326 ±0.25	65.205 ±0.19	45.501 ±0.50
9	58.931 ±0.57	54.115 ±0.27	46.310 ±0.65	51.405 ±0.19	72.112 ±0.25	60.221 ±0.68	46.517 ±0.40	62.129 ±0.52	67.306 ±0.20	48.427 ±0.55
10	60.542 ±0.48	57.418 ±0.15	50.216 ±0.11	55.215 ±0.25	75.206 ±0.15	65.315 ±0.15	50.376 ±0.60	65.675 ±0.59	70.310 ±0.70	50.218 ±0.45
11	62.601 ±0.62	60.102 ±0.17	53.380 ±0.51	60.302 ±0.54	78.815 ±0.18	69.497 ±0.91	53.225 ±0.65	67.298 ±0.61	72.204 ±0.45	55.518 ±0.55
12	65.514 ±0.16	62.312 ±0.20	57.615 ±0.55	62.217 ±0.26	80.706 ±0.30	72.613 ±0.82	56.645 ±0.31	69.378 ±0.11	74.520 ±0.38	56.401 ±0.52
16	67.211 ±0.19	63.416 ±0.25	60.508 ±0.40	65.116 ±0.32	82.615 ±0.25	74.718 ±0.18	60.515 ±0.42	70.125 ±0.32	76.671 ±0.22	60.321 ±0.71
20	70.312 ±0.20	65.520 ±0.30	61.402 ±0.22	67.184 ±0.29	84.518 ±0.31	76.814 ±0.93	62.712 ±0.32	71.419 ±0.43	78.791 ±0.18	63.571 ±0.62
24	74.415 ±0.25	66.210 ±0.10	62.819 ±0.32	69.181 ±0.16	87.708 ±0.32	77.102 ±0.18	67.89± 0.19	72.810 ±0.15	80.810 ±0.25	69.291 ±0.80

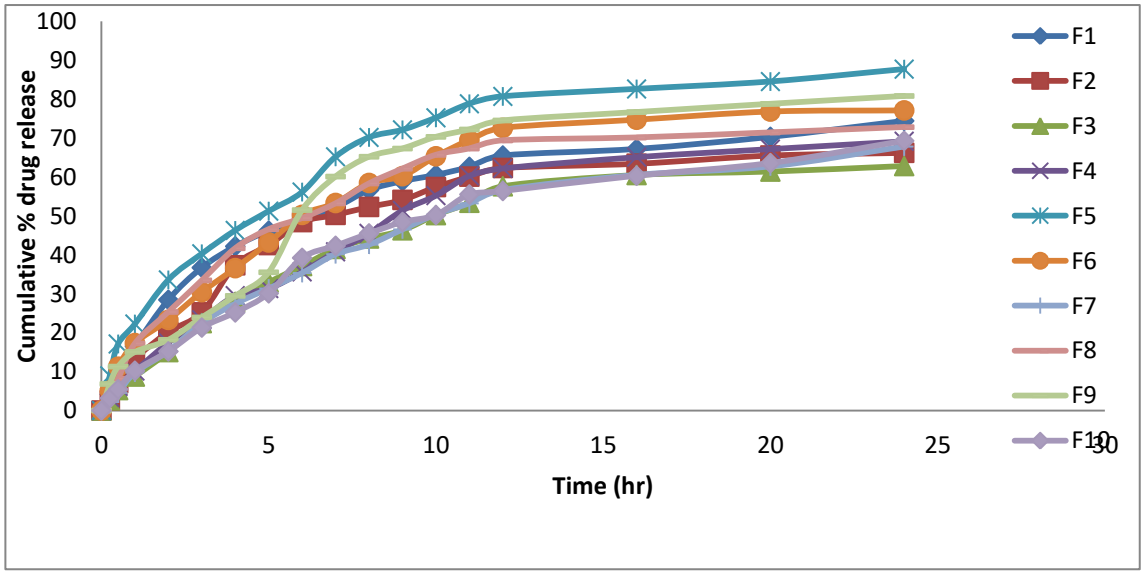

Fig. 4: Drug release profile of formulation F1 to F10.

The cumulative release of F5 is best among all formulations. Hence skin irritation study was performed only on F5 formulation.

Kinetic analysis of dissolution data [15]

The *in- vitro* study data of optimized formulation of glimepiride transdermal patch (F5) was fitted to zero order, first order, Higuchi's and Korsmeyer-Peppas model to ascertain the kinetic modeling of drug release.

Table-5: showing kinetic analysis of drug release data of selected formulation F5.

Time (h)	Root time	Log time	% Drug release	Log % Drug release	%Drug remained	Log % drug remained
0	0	0	0	0	0	0
0.25	0.5	-0.602	8.918	9.950	91.082	1.959
0.5	0.707	-0.301	17.101	1.233	82.899	1.918
1	1.000	0.000	22.221	1.346	77.779	1.890
2	1.414	0.301	33.561	1.525	66.439	1.822
3	1.732	0.477	40.270	1.604	59.730	1.776
4	2.000	0.602	46.281	1.665	53.719	1.730
5	2.236	0.698	51.226	1.709	48.774	1.688
6	2.449	0.778	56.128	1.749	43.872	1.642
7	2.645	0.854	65.182	1.814	34.818	1.541
8	2.828	0.903	70.167	1.846	29.833	1.474
9	3.000	0.954	72.112	1.858	27.888	1.445
10	3.162	1.000	75.206	1.876	24.794	1.394
11	3.316	1.041	78.815	1.896	21.185	1.326
12	3.464	1.079	80.706	1.906	19.294	1.285
16	4.000	1.204	82.615	1.917	17.385	1.240
20	4.472	1.301	84.518	1.926	15.482	1.189
24	4.898	1.380	87.708	1.943	12.292	1.089

The following methods were adopted for deciding the most appropriate model,

1. Percent drug released versus time (zero-order kinetic model)
2. Log percent drug remaining versus time. (first-order kinetic model)
3. Percent drug released versus square root of time (Higuchi's model)
4. Log percent drug released versus log time (Korsmeyer-Peppas model)

The data were processed for regression analysis using MS-EXCEL statistical function. The kinetic analysis data of the formulation F5 shown in Table 5. At the outset drug release data of the formulation was fitted to zero order, first order and Higuchi's model and from the respective profiles values of slope, intercept and r^2 were calculated in each case. These values are shown in Table 6. As the model with highest correlation coefficient (r^2) was considered to be best model therefore form the kinetic parameters shown in Table 6. It can be concluded that the release of drug from formulation F5 of glimepiride followed Higuchi's model. Hence in current investigation, *in -vitro* release profile could be best expressed by Higuchi's model for the formulation F5 which shows good linearity (r^2) and indicated that diffusion is dominant mechanism of drug release from glimepiride formulation.

The parameters obtained from kinetic analysis of F5 after fitting the data into various kinetic models are shown in Table 6. From the table it has been observed that the regression value (n-value) of the formulation was 0.944 suggesting that the drug was released by Fickian diffusion.

Table-6: Summary of parameters obtained from kinetic analysis of F5.

Zero Order	Slope(K)	3.533
	Intercept	26.80
	r^2	0.758
First Order	Slope(K/2.303)	-0.0086
	K	-0.020
	Intercept	1.626
	r^2	0.099
Higuchi's model	Slope(K)	19.86
	Intercept	5.683
	r^2	0.944
Korsemeyer-Peppas model	Slope(n)	-1.412
	Intercept(log K)	0.4795
	K	3.017
	r^2	0.158

Skin irritation study

The selected formulation was tested for its potential to cause skin irritation/sensitization in mice. The mice were divided into three groups (each group having 6 mice). On the previous day of the experiment, the hair of the dorsal portion of the mice were removed physically with the help of hair removal cream and the skin was cleared with rectified spirit. The animals of group I served as control group, standard without any treatment. The animals of the group II served as the test group "a", and treated with placebo patch (without

drug, 2.0×2.0 cm^2). The animals of group III served as the test group "b" and treated with transdermal patches of glimepiride (2.0×2.0 cm^2). After 24 h of exposure, each patch was removed with the help of alcohol swab and the test site was rinsed with tap water. The application sites were examined and scored for signs of erythema.[16,17]

The study was approved by ethics committee of Lord Shiva College of Pharmacy, Sirsa (Hry).

Table-7: Skin irritation scores following transdermal patch application of Formulation F5.

Animal Code	**Group** I **(Control)**	**Group** II **(test "a" group)**	**Group** III **(test "b" group)**
	Erythema	**Erythema**	**Erythema**
I	0	0	0
II	0	0	0
III	0	0	0
IV	0	0	0
V	0	0	0
VI	0	0	0

Results of skin irritancy study are shown in Table 7, which revealed that neither blank patch nor patch containing glimepiride caused any noticeable signs of erythema shown in on mice skin throughout the period of 24 h. Hence, the formulated transdermal patches were declared to be free from skin irritation and compatible with the studied mice animal skin. Fig. 5 (a), (b) & (c) depicts mice skin after removal of hair, (b) having transdermal patches of formulation F5 & (c) skin after removal of patch.

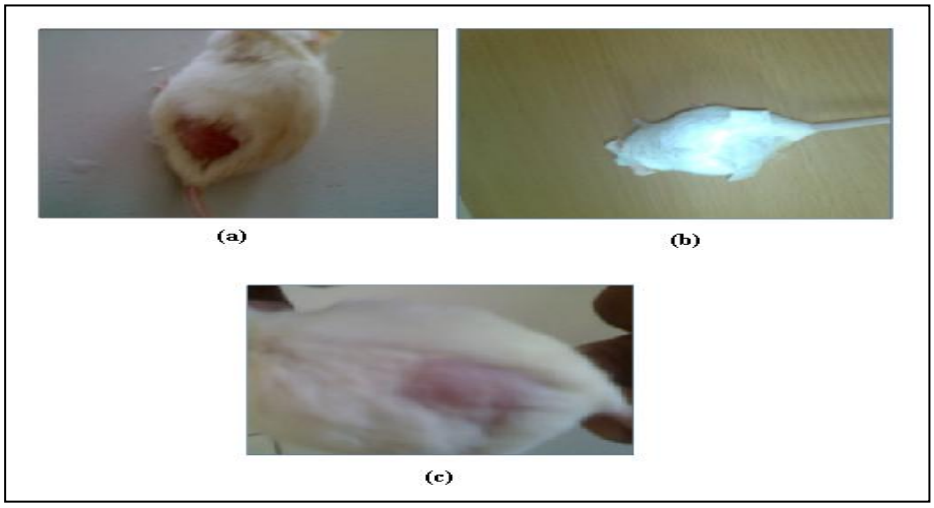

Fig. 5 (a) Mice skin after removal of hair, (b) Having transdermal patch of formulation F5 & (c) After removal of transdermal patch.

Conclusion

Glimepiride is an effective anti-diabetic drug particularly in non- insulin dependent diabeties mellitus. It is second generation sulfonylurea which actually lowers the blood glucose level in humans by stimulating the pancreatic cells and thereby releasing insulin. Low molecular weight, good permeability & short biological half-life of glimepiride made it suitable candidate for transdermal drug delivery. The main objective of formulating the transdermal delivery system of glimepiride was to prolong the drug release time, to reduce its frequency of administration and to improve patient compliances.

The results of this study, reveals that transdermal patches of glimepiride were successfully developed using polymers *ie* HPMC E15LV, PVPK30 & PVA. *In-vitro* dissolution studies suggest that transdermal patches of glimepiride may provide much better maintenance of therapeutic levels of drug in blood and for a prolonged period of time as well. The non-irritant nature of patches also revealed the advantage of using the patch over skin.

The selected formulation F5 satisfied all the pharmaceutical parameters of transdermal films and appears to be promising, would be able to after advantages such as sustained drug release, reducing frequency of drug administration, improving bioavailability, and thereby may help to improve patient compliance. On the basis of drug release behavior using kinetic models like zero order, first order, Higuchi's, Peppas etc. Finally it has been observed that F5 exhibits Fickians release. Also, this technology can be explored for other antidiabetic molecules as well so as to achieve better control over the disease.

References

1. Jalwal P, Jangra A, Dhaiya L, Sangwan Y, Saroha R. A review on transdermal patches Pharm Res. J. 2010; 3:139-149.
2. Patel D, Chaudhary SA, Parmar B, Bhura N. Transdermal drug delivery system: a review. The Pharm Innovation. 2012; 1(4):66-75.
3. Mehta R. Topical and transdermal drug delivery: what a pharmacist needs to know. InetCE. J. 1st Ed. Arizona; 2004:1-10.
4. Ramteke KH, Dhole SN, Patil SV. Transdermal drug delivery system: a review. J Advanced Sci. Res. 2012; 3(1):22-35.

5. Pathan IB, Setty CM. Chemical penetration enhancers for transdermal drug delivery systems. Tropical J Pharm Res. 2009; 8(2):173-179.
6. Tripathi KD, Essentials of medical Pharmacology 6th Ed. Jaypee brother's medical Publishers Pvt. Ltd, New Delhi. Page no. 266-268.
7. Prabhakar P, Koland M, Vijanarayan K, Harish NM, Shankar G, Ahemad MG, Narayan RC Satyanarayana D. Preparation and evaluation of transdermal patches of Papaverine hydrochloride. Int. J Res. Pharm Sci. 2010; 1(3):259-266.
8. Ahad HA, Kumar CS, Anuradha CM, Reddy KK, Sreeamulu J, Sushma K, Krishna HZ, Savitri R. Fabrication and *in-vitro* permeation studies of Indomethacin-ficus carica fruits mucilage patches. Int. J Applied Bio. Pharm Tech. 2010; 1(3):786-792.
9. Pachisia N, Agarwal SS. Formulation, development and evaluation of transdermal drug delivery system of Glimepiride. Int. J Pharm Sci. Res. 2012; 2(1):1-8.
10. Patel JR, Gupta JRD, Tripathi P, Dubey P, Irchhiaya R, Garud N. Formulation and evaluation of matrix type transdermal patches of Glibenclamide. Int. J Pharm Sci. Drug Res. 2009; 1(1):46-50.
11. Rathod K, Shah C, Shah H. To optimize the effect of polymers on matrix type transdermal patch of Trandolopril. IJPRNK. 2014; 3(2):540-554.
12. Nessem DI, Eid SF, Houseny EI. Development of novel transdermal self adhesive films Tenoxicam an anti-inflammatory drug. Life Sci. 2011; 89:430-438.
13. Ghosal K, Rajabalaya R, Kishore AM, Chowdhury B, Nanda A. Evaluation of physicochemical properties and *in-vitro* release profile of Glipizide- matrix patch. Brazzilian J Pharm Sci. 2010; 46(2):213-218.
14. Kavitha K and More MR. Design and evaluation of transdermal system films of Lornoxicam. Int. J Pharma Bio. Sci. 2011; 2(2):54-62.
15. Costa P, Lobo JMS. Modeling and comparison of dissolution profile. Eup. J Pharm Sci. 2001; 13:123-133.
16. Ramkanth S, Madhusudhana CC, Sudhakar Y. Development and evaluation of transdermal drug delivery system of Metoprolol. Int. J Res. Pharm. Sci. 2012; 3(4):698-708.

17. Narasima RR, Askulla S, Bhavya B, Prasoona Ch, Koppu P. Design and evaluation of Glipizide transdermal patches. Int. J Res. Pharm Biomed. Sci. 2011; 2(4):1620-1633.

18. Madhulatha A and Naga RT. Formulation and evaluation of Ibuprofen transdermal patches. Int. J Res. Pharm Bio. Sci. 2013; 4(1):351-360.

Corresponding Author:

Anupama Kumari*

Email: *robinshrm7@gmail.com*