

COMPARATIVE EVALUATION OF SELECTED POLYMERS AND PLASTICIZER ON TRANSDERMAL DRUG DELIVERY SYSTEM

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ABSTRACT

Objective: The present work was aimed at preparation of transdermal patches by a solvent casting method using a varying concentration of polymers i.e. methocel (K15 and K100), ethocel (4 and 10), gelatin, chitosan, eudragit (RL and RS) grade using plasticizer (glycerin and propylene glycol).

Methods: The ratio of drug to polymers and plasticizer was varied and the effect of formulation variables was studied. Prepared transdermal patches were evaluated for physicochemical properties, *in-vitro* permeation studies, content uniformity, primary skin irritation studies and FT-IR studies.

Results: The formulated transdermal patch by using Methocel K 100 M showed good physical properties. The average weight of patches prepared using glycerin as a plasticizer were ranged from 42.33-67.00 mg and propylene glycol as a plasticizer were ranged from 40.67-67.67 mg. The percentage moisture absorption varies from 1.76 to 10.73 for patches formulated using glycerin and 2.28 to 7.97 for propylene glycol patches. The percentage moisture loss from patches prepared using glycerin was ranged from 2.75 to 11.54 and 2.87 to 12.02 from propylene glycol. The water vapour transmission rate from patches prepared using glycerin was ranged from 0.25 to 0.92 and 0.41 to 1.76. The formulated patch showed the acceptable quantity of medicament ranged from (100.20-101.05%). This result met the test content uniformity as per BP (85% to 115%). According to that, the drug was consistent throughout the patches. The formulation PGD is considered as the best formulation, since it shows a maximum *in vitro* drug release as 43.75 % at 24 h. The drug release kinetics studied showed that the majority of formulations was following zero order.

Conclusion: In conclusion, controlled release transdermal drug delivery system patches of aliskiren can be prepared using polymer combinations, with a different plasticizer. The release rate of drug depends upon the polymer. However, release kinetics followed zero order.

Keywords: Transdermal Patches, Aliskiren Hemifumarate, Methocel (K15 and K100), Ethocel (4 and 10), Gelatin, Chitosan, Eudragit (RL and RS), Glycerin, Propylene glycol, Solvent casting method, Hypertension

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INTRODUCTION

In the current scenario, hypertension is the major factor for cardiovascular disease and the leading cause of death in economically developed countries. The renin-angiotensin system (RAS) is the main regulator of blood pressure and body fluid volume and acts primarily via the effects of the octapeptide hormone, angiotensin II (AngII). Ang II is formed in a two-step: angiotensinogen converted to angiotensin I (AngI), which is then converted by angiotensin converting enzyme (ACE) into AngII. Ang II increases blood pressure and exerts direct growth-promoting effects on cardiac and renal tissue that causes organ damage [1-3]. Renin inhibitors avoid the formation of AngI and AngII and so may act differently from ARBs, which increase angiotensin peptide levels, and ACE inhibitors, which increase AngI levels and do not block ACE-independent AngII production [4-7].

From past few years, topical delivery for treatment of hypertension shows better results. The barrier causing agent during transdermal delivery is "Skin". Skin plays a vital role for the transportation of the drug. There are three routes from which molecules can penetrate the skin: (1) intracellular, (2) intercellular lipids, and (3) appendages. Absorption through the skin is affected by a number of factors including the origin (human, animal), type of skin, physicochemical properties of the compound and formulations, as well as possible skin pretreatment and environmental factors [6-9].

Major advantages of transdermal drug delivery: the constant level of drug is maintained within the therapeutic window during the whole period of the administration; the pre-systemic first-pass effect can be avoided which can result in higher bioavailability and fewer adverse effects than in the case of oral administration; the drug administration can be stopped instantly in situations where drug input is no longer desirable; it allows a reduced frequency of dosing which is particularly favourable for compounds with short biological half-life [10-14].

The ideal properties of a molecule penetrating intact stratum corneum (sc) well are: Molecular mass less than 600 Da, when the diffusion coefficient in sc tends to be high, Log P value between 1 and 3, High, but balanced, sc/vehicle partition coefficient, such that the drug can diffuse out of the vehicle, partition into, and move across, the sc without becoming sequestered within it [6, 9].

Aliskiren hemifumarate is selected for the treatment of hypertension because it rapidly absorbed through oral administration, with a low bioavailability ~2.6%. The terminal half-life ranges between 23 to 36 h. Aliskiren is eliminated primarily as unchanged drug in the feces; less than 1% was excreted in the urine. Aliskiren is a hydrophilic molecule ($\log P_{\text{oct-water}} = 2.45$ at pH 7.4) with favourable physicochemical properties including high aqueous solubility (>350 mg/ml at pH 7.4) that were considered an important prerequisite for improved oral bioavailability. Aliskiren has as its free base ($pK_a = 9.49$) the molecular formula $C_{30}H_{53}N_3O_6$ and a molecular mass of 609.8 g/mol as hemifumarate salt [1, 15, 16]. The aim of the study was to reduce the dosing frequency, increase the bioavailability of the drug by novel drug delivery over conventional formulation.

MATERIALS AND METHODS

Materials

Gift sample of aliskiren hemifumarate was provided by dr. morepen, methocel and ethocel from colorcon Mumbai. All other reagents/solvents used in this study are of analytical grade (sigma aldrich). Transdermal films containing aliskiren hemifumarate were prepared by solvent casting technique using mercury as a substrate. Overall forty-eight formulations were formulated using a different type of polymer in varying ratio and different plasticizer [17].

The animal used for skin irritation studies were adult rats weighing from 200-220 g, from the animal house of Innovative College of pharmacy, Greater noida. The experiment was conducted out in the

facility having an approved animal house (1346/c/10/CPCSEA). The animals were housed in polypropylene cages, 4 per cage with free access to water and standard laboratory diet (Lipton feed, Mumbai, India). They were kept at 25±1 °C and 45-55% relative humidity with a 12h light/dark cycle. No rats were harmed during the study and after completion of the experiment, rats were housed.

Experimental methods

Preparation of transdermal patches

Transdermal patches containing aliskiren hemifumarate were prepared by a solvent casting method. As shown in table 1, casting solutions were prepared by dissolving appropriate ratio of polymer,

the plasticizer in a suitable solvent using magnetic stirrer. The mixture was stirred continuously in such a manner that evaporation of the solvent was minimized. The drug was added slowly to the solution and dissolved by continuously stirring for 30 min.

Casting of matrices

For the formulation of films, mercury was spread uniformly on a glass petridish. The glass mould was kept on a mercury surface. About 5 ml of the solution was poured on the mercury. The rate of evaporation was controlled by inverting the funnel over the mould. After 6-7 h, the dried patches were removed from the mould and wrapped in aluminum foil and stored over fused calcium chloride in a desiccator at room temperature for further use.

Table 1: Composition of transdermal patches using glycerin and propylene glycol as plasticizer

S. No.	Formulation	Code [@]	Composition (Drug: polymer)	Plasticizer		Casting solvent (2:2:1)
				Glycerin (% w/w)*	Propylene glycol (% w/w)*	
1	Methocel K 15 M	A	1:1	150	150	Chloroform: Dichloromethane: Ethanol
2	Methocel K 15 M	B	1:1.5	150	150	---
3	Methocel K 15 M	C	1:2	150	150	---
4	Methocel K 100 M	D	1:1	150	150	---
5	Methocel K 100 M	E	1:1.5	150	150	---
6	Methocel K 100 M	F	1:2	150	150	---
7	Ethocel Standard	G	1:1	150	150	Chloroform
8	Ethocel Standard 4	H	1:1.5	150	150	Chloroform
9	Ethocel Standard 4	I	1:2	150	150	Chloroform
10	Ethocel Standard 10	J	1:1	150	150	Chloroform
11	Ethocel Standard 10	K	1:1.5	150	150	Chloroform
12	Ethocel Standard 10	L	1:2	150	150	Chloroform
13	Chitosan	M	1:1	150	150	Water
14	Chitosan	N	1:1.5	150	150	Water
15	Chitosan	O	1:2	150	150	Water
16	Gelatin	P	1:1	150	150	Water
17	Gelatin	Q	1:1.5	150	150	Water
18	Gelatin	R	1:2	150	150	Water
19	Eudragit RL	S	1:1	150	150	Acetone
20	Eudragit RL	T	1:1.5	150	150	Acetone
21	Eudragit RL	U	1:2	150	150	Acetone
22	Eudragit RS	V	1:1	150	150	Acetone
23	Eudragit RS	W	1:1.5	150	150	Acetone
24	Eudragit RS	X	1:2	150	150	Acetone

*% w/w of the polymer, @formulation code for propylene glycol: PG used as a prefix before code.

Compatibility studies of drug and polymers

The Fourier transform infrared (Perkin Elmer IR spectrometer 4000-400 V_{max} in cm^{-1}) analysis was the most powerful technique for qualitative compound identification. The main application of Fourier transform infrared spectrophotometry was a determination of the identity of a compound by means of spectral comparison with that of a reference and verification of the presence of functional groups in an unknown molecule. The potassium bromide pellet of the drug was prepared by grinding 3-5 mg of the sample with 100-150 mg of potassium bromide in pressure compression machine. The sample pellet was mounted in fourier transform infrared compartment and scanned between at wavelength 4000 cm^{-1} -400 cm^{-1} . The principal peaks of pure aliskiren hemifumarate and the selected polymers were evaluated. The resulted values show that the peaks don't-shift significantly in the fourier transform infrared spectra. The comparison with the pure drug as seen in fig. 1 and 2, respectively, indicating the compatibility of the drug with the polymers used.

Evaluation of transdermal patches

The patches were evaluated for the following physicochemical properties.

Weight variation

Uniformity of weight was determined by weighing three 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.

Percentage moisture absorption

The films were weighed accurately and placed in the desiccator containing 100 ml of saturated solution of aluminium chloride, which maintains 79.50% RH. After 3 d, the films were taken out and weighed. The percentage moisture absorption was calculated using the formula.

Percentage moisture absorption =

$$\frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

Percentage moisture loss

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

Percentage moisture loss =

$$\frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

Water vapour transmission rate

Glass vials of equal diameter were used as transmission cells. These transmission cells were washed thoroughly and dried in an oven. About 1 g anhydrous calcium chloride was placed in the cells and the

respective polymer film was fixed over the brim. The cells were accurately weighed and kept in a closed dessicator containing a saturated solution of potassium chloride to maintain a humidity of 84%. The cells were taken out and weighed after 6, 12, 24, 36, 48, and, 72 h of storage. The amount of water vapour transmitted was calculated using the formula.

Water vapour transmission rate =

$$\frac{\text{Final weight} - \text{Initial weight}}{\text{Time} \times \text{Area}} \times 100$$

Thickness

The thickness of the patch was measured at five different points using a screw gauge (Mitutoyo Japan) and average thickness recorded.

Content uniformity

A film was cut into small pieces and put in 100 ml buffer (pH 7.4). This was shaken on a mechanical shaker for 2 h to get a homogeneous solution and filtered. The resulting solutions were quantitatively transferred to volumetric flasks, and appropriate dilutions were made with pH 7.4 Phosphate buffer. The resulting solutions were filtered and analyzed for drug content at 279 nm in UV spectrophotometer. The average reading of three patches was taken as the content of drug in one patch.

In vitro permeation study

For the study of *in vitro* release patterns from the prepared TDDS formulation, a franz diffusion cell was used. The films were placed in between the donor and donor-receptor compartment in such a way that the drug releasing surface faced toward the receptor compartment. The receptor compartment was filled with phosphate buffer and stirred with magnetic bead and the temperature was controlled at 37 ± 1 °C.

A sample of 5 ml was withdrawn at predetermined intervals, being replenished by equal volumes of the elution medium. This was carried out for a period of 24 h. The drug concentration in the aliquot was determined and calculated and shown graphically from fig. 3 to 6.

Primary skin irritation studies

The mice were divided into 4 groups (n=6). On the previous day of the experiment, the hair on the back-side area of mice was removed. The animal of group I served as normal, without any treatment. Group II of animals was applied with marketed adhesive tape (official adhesive tape in USP). Transdermal systems (blank, without drug and drug loaded) were applied onto the nude skin of animals of group III and IV. The application sites were graded according to visual scoring scale, always by the same investigator. The erythema scale was as follows: 0, none; 1, slight; 2, well defined; 3, moderate and 4, severe

The patches were tested for their potential to cause skin irritation/sensitization in healthy albino rats of 200-220 gms. The skin from the back of each rat was depilated 24 h prior to the application of the patch.

The skin was cleared with rectified spirit. The patches were placed over the skin with the help of adhesive tape. They were removed after 24 h exposure. Upon removal of patches, the resulting reaction was evaluated according to US-FDA grading scale. [17-20].

RESULTS AND DISCUSSION

FTIR studies

The infrared spectral analysis of aliskiren hemifumarate alone showed that, the principle peaks were observed at wave numbers of 2932.66, 2969.47, 2875.29 cm^{-1} , that can be attributed to the asymmetric C-H stretching vibration of drug and also the characteristic bands at 1306.24 cm^{-1} , 1425.59 cm^{-1} , 1445.15 cm^{-1} and 1515.86 cm^{-1} , due to as (C=O). The two bands also meet at 1609.29 cm^{-1} and 1664.08 cm^{-1} being attributed to (C=O). The band at 1565.98 cm^{-1} is related to the stretching vibrations of the amine group. Bending vibrations of methylene and methyl groups are located at 1236.03 cm^{-1} and 1258.99 cm^{-1} , respectively. Confirming the purity of the drug as per established standards. In the infrared spectra of the physical mixture of drug and polymers, the major peaks of aliskiren hemifumarate were at same wave numbers. However, some additional peaks were observed in the mixture, which could be due to the presence of polymer.

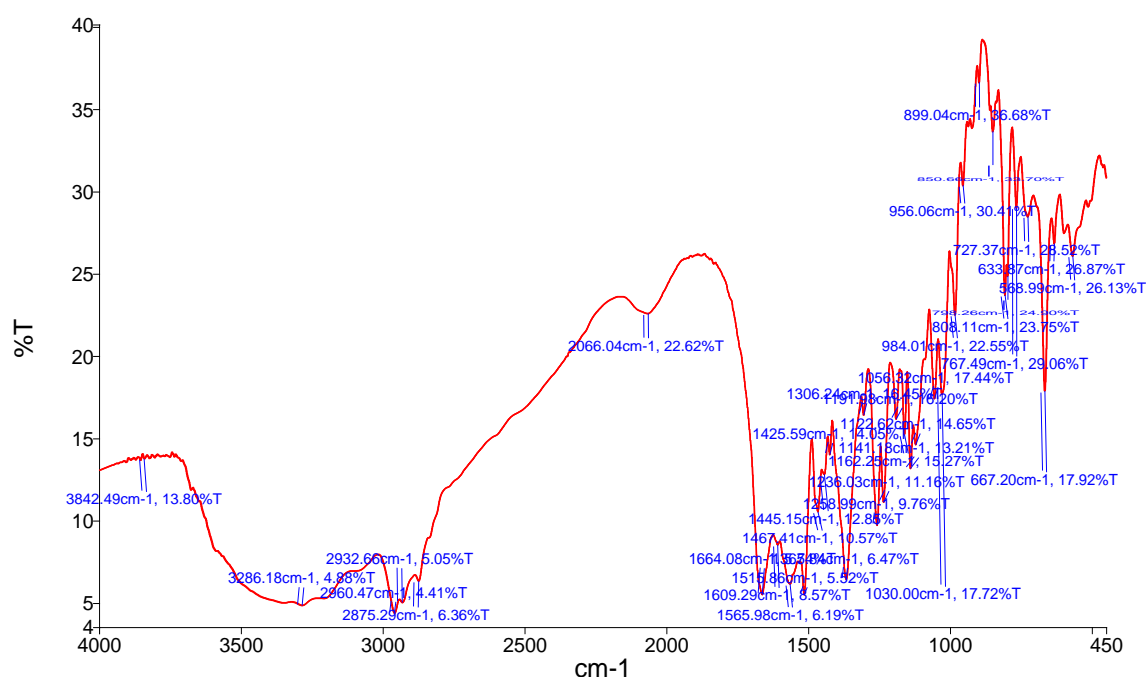


Fig. 1: FTIR spectra of aliskiren hemifumarate

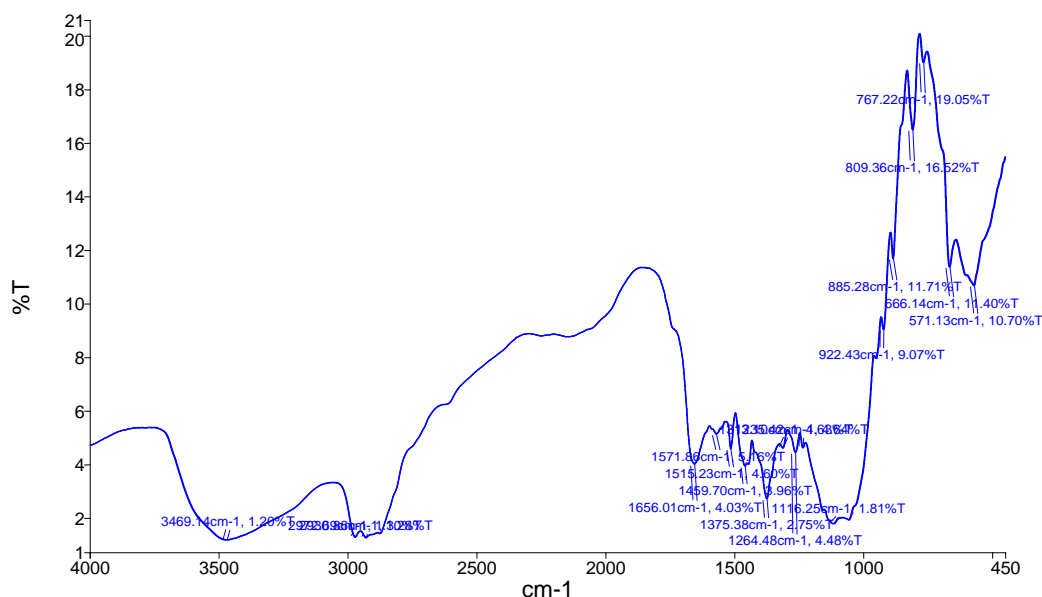


Fig. 2: FTIR spectra of aliskiren hemifumarate with polymers

Characterization of aliskiren hemifumarate transdermal patches for optimized formulations

The average weights of the formulations prepared using glycerin as a plasticizer were ranged from 42.33-67.00 mg and propylene glycol as a plasticizer were ranged from 40.67-67.67 mg. The difference in weight depends on varying polymer concentration.

Moisture content and moisture uptake studies indicated that the increase in the concentration of hydrophilic polymer was directly proportional to the increase in moisture content and moisture uptake of the patches. The moisture content of the prepared formulations was low, which could help the formulations remain stable and reduce brittleness during long-term storage. The moisture uptake of the formulations was also low, which could protect the formulations from microbial

contamination and reduce bulkiness. The percentage moisture absorption varies from 1.76 to 10.73 for patches formulated using glycerin and 2.28 to 7.97 for propylene glycol patches.

The percentage moisture loss from patches prepared using glycerin was range from 2.75 to 11.54 and 2.87 to 12.02 from propylene glycol.

The water vapour transmission rate from patches prepared using glycerin was range from 0.25 to 0.92 and 0.41 to 1.76.

Thickness and folding of both patches were satisfactory.

Good uniformity of drug content among the formulated patches. The acceptable quantity of medicament ranged from (100.20-101.05%). This result met the test content uniformly as per BP (85% to 115%). According to that, the drug was consistent throughout the patches.

Table 2: Result showing effect of physicochemical properties of patches prepared using glycerin as plasticizer

Formulation code	Weight variation (mg)		Percentage moisture absorption		Percentage moisture loss		Water vapor transmission rate(g/cm ² /h)		Thickness(mm)		Content uniformity(mg)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
A	53.33	0.58	4.26	0.294	3.16	0.621	0.55	0.02	0.092	0.003	4.580	0.010
B	58.33	0.58	5.16	1.063	3.85	0.237	0.54	0.30	0.066	0.005	4.553	0.015
C	65.00	1.00	4.44	0.962	4.39	0.431	0.78	0.58	0.069	0.002	4.563	0.025
D	42.33	1.53	4.79	1.086	2.79	0.715	0.53	0.17	0.043	0.002	4.547	0.023
E	52.00	2.65	5.59	1.506	4.96	0.892	0.46	0.02	0.057	0.003	4.557	0.012
F	61.67	1.15	5.66	1.069	5.60	0.463	0.34	0.01	0.079	0.006	4.567	0.015
G	44.00	3.00	5.65	0.894	4.89	0.915	0.35	0.01	0.048	0.003	4.547	0.012
H	52.00	1.00	6.04	0.344	5.56	0.475	0.46	0.02	0.052	0.004	4.570	0.010
I	57.67	1.53	5.27	0.361	6.40	0.845	0.56	0.04	0.155	0.226	4.567	0.023
J	49.00	2.00	6.14	0.290	5.08	0.751	0.48	0.04	0.061	0.002	4.570	0.020
K	54.33	2.52	5.66	0.680	5.16	0.300	0.58	0.08	0.066	0.003	4.563	0.006
L	63.00	2.65	7.32	1.189	6.55	0.221	0.39	0.13	0.072	0.003	4.557	0.021
M	49.67	2.08	3.55	0.773	7.71	0.614	0.76	0.02	0.046	0.003	4.580	0.010
N	57.00	2.00	5.51	1.129	8.46	0.278	0.75	0.08	0.052	0.002	4.557	0.012
O	60.00	1.00	7.24	0.295	10.43	0.517	0.89	0.04	0.060	0.002	4.557	0.012
P	47.67	1.53	7.47	1.055	7.98	0.235	0.73	0.02	0.035	0.003	4.570	0.020
Q	51.33	2.08	8.66	0.669	9.59	0.597	0.87	0.07	0.041	0.002	4.567	0.015
R	67.00	1.00	10.73	0.570	11.54	0.255	0.92	0.08	0.045	0.003	4.563	0.021
S	52.33	1.53	2.65	0.315	3.15	0.245	0.34	0.05	0.040	0.002	4.567	0.015
T	61.00	2.00	1.76	0.598	4.12	0.318	0.41	0.04	0.044	0.002	4.563	0.012
U	65.33	1.53	3.49	1.072	5.08	0.372	0.59	0.04	0.050	0.002	4.557	0.015
V	49.67	2.08	4.09	0.774	2.75	0.365	0.25	0.09	0.042	0.002	4.560	0.000
W	54.33	2.31	4.46	0.730	4.14	0.238	0.49	0.05	0.050	0.002	4.563	0.021
X	59.33	1.53	6.10	0.402	4.82	0.297	0.44	0.09	0.056	0.002	4.543	0.015

(mean value±SD) (n=3);SD: Standard deviation

Table 3: Result showing effect of physicochemical properties of patches prepared using propylene glycol as plasticizer

Formulation code	Weight variation(mg)		Percentage moisture absorption		Percentage moisture loss		Water vapor transmission rate(g/cm ² /h)		Thickness (mm)		Content uniformity(mg)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
PGA	53.67	0.58	4.43	0.09	2.87	0.94	0.54	0.03	0.09	0.00	4.51	0.02
PGB	57.33	0.58	4.93	0.15	4.32	0.78	0.85	0.09	0.07	0.00	4.54	0.02
PGC	64.67	0.58	5.25	0.25	4.02	0.34	1.49	0.64	0.07	0.00	4.52	0.03
PGD	40.67	0.58	3.87	0.78	3.14	0.40	0.83	0.09	0.05	0.00	4.55	0.03
PGE	53.67	1.53	6.22	0.44	4.90	0.78	0.91	0.31	0.06	0.00	4.55	0.04
PGF	63.67	0.58	5.97	1.71	6.08	0.75	0.52	0.11	0.38	0.41	4.56	0.01
PGG	44.67	2.08	5.25	1.04	4.53	0.99	0.41	0.02	0.05	0.00	4.52	0.02
PGH	52.00	0.00	6.11	0.44	4.77	1.17	0.52	0.04	0.05	0.00	4.54	0.04
PGI	57.67	0.58	4.83	0.81	7.11	0.98	0.64	0.03	0.06	0.00	4.57	0.02
PGJ	51.00	1.00	7.20	0.21	5.22	0.89	0.57	0.10	0.06	0.00	4.55	0.02
PGK	55.33	0.58	4.65	0.94	4.93	1.52	0.83	0.12	0.07	0.00	4.54	0.04
PGL	65.00	1.00	7.97	0.27	6.97	0.58	0.54	0.07	0.08	0.00	4.54	0.03
PGM	48.33	1.15	4.89	1.72	8.01	1.03	0.93	0.07	0.05	0.00	4.55	0.03
PGN	57.33	1.15	5.93	0.63	8.81	0.21	1.08	0.25	0.05	0.00	4.54	0.04
PGO	59.67	0.58	8.24	0.66	10.84	0.61	1.14	0.18	0.06	0.00	4.53	0.02
PGP	47.67	1.15	7.49	1.01	8.52	0.99	1.76	0.75	0.03	0.00	4.54	0.03
PGQ	51.67	0.58	9.21	0.44	11.08	0.59	0.95	0.05	0.04	0.00	4.53	0.05
PGR	66.67	1.53	9.48	0.50	12.02	0.43	0.97	0.05	0.05	0.00	4.52	0.02
PGS	53.67	0.58	2.69	0.76	3.39	0.41	0.62	0.17	0.04	0.00	4.55	0.02
PGT	63.00	1.00	2.28	0.51	4.30	0.58	0.51	0.07	0.05	0.00	4.56	0.01
PGU	67.67	1.53	4.28	0.71	5.16	0.29	0.83	0.14	0.05	0.00	4.52	0.03
PGV	51.00	2.00	4.47	0.50	3.13	1.37	0.86	0.37	0.04	0.00	4.52	0.01
PGW	54.67	1.53	4.96	0.39	4.16	1.25	0.86	0.18	0.05	0.00	4.53	0.04
PGX	61.33	1.15	5.89	1.05	4.90	1.17	0.93	0.24	0.06	0.00	4.52	0.01

(mean value±SD) (n=3);SD: Standard deviation

In vitro permeation studies

The cumulative percentage drug permeated by the individual path in the *in vitro* skin permeation studies were based on the mean amount of drug present in the respective patch. The *in vitro* drug release profile was studied using the best fit model from formulations

prepared using varying concentration of polymer and different plasticizer. The percentage drug release was found best in formulation PGD with 43.75 % prepared with Methocel K 100 M using propylene glycol as a plasticizer. The plot of cumulative percent permeated for all the formulations was shown in the fig. 3 to 6. All the formulations show the zero order release.

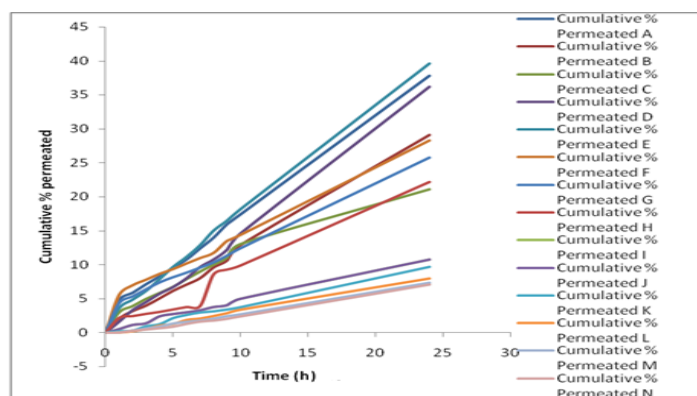


Fig. 3: Plot of cumulative percent permeated versus time for formulations A-N

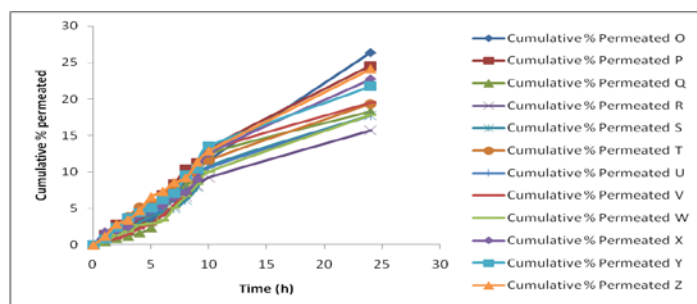


Fig. 4: Plot of cumulative percent permeated versus time for formulations O-Z

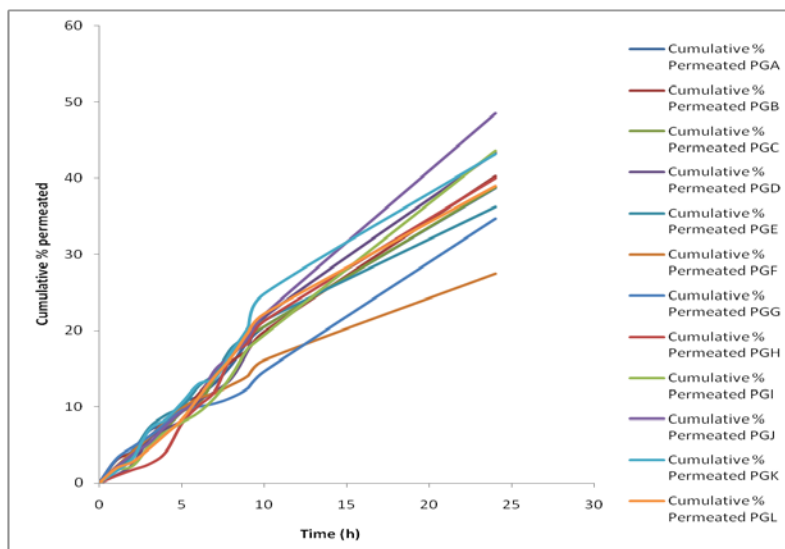


Fig. 5: Plot of cumulative percent permeated versus time for formulations PGA-PGL

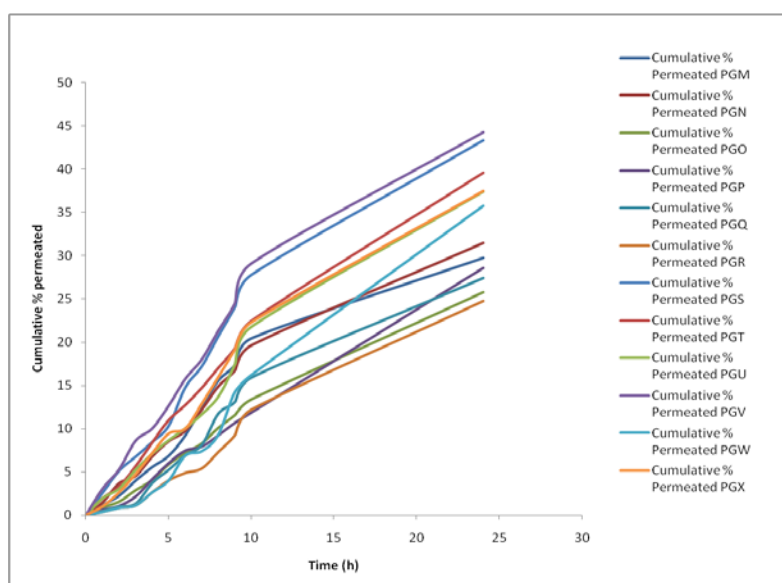


Fig. 6: Plot of cumulative percent permeated versus time for formulations PGM-PGX

Primary skin irritation studies

The skin irritation test of the transdermal formulations PGD showed a skin irritation score (erythema and edema) of less than 2. The compounds producing scores of 2 or less are considered negative (no skin irritation). Hence, the developed transdermal formulations are free of skin irritation.

DISCUSSION

Transdermal route enhances the bioavailability of the drug by avoiding the first pass metabolism and increases the therapeutic efficacy of the drug by reaching into the systemic circulation. This is the most suitable system for a long-term treatment or for a multi-dose treatment because transdermal patches are prepared for a long period of time in a single dose providing treatment from a day to even up to seven days. Synthetic and natural polymers were selected on the basis of their adhering property and nontoxicity. The result of the study showed good controlled release. The result from present study concluded that aliskiren in combination with Methocel K 100M with an incorporation of propylene glycol produced a smooth, flexible and transparent film. FTIR studies showed characteristic

peaks of aliskiren hemifumarate, confirming the purity of the drug. FT-IR spectral studies indicated there was no interaction between aliskiren hemifumarate and polymers used for the patches.

The patches were prepared in varying composition of the polymers and evaluated it for physical parameters such as weight variation, thickness, drug content, water vapour transmission rate, % moisture loss and % moisture absorption. The drug content of transdermal drug delivery system (TDDS) patches ranged from 100.20-101.05%. Among all these formulations, the formulation PGD showed the maximum % drug cumulative release i.e. 43.75% up to 24 h of the study.

CONCLUSION

The primary objective of the study was to increase the bioavailability of the drug and secondary to study the effect of different polymers and plasticizer in the formulation. It can be concluded that the patches prepared using propylene glycol (PGD) shown better physicochemical properties and release profile over the patches prepared using glycerin. It can be used for an extended period without the risk of skin irritation. This will enhance the patient compliance throughout reduction of dosing administration.

AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICTS OF INTERESTS

Declare none

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