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Fabrication and assessment of transdermal patches accustom with antihypertensive medicaition

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ABSTRACT

Basically, to provide a continuous drug infusion through an intact skin, various transdermal systems have been designed for topical application and it control the delivery of drug and its permeation via the skin tissue. Historically, developments related to TDDS have been incremental, concentrating on overcoming issue related with the skin barrier properties, minimizing skin irritation and improving the outlook related with passive patch systems. TDDS defined as self-contained, discrete dosage form applied to the unharmed skin then it deliver the drug, via skin at controlled manner in the systemic circulation. Transdermal drug delivery via the skin provides a suitable route of administration for a various clinical indications. Captopril is an angiotensin-converting enzyme inhibitor, which reduces peripheral resistance end lowers blood pressure. It is extensively used for the treatment of hypertension and congestive failure. And hence only in our current research we have, fabricated a transdermal delivery system comprising Captopril for the better patient compliance. The transdermal patches were prepared by solution casting technique employing a glass substrate. Membrane type transdermal systems with Captopril prepared using HPMC alone and by employing various proportions of HPMCK15M, PVPK30, and Ethyl Cellulose. It has been observed, that current method for the fabrication of transdermal patches accustom with antihypertensive drug has been found to be significant, conducive and remarkable.

Keywords: Transdermal system, Fabrication, Evaluation, Captopril and drug permeation.

INTRODUCTION

TDDS defined as self-contained, discrete dosage form applied to the unharmed skin then it deliver the drug, via skin at controlled manner in the systemic circulation. Transdermal drug delivery via the skin provides a suitable route of administration for a various clinical indications. The skin is the largest and most readily accessible organ in the body and its use for topical and systemic effect of drug has been well documented. Many formulations used traditionally

include ointments, gels, creams etc. Alza Corporation developed first transdermal patch for motion sickness [1-6]. Modern commercial drug products accepted the benefits and applicability of this method of administrations. There are several products in last-stage development for various therapeutic areas like parkinson disease, sexual dysfunction, hypertension in angina, motion sickness. TDDS represent a convenient option for drug delivery because of flexibility, dose change facility according to patient demand and self regulation of dosage by patient. TDD can use in a patient with minimal co-operation here other person also involve in the administration process other than the patient. The non-invasive nature of transdermal delivery systems easily accessible to a large patient populations and most acceptable alternative for drug dosing [1-5].

MATERIALS AND METHODS

Estimation of partition coefficient

The partition coefficient was determined with n-octanol and PBS pH 7.4 as oil and aquous phase respectively. The n-octanol: phosphate buffer saline partition coefficient used to study lipophilicity. 100mg of drug was dissolved in 10 ml n-octanol and was shaken at 370C for 24 h in a sealed container. The two phases were separated and then they were analyzed spectrophotometerically (ShimadzuUV-1800, Japan) for respective drug contents. The Ko/w was calculated using following expression [6-10];

Preparation of calibration curve for Captopril

Captopril was dissolved in 10 ml methanol and volume is made up to 100 ml in volumetric flask with PBS pH 7.4. From stock solution 1 ml was pipette out (100 µg/ml) then further diluted to get solutions having concentrations 2µg/ml to 24 µg/ml. Absorbance of these solutions were measured using UV Spectrophotometer at 220 nm with PBS pH 7.4 as a blank [7-10]. The calibration curve was produced for entire range from 2 to 10 µg/ml [11-13].

Compatibility study

FTIR absorption spectra of Captopril, polymers (HPMCK15M, PVPK30, and EC) and dry sample of drug was directly placed after mixing and triturating. Also combined mixture of Captopril and polymer was recorded by using FTIR spectrophotometer (Bruker FTIR).

Preparations of transdermal patches

The transdermal patches of composition listed in table no.5.3 were prepared by solution casting technique employing a glass substrate (Bangles wrapped with aluminium foil). Membrane type transdermal systems with Captopril prepared using HPMC alone and by employing various proportions of HPMCK15M, PVPK30, and Ethyl Cellulose. The polymers was accurately weigh and dissolved in a suitable solvent mixed until clear solution formed with magnetic stirrer then added Captopril to the uniform polymeric solution and mixed completely to form uniform solution. PEG400 and dibutyl phthalate added as a plasticizer. DMSO and tween-80 were used as a penetration enhancer. The polymer solution was poured into bangles placed in a suitable level, hard rigid surface and patches were dried at a room temperature in a dust free environment for 24 hrs [11-13] an inverted funnel was covered over the bangles to avoid fast evaporation of the solvent. Patches of 3.14 cm^2 were prepared by cutting and packed in an aluminum foil and kept in a desiccator.

RESULTS AND DISCUSSION

Table No. 1 Composition of Captopril transdermal patches

Formulation	F1	F2	F3	F4	F5	F6	F7
Drug (mg)	65	65	65	65	65	65	65
HPMCK15M (mg)	500	450	400	300	-	-	-
PVPK30 (mg)	-	50	100	200	400	300	200
EC (mg)	-	-	-	-	100	200	300
PEG-400*(ml)	0.18	0.18	0.18	0.18	-	-	-
Dibutyl phthalate *(ml)	-	-	-	-	0.2	0.2	0.2
Tween 80*(ml)	0.14	0.14	0.14	0.14	-	-	-

DMSO* (ml)	-	-	-	-	0.11	0.11	0.11
DCM/Methanol (ml)	12	12	12	12	-	-	-
Chloroform (ml)	-	-	-	-	5	5	5

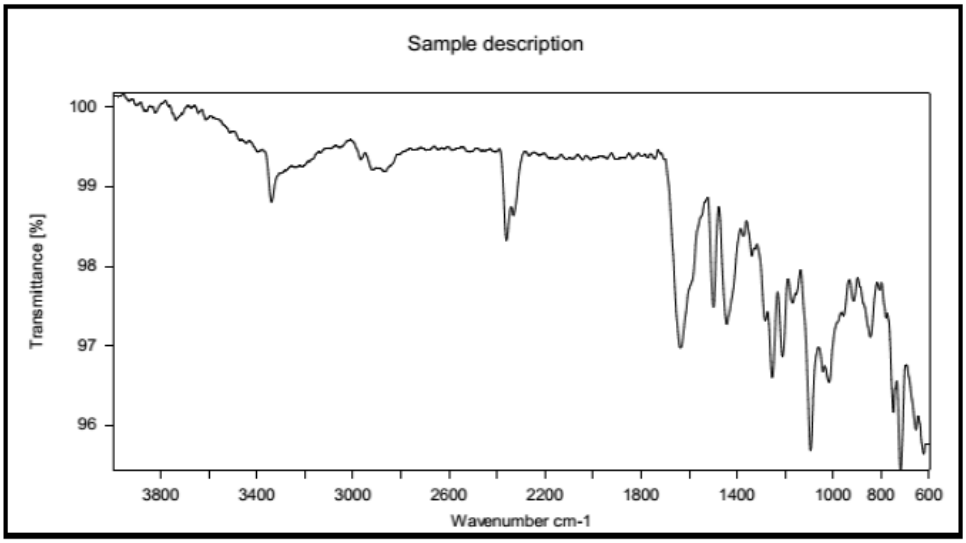

Figure No 1. FTIR Spectra of Captopril TDDS

The compatibility studies were performed to find out interaction of drug with the polymer that is used in the formulation of TDDS. The FT-IR spectrum of the drug and polymer did not show presence of any additional peaks for new functional groups. These results suggest compatibility between drug and polymer.

Table No. 2 Physicochemical Evaluation data of Transdermal Patches of Captopril

Formulation Code	% Elongation	% Moisture Content	% Moisture uptake	Swelling index
F_1	24.13	1.85	4.87	24.17
F_2	22.70	1.6	3.6	25.75
F_3	26.00	3.1	4.3	25.50
F_4	26.25	3.2	4.7	23.41
F_5	27.94	3.23	5.7	22.82
F_6	26.06	2.7	4.76	25.18
F7	25.25	2.8	4.77	26.19

Table No. 3 *In-vitro* Drug Permeation of Captopril Data Batches F1-F7

Cumulative drug permeated in (µg/cm^2)						
F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**
729	156	177	174	122	182	174
1216	290	299	298	242	321	321
1511	564	565	559	702	595	595
1656	754	675	703	729	822	821
_	1012	956	982	961	1015	1015
_	1251	1188	1214	1243	1295	1215
_	1498	1387	1418	1442	1496	1296
_	1592	1593	1641	1668	1640	1441
_	1722	1828	1925	1905	1741	1597

Table No. 4 Stability Study of batch F5

Sr. no	Evaluation Parameter	At o day	After 90 days
1	Thickness (mm)	0.35	0.34
2	Weight variation	0.225	0.224
3	% Drug Content	96.36	95.68
4	Folding endurance	58	57
5	Tensile Strength Kg/mm^2	2.41	2.40
6	% Elongation	28.04	26.41
7	% Moisture content	3.23	2.5
8	% Moisture uptake	5.7	4.89
9	Swelling index	22.82	22.46

Table No. 5 Drug permeation study: F5

Time in (hrs)	% Cumulative permeated (At 0 day)	% Cumulative Permeated (After 90 days)
2	5.87	4.53
4	11.70	10.47
6	33.95	32.31
8	35.26	34.18
10	46.45	44.85
12	60.05	59.39
16	69.64	68.58
20	80.58	79.18
24	92.05	91.38

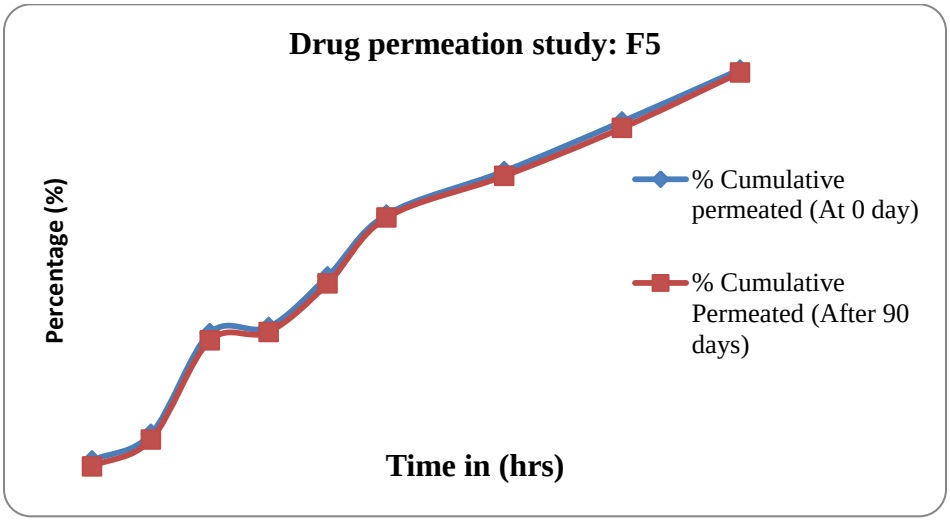

Figure No 2. Drug Permeation study of F5

CONCLUSION

In due course, based on results of various evaluation parameters like thickness, strength, elongation, better compatibility and stability the transdermal matrix patches was successfully designed and developed by trial and error method. Formulations were prepared by employing combination of HPMCK15M, PVPK30, and EC in various ratios. From the research, various conclusions were drawn. The patches showed good thickness, tensile strength and content uniformity of drug. The used polymers employed to design transdermal patches in different proportion. The Captopril penetration from formulated transdermal patches was found to follow diffusion mechanism and obeys zero order release.

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