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DESIGN AND DEVELOPMENT OF TRANSDERMAL PATCH OF BUCLIZINE HYDROCHLORIDE.

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ABSTRACT
Matrix type Transdermal drug delivery system of Buclizine Hydrochloride , an Antiallergic drug were prepared. Using different polymers like, HydroxyPropyl Methyl Cellulose and Eudragit L100 in varied ratios. The present study aims to formulate and evaluate Transdermal drug delivery for sustained release of Buclizine Hydrochloride. Physicochemical parameter was characterized. The permeability studies indicate that the drug is suitable for Transdermal drug delivery. The patches were evaluated for various parameters like Thickness, Drug Content, Diffusion and Dissolution studies. The patches were further evaluated by IR to ensure uniform distribution of the drug and compatibility of drug with polymer. The Optimized formulation: Eudragit L100 with enhancer Dimethyl sulphoxide 96% drug release after 12 hours compared with eucalyptus oil.

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INTRODUCTION

Buclizine Hydrochloride , an Antiallergic drug has a half-life of 3 to5 hours and a bioavailability of 30-40%. It undergoes extensive first pass metabolism. The present study aims to formulate and evaluate Transdermal drug delivery for sustained release of Buclizine Hydrochloride. Transdermal drug delivery systems are capable of controlling the rate of drug delivery, sustaining the duration of therapeutical activity and targeting the delivery of drug to a tissue1.In response to these advances, several Transdermal drug delivery systems have been developed to achieve the objective of systemic medication through application on the intact skin surface2.The advantage of Transdermal drug delivery system is that they can provide sustained drug delivery and enhance constant drug concentrations in plasma over a prolonged period of time. Thus it is anticipated that Transdermal drug delivery systems can be designed to deliver drugs at appropriate rates to maintain suitable plasma–drug levels for therapeutic efficiency, without the periodic into plasma concentration that would accompany toxicity or lack of efficiency. Ultimately the success of all Transdermal systems depends on the ability of the drug to permeate skin in sufficient quantities to achieve its desirable therapeutic effects. Transdermal therapeutic

systemic are defined as self- contained, discrete dosage form when applied to skin a controlled rate to the systemic circulation. One of the approaches of transdermal therapeutics system (TTS) is maintenance of blood concentration of drug at therapeutic level by means of controlled permeation throughout the skin (therefore avoiding the fist-fast effect) during a long period of time and using only one administration3

MATERIALS AND METHODS

Materials

Buclizine Hydrochloride was gift sample from srikem lab. Mumbai. -, Eudragit RL 100(ERL 100),) and Hydroxypropyl Methyl Cellulose (HPMC) were gift samples from Lupin, Goa, India. Dimethyl sulphoxide (DMSO), Eucalyptus oil (S.D fine chemical lab, Mumbai, India). , Dibutyl phthalate (DBP), chloform, methanol.(loba chemical Mumbai)

Method

Solvent Evaporation Method [4,]

Accurately weighed quantities of polymers were mixed in different compositions with suitable solvent. was taken in a beaker (Sonication for 1to 2 hr) Then 40 mg of drug was slowly added. (Sonication for 1 hr) Then required quantity of DMSO was added as penetration enhancer and DBP as plasticizer. Then it was poured in a glass Petri dish. Then placed in hot air oven for evaporation. at 40oC. The rate of evaporation of the solvent was controlled by placing an inverted funnel over the Petri dish. The films were removed by using sharp blade by inserting along the edges of the film. The dried films were wrapped in butter paper and stored in a closed

Container away from light and in cool place.

EVALUATION PARAMETERS [5, 6, 7, 8]

1. Physical appearance

All the Transdermal patches were visually inspected for Transparency, Stickiness, flexibility and smoothness.

2. Weight uniformity

It was determined by weighing five film formulations individually on a digital balance. The average value was taken as a weight of the films.

3. Folding endurance

A strip of film (2× 2 cm) 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.

4. Thickness

The thickness of the drug loaded film was measured in different point by using digital micrometer and determine average thickness.

5. Percent Moisture Absorption

The weighed films were kept in desiccators at room temperature for 24hrs containing saturated solution of potassium chloride in order to maintain 84% RH. After 24hrs the films are to be reweighed and determine the percentage moisture uptake from the below mentioned.

$$\% \text{ Percent Moisture Absorption} = \frac{\text{Final Weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

6. Percent Moisture Loss

The prepared films were weighed individually and to be kept in a desiccators containing fused calcium chloride at room temperature for 24 hrs. After 24hrs the films are to be reweighed and determine the percentage moisture content from the below mentioned formula.

$$\% \text{ Moisture Loss} = \frac{\text{Inital weight} - \text{Final weight}}{\text{Inital weight}} \times 100$$

7. Drug content

The patches (1 cm^2) were cut and added to a volumetric flask containing 10 ml of phosphate buffer of pH 7.4 (solution).From solution 1, 01 ml solution was taken and the volume was made (20 ml)with phosphate buffer saline (pH 7.4).The contents were filtered using whatman filter paper and the filter was examined for the drug content against the reference solution consisting of placebo film (contains no drug) at 230 nm specrtophotometrically.

8. *In vitro* drug release through cellophane membrane.

Chien diffusion cell was used in our studies for in-vitro drug release. The cell consists of two chambers, the donor and the receptor. The donor compartment is open at the top and is exposed to

the atmosphere. The receptor compartment is surrounded by a water jacket for maintaining the temperature at 37 oC ± 2o C and is provided with a sampling port. The diffusion medium was phosphate buffer of pH 7.4, which was stirred with magnetic bead (operated by a magnetic stirrer). cellophane membrane was placed between the two chambers. Diffusion media was stirred to prevent the formation of concentrated drug solution just beneath the membrane. Samples from the receptor compartment were taken at various intervals of time over a period of 12 hours and the concentration of the drug was determined by UV Spectrophotometric method using the standard

9. *In situ* drug release through Goat skin

Preparation of the skin barrier: fresh full thickness goat skin was used for the study. The skin was immersed in water at 60ºc for a period of 5 minutes .The epidermis was peeled from the dermis .Theisolated epidermis (25 ± 5 cm thick) was rapidly rinsed to remove surface lipids and then rinsed with water and used immediately. The *in vitro* skin permeation from the prepared polymeric patches across the goat skin barrier was studied using diffusion cell. Phosphate buffer of pH 7.4 was used as an elution medium. The patches to be studied were placed in between the donor and the receptor compartment in such a way that the drug releasing surface faced toward the receptor compartment. The temperature of the whole assembly was maintained at 37 ± 1ºC by thermostatic arrangements. An aliquot of 1 ml was withdrawn at a suitable interval and an equivalent volume of fresh buffer was replaced. The amount of drug permeated across the skin was determined on a UV spectrophotometer at 230 nm.

CONCLUSION

- All a nine batches shows good physical appearance, optimum thickness, and folding indurance . It was due to the optimum concentration of polymer and plasticizer .
- Drug content of all batches was in the range 92 to 99.20 %
- The batch containing Eudragit L 100 and DMSO as penetration enhancer shows good in vitro drug release.
- Eucalyptus oil is a natural penetration enhancer but DMSO shows better penetration activity.

Table.No.1 Formulation of transdermal patch of buclizine HCL. With different concentration of polymer.

Sr. no	Ingredients	Formulation codes								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Buclizine Hydrochloride (mg)	40	40	40	40	40	40	40	40	40
2	HPMC (mg)	100	100	100	200	200	200	--	--	--
3	Eudragit L100 (mg)	100	100	100	--	--	--	200	200	200
4	Dimethyl sulphoxid(ml)	0.6	--	0.3	0.6	--	0.3	0.6	--	0.3
5	Eucalyptus oil(ml)	--	0.6	0.3	--	0.6	0.3	--	0.6	0.3
6	Dibutyl phthalate(ml)	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08
7	Methanol (ml)	4	4	4	4	4	4	4	4	4
8	Chloroform (ml)	4	4	4	4	4	4	4	4	4

Fig. no 1. Formulated Transdermal patch.

Table no.2 Evaluation of TDDS patch

Sr no	Formulation code	physical appearance	Weight* (mg)	Thickness* (mm)	Folding Endurance
1	F1	++	360.5(±0.50)	0.065(±0.005)	>200
2	F2	++	420.8(±0.82)	0.082(±0.006)	>200
3	F3	++	490.6(±0.52)	0.094(±0.008)	>175
4	F4	++	363.0(±0.70)	0.122(±0.005)	>200
5	F5	++	430.6(±0.85)	0.134(±0.006)	>200
6	F6	++	494.8(±0.82)	0.15(±0.008)	>200
7	F7	++	365.5(±0.87)	0.065(±0.006)	>300
8	F8	++	365.2(±0.52)	0.124(±0.005)	>200
9	F9	++	370.8(±0.80)	0.067(±0.008)	>250

Formulation code	Drug content (%)*	% Moisture absorption	% Moisture loss
F1	96.02(± 0.62)	3.02(± 0.057)	1.22(± 0.98)
F2	98.10(±0.34)	2.34(± 0.038)	1.33(± 0.62)
F3	93.12(± 0.62)	2.21(± 0.073)	1.54(± 1.22)
F4	97.25(±0.52)	1.83(± 0.032)	2.01(± 0.82)
F5	96.30(±0.35)	1.72(± 0.062)	2.81(± 0.62)
F6	97.25(±0.95)	1.52(± 0.042)	2.22(± 0.92)
F7	99.20 (± 0.70)	1.34(± 0.022)	2.34(± 0.72)
F8	97.80(± 0.30)	1.45(± 0.036)	1.99(± 0.68)
F9	92.00(±0.30)	2.44(± 0.065)	1.85(± 0.42)

Table no. 3 Evaluation parameter of transdermal PATCH % drug content, % moisture absorption, % moisture loss

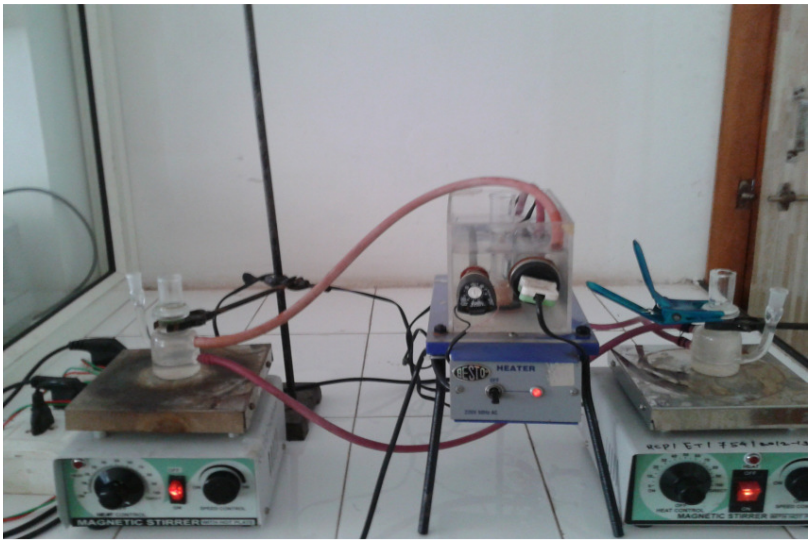
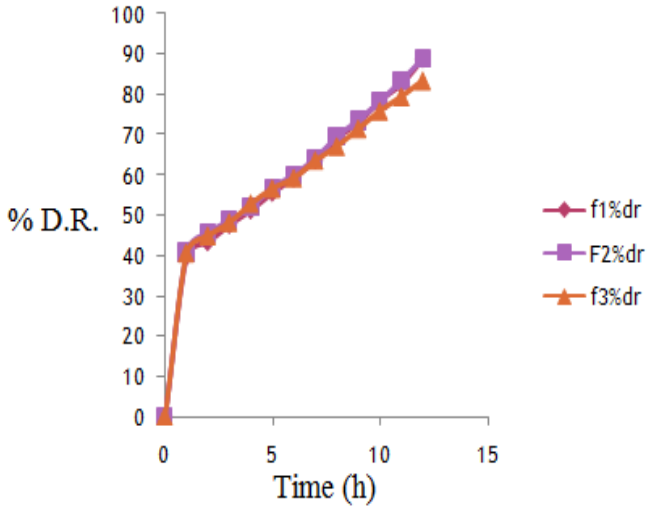


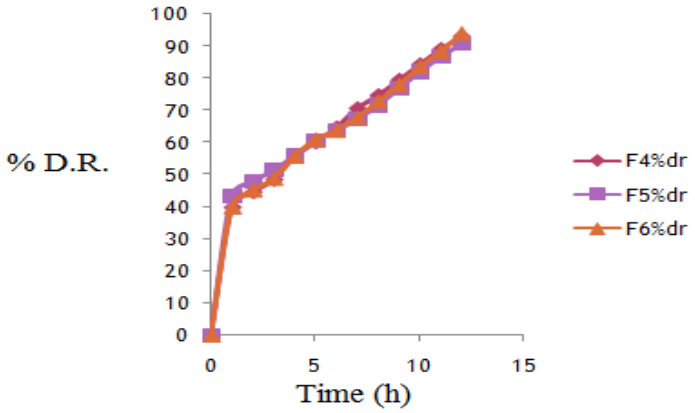
Fig no. 2 Assembly of diffusion cell

Table no. 4 To determine % drug release by using keshary-chien diffusion cell

Time(hr)	F1 %DR	F2 %DR	F3 %DR	F4 %DR	F5 %DR	F6 %DR	F7 %DR	F8 %DR	F9 %DR
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1	39.76	40.79	40.63	39.84	43.41	39.84	39.84	38.65	40.23
2	43.41	47.79	44.52	44.60	47.77	45.07	45.15	44.60	43.80
3	47.69	48.73	48.25	48.49	51.34	48.60	49.76	49.12	47.77
4	51.34	52.14	52.93	55.55	55.71	55.63	56.90	55.71	52.93
5	55.71	56.9	56.66	60.07	60.31	60.87	61.66	59.68	55.63
6	59.28	60.07	59.28	64.60	63.65	63.65	65.23	63.65	57.69
7	63.8	64.28	63.65	70.63	67.22	67.31	71.58	68.80	63.65
8	69.12	69.6	67.14	74.68	71.50	72.69	74.74	71.58	68.80
9	73.17	73.65	71.58	79.44	76.74	77.75	79.52	74.44	71.58
10	78.49	78.33	75.95	84.28	81.90	83.49	85.77	79.52	75.71
11	82.69	83.49	79.52	89.04	86.66	88.45	90.63	83.49	79.52
12	89.04	89.04	83.49	93.08	90.63	93.80	96.98	87.46	86.46

% D.R .By using graph





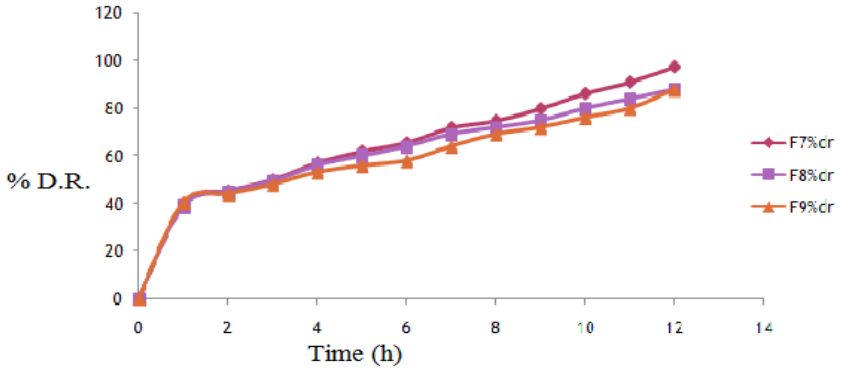
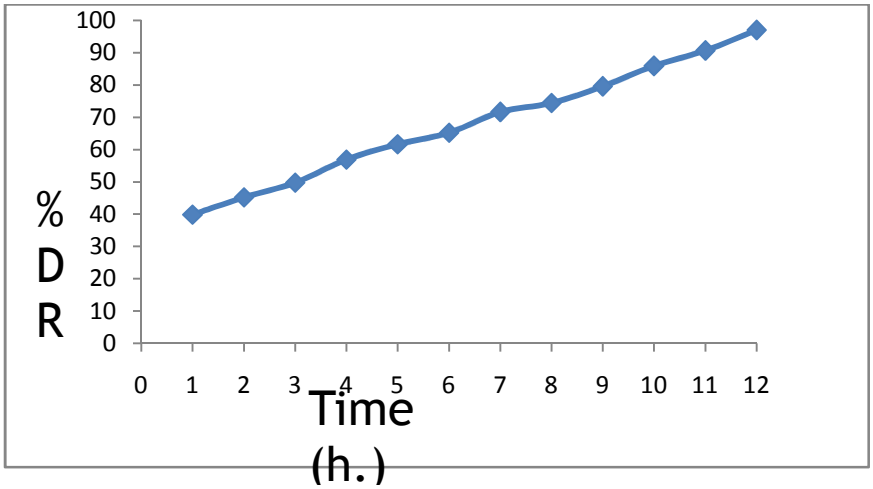


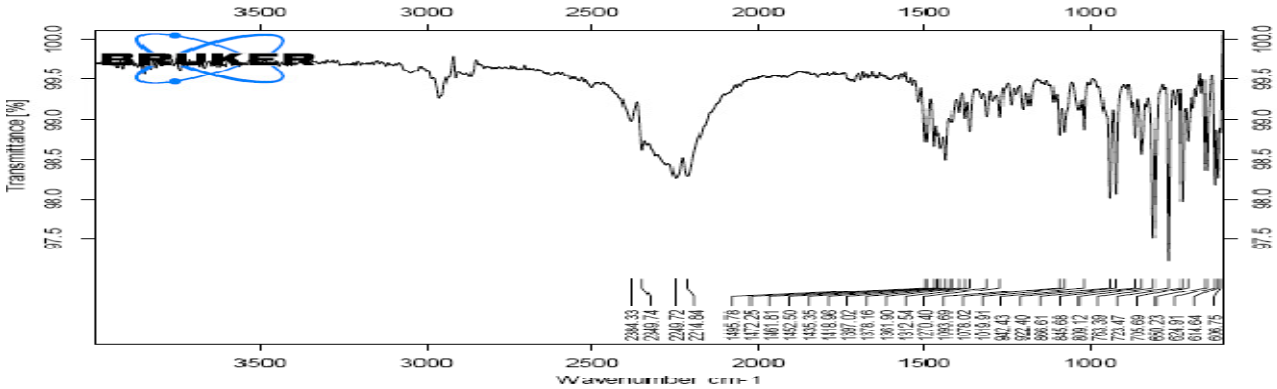
Table no. 5 Drug Release kinetics (Batch f7)

Models	R^2
Zero order	0.998
First order	0.834
Korsmeyer peppas	0.956
Higuchi	0.983
Hixson-crowell	0.993

Zero order

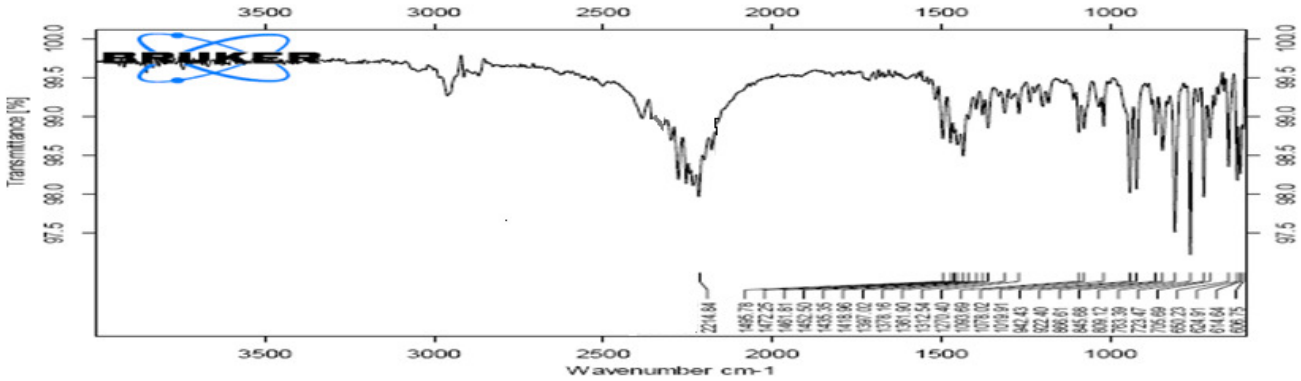


IR Spectra of Buclizine .HCL



STANADARD PEAK (cm^{-1})	OBSERVE PEAK (cm^{-1})	FUNCTIONAL GROUP
1400-1500	1435.35	C-C Aromatic
1250-1335	1270.40	C-N Aromatic Amine
550-850	723.47	C-Cl Alkyl halide
675-900	886.61	C-H Aromatic

IR spectra of optimized Batch F7



STANADARD PEAK (cm^{-1})	OBSERVE PEAK (cm^{-1})	FUNCTIONAL GROUP
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1250-1335	1270.40	C-N Aromatic Amine
550-850	723.47	C-Cl Alkyl halide
675-900	886.61	C-H Aromatic

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