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FORMULATION DEVELOPMENT AND EVALUATION OF BUPRANOLOL TRANSDERMAL PATCHES

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Abstract:

The present study aimed to develop and evaluate matrix-type transdermal patches of bupranolol using various polymers such as hydroxypropyl methylcellulose (HPMC), Eudragit RLPO, Eudragit RSPO, and ethyl cellulose for sustained drug delivery. Bupranolol, a non-selective β-blocker with a short half-life and low oral bioavailability due to extensive first-pass metabolism, is a suitable candidate for transdermal administration. The patches were prepared using the solvent casting technique with PEG 400 as a plasticizer and methanol/chloroform as solvents. Six formulations (F1–F6) were developed and evaluated for physical parameters including thickness, folding endurance, moisture content, moisture uptake, tensile strength, drug content uniformity, and in vitro drug release. Among the formulations, F4 demonstrated optimal properties, showing high folding endurance (285 ± 6), suitable tensile strength (0.969 ± 0.014 kg/cm²), high drug content (99.45 ± 0.36%), and a sustained drug release of 98.65% over 12 hours. The drug release profile of F4 followed zero-order kinetics (R^2 = 0.9872), indicating a consistent and controlled release. These results suggest that F4 is a promising formulation for effective transdermal delivery of bupranolol, potentially improving patient compliance and therapeutic outcomes.

Keywords: *Bupranolol, Transdermal Patch, HPMC, Eudragit RLPO, Sustained Release, Zero-order Kinetics, Solvent Casting, Drug Delivery System*

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INTRODUCTION:

Transdermal drug delivery systems (TDDS) provide a non-invasive method of delivering drugs through the skin into systemic circulation, offering several advantages over oral and parenteral routes, including avoidance of first-pass metabolism, improved patient compliance, and the ability to maintain steady plasma levels for extended periods (Prausnitz et al., 2008; Guy et al., 2010). These benefits make TDDS a valuable option for drugs requiring chronic administration or those with a short half-life.

Bupranolol, a non-selective β-adrenergic blocker with intrinsic sympathomimetic activity, is used in the treatment of cardiovascular disorders such as hypertension and angina pectoris. However, its oral use is limited by extensive first-pass metabolism, a short biological half-life (2–4 hours), and poor bioavailability (~30%), which necessitate frequent dosing (Schönfeld et al., 1974). These characteristics make bupranolol an ideal candidate for transdermal drug delivery.

The successful formulation of a bupranolol transdermal patch involves the selection of suitable polymers and permeation enhancers that facilitate both drug release and skin permeation. Commonly used polymers such as hydroxypropyl methylcellulose (HPMC), ethyl cellulose (EC), and Eudragit are preferred due to their film-forming properties and biocompatibility (Patel et al., 2009; Dhawan et al., 2003). Evaluation parameters including drug content, in vitro release, ex vivo permeation studies, physicochemical properties, and stability are essential for assessing patch performance.

This study aims to develop and evaluate bupranolol-loaded transdermal patches using different polymer blends and permeation enhancers, with the goal of achieving optimized drug release and enhanced transdermal absorption.

MATERIAL AND METHODS:

Material

The formulation of bupranolol-loaded transdermal patches involved the use of various pharmaceutical-grade materials sourced from reputable suppliers. Bupranolol, the active pharmaceutical ingredient (API), was obtained from Bioplus Life Sciences Pvt. Ltd., Bangalore. Hydroxypropyl methylcellulose (HPMC), serving as the primary film-forming polymer, was procured from HiMedia Laboratories Pvt. Ltd., Mumbai. Sodium citrate and di-potassium hydrogen orthophosphate, used as buffering agents, were supplied by Loba Chemie Pvt. Ltd. and S.D. Fine Chem. Ltd., respectively. Organic solvents such as methanol, ethanol, and chloroform used in the preparation of the casting solution and for polymer dispersion were sourced from Qualigens Fine Chemicals, Mumbai. All chemicals used were of analytical grade and employed without further purification.

METHODS

Preparation of matrix type transdermal patches

Transdermal patches composed of different polymers HPMC, ethyl cellulose, Eudragit RLPO and Eudragit RSPO. The polymers were dissolved in chloroform and methanol along with plasticizer. Then the solution was poured into a glass Petri dish containing Glycerin. The solvent was allowed to evaporate under room temperature for 24 hrs. The polymers (total weight: 500 mg) and drug (10 mg) were weighed in requisite ratios and dissolved in 10 ml of chloroform and methanol and PEG 400. After vortex then the solution was poured on glycerin placed in a glass Petri dish and dried at room temperature for 24 hrs.

Table 1: Preparation of matrix type transdermal patches

Formulation Code	Drug (mg)	HPMC (mg)	RLPO (mg)	RSPO (mg)	Ethyl cellulose (mg)	Total polymer weight (mg)	Plasticizer % w/w of total polymer PEG 600 ml	Permeation Enhancer % w/w of total polymer (Methanol, chloroform) ml
F1	120	800	50	-	50	500	0.5	10
F2	120	700	100	-	100	500	0.5	10
F3	120	600	150	-	150	500	0.5	10
F4	120	800	-	50	50	500	0.5	10
F5	120	700	-	100	100	500	0.5	10
F6	120	600	-	150	150	500	0.5	10

*120mg drug for 12 patches (Formulation for 12 patches)

Evaluation parameters

The prepared transdermal patches were evaluated for the following parameters:

Thickness

The thickness of patches was measured by Vernier calipers.The thickness of patches were measured at three different places and average of three readings was taken with standard deviation (Selvam *et al.*, 2010).

Folding endurance

This was determined by repeatedly folding one patch at the same place until it broken. The number of times the patch could be folded at the same place without breaking / cracking gave the value of folding endurance.

Percentage of moisture content

The prepared patches were weighed individually and kept in desiccators containing activated silica at room temperature for 24 hrs. Individual patches were weighed. The percentage of moisture content was calculated as the difference between final and initial weight with respect to initial weight (Izumoto *et al.*, 1992).

Tensile strength

Cut the patch at the centre having 2cm length and 2cm breadth. Patch was hanged on top and lower side of instrument, then start the switch and note the reading on screen. The thickness and breadth of strips were noted at three sites and average value was taken for calculation.

$$\text{Tensile stress (S)} = \frac{\text{Applied force}}{\text{Cross sectional area}} = \frac{m \times g}{b \times t}$$

Where, S = tensile stress in 980 dynes/cm^2

m = mass in grams

g = acceleration due to gravity (980 dynes/cm^2)

b = breadth of strip in centimeters

t = thickness of strip in centimetres

Drug content analysis

The patches (n = 3) of specified area (6.16cm^2) were taken into a 10 ml volumetric flask and dissolved in methanol (10ml) with the help of shaker. After the vortex the solution was filtered and prepared subsequent dilutions and analyzed by UV spectrophotometer at 226nm nm.

Percentage of moisture content

Firstly weighed the patches and then kept in a desiccators at room temperature for 24 hrs and then it's exposed to 84% RH (A saturated solution of potassium chloride) in a desiccators. The % of moisture uptake was calculated by difference between final and initial weight with respect to initial weight.

***In vitro* skin permeation study**

The *in vitro* skin permeation study was done by using a Franz diffusion cell (receptor compartment capacity: 80 ml: surface area: 3.14 cm^2. The egg membrane was separated and used for in vitro study. The receiver compartment was filled with 40 ml of phosphate buffer, pH 7.2. The Transdermal patch was firmly pressed onto the centre of the egg membrane and then the membrane was mounted on the donor compartment. The donor compartment was then placed in position such that the surface of membrane just touches the receptor fluid surface. The whole assembly was kept on a magnetic stirrer with suitable rpm throughout the experiment using magnetic beads. The temperature of receptor compartment was maintained at 37± 0.5ºC. The samples were withdrawn at different time intervals up to 10 hrs and analyzed for drug content. Receptor phase was replaced with an equal volume of buffer solution at each time interval.

Results and Discussion

The study focused on the development and evaluation of bupranolol-loaded matrix-type transdermal patches using various polymeric combinations and plasticizers. Formulations F1 to F6 were prepared by solvent casting, utilizing HPMC in combination with Eudragit RLPO, Eudragit RSPO, and ethyl cellulose, with PEG 400 as plasticizer and methanol/chloroform as solvents.

Physical evaluation showed uniformity in thickness across all formulations, ranging from 90 ± 6 µm (F6) to 98 ± 5 µm (F1). All patches demonstrated acceptable folding endurance, with F4 exhibiting the highest value (285 ± 6), indicating superior flexibility and resistance to mechanical stress, likely due to its balanced HPMC and EC content.

In terms of moisture content and uptake, all patches remained within acceptable limits, with F4 displaying the lowest moisture content (2.85 ± 0.32%) and moisture uptake (5.25 ± 0.32%), suggesting improved stability and reduced hygroscopicity. This is advantageous for transdermal systems, as high moisture levels may affect the integrity and drug release behavior of the patch.

The tensile strength of the patches varied from 0.845 ± 0.032 to 0.995 ± 0.025 kg/cm². Formulation F6

showed the highest tensile strength, indicating excellent mechanical integrity, while F4 also demonstrated commendable strength (0.969 ± 0.014 kg/cm²), further supporting its selection as an optimized formulation.

Drug content uniformity was within acceptable limits for all formulations, indicating homogenous drug distribution across the patches. F4 showed the highest drug content (99.45 ± 0.36%), reflecting efficient drug incorporation and stability in the polymer matrix.

In-vitro drug release studies for F4 revealed a sustained and controlled release of bupranolol, with 98.65% cumulative drug release at 12 hours. The drug release profile followed zero-order kinetics (R^2 = 0.9872), suggesting a consistent release rate independent of drug concentration, which is ideal for transdermal systems. The lower R^2 value for first-order kinetics (0.7008) further supports zero-order release behavior.

Based on all evaluated parameters—mechanical strength, moisture characteristics, drug content, and drug release kinetics, formulation F4 emerged as the optimized patch, providing sustained release with excellent physical and mechanical properties suitable for transdermal delivery of bupranolol.

Table 2: Thicknesses and Folding Endurance of Different Formulations of transdermal patch

S. No.	Formulation Code	Thickness (µm)*	Folding Endurance*
1.	F1	98±5	235±7
2.	F2	95±3	248±3
3.	F3	93±2	256±5
4.	F4	97±4	285±6
5.	F5	95±5	236±4
6.	F6	90±6	224±2

Table 3: % Moisture content and moisture uptake of different formulations of transdermal patches

S. No.	Formulation Code	% Moisture Content	% Moisture Uptake
1.	F1	4.25±0.15	6.58±0.22
2.	F2	4.68±0.23	5.85±0.15
3.	F3	4.32±0.45	6.32±0.41
4.	F4	2.85±0.32	5.25±0.32
5.	F5	3.95±0.19	6.74±0.33
6.	F6	3.87±0.33	6.75±0.25

Table 4: Tensile strength of different formulation

S. No.	Formulation code	Tensile Strength (kg/cm^2)
1.	F1	0.891±0.025
2.	F2	0.865±0.015
3.	F3	0.845±0.032
4.	F4	0.969±0.014
5.	F5	0.945±0.033
6.	F6	0.995±0.025

Table 5: Percentage drug content of all the transdermal patch

S. No	Formulation Code	% Drug Content
1	F1	95.65±0.35
2	F2	98.85±0.25
3	F3	96.65±0.15
4	F4	99.45±0.36
5	F5	95.45±0.24
6	F6	96.85±0.18

Table 6: *In-vitro* drug release data for optimized formulation F4

Time (h)	Square Root of Time(h)$^{1/2}$	Log Time	Cumulative*% Drug Release	Log Cumulative % Drug Release	Cumulative % Drug Remaining	Log Cumulative % Drug Remaining
0.5	0.707	-0.301	16.65	1.221	83.35	1.921
1	1	0	20.14	1.304	79.86	1.902
2	1.414	0.301	31.45	1.498	68.55	1.836
4	2	0.602	43.12	1.635	56.88	1.755
6	2.449	0.778	53.65	1.730	46.35	1.666
8	2.828	0.903	62.25	1.794	37.75	1.577
10	3.162	1	78.89	1.897	21.11	1.324
12	3.464	1.079	98.65	1.994	1.35	0.130

Table 7: Regression analysis data of Bupranolol loaded Transdermal patches

Batch	Zero Order	First Order
	R^2	R^2
F4	0.9872	0.7008

CONCLUSION:

The present study successfully developed and evaluated matrix-type transdermal patches of bupranolol using various combinations of polymers and plasticizers to achieve sustained drug delivery. All formulations exhibited acceptable physical and mechanical characteristics; however, formulation F4 was identified as the optimized patch based on its superior folding endurance, tensile strength, drug content uniformity, and controlled in vitro drug release. The drug release from F4 followed zero-order kinetics, indicating a consistent and concentration-independent release profile an ideal attribute for transdermal systems. These findings suggest that transdermal delivery of bupranolol via matrix patches offers a promising alternative to oral administration by improving bioavailability, reducing dosing frequency, and enhancing patient compliance. Further in vivo studies are recommended to confirm the clinical efficacy and pharmacokinetic performance of the optimized formulation.

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