International Journal of Pharmaceutics & Drug Research
ISSN: 2347-6346
Available online at http://ijpdr.com

Original Research Article

FORMULATION AND EVALUATION OF FELBINAC LOADED TRANSFEROSOMES GEL FOR ANTI-INFLAMMATORY EFFECT

Namrata Raj*, Mr. Brajesh Kumar Pathak, Dr. Ashish Manigauha

Mittal Institute of Pharmacy, Bhopal (M.P.)

***Correspondence Info:**
Namrata Raj
Mittal Institute of Pharmacy, Bhopal (M.P.)
Email: namrataraj43@gmail.com

***Article History:**

Received: 12/04/2023
Revised: 20/05/2023
Accepted: 29/05/2023

ABSTRACT

One of the main causes of heart disease is hypertension, and in recent years, both the age-adjusted mortality rates for these conditions have been rising. In order to improve the therapeutic efficacy of the treatment and lessen its negative effects, transdermal patches distribute the drug via the skin in a controlled and predetermined manner. Thus, this study aims at formulation & evaluation of transdermal patch of Nitrendipine to treat hypertension. The formulation of patch was done by standard procedure & its evaluation was performed for various parameters. Results revealed that For F3 formulation the maximum thickness was found to be 92±4 µm & folding endurance was noticed as 195±4. The % moisture content & uptake for F3 was found to be 5.11±0.28 % and 2.15±0.11% respectively. Tensile strength for F3 was observed as 0.68±0.04 kg/cm2. The % drug content for F3 was also highest which is 99.12±0.25. The In vitro % permeation profile observed maximum for F5 which is 99.85 for 12hr. In-vitro drug release data for optimized formulation F3 revealed that Nitrendipine transdermal patches follow zero order kinetics which is evident from R^2 value 0.957. Thus, from the results it can be concluded that the transdermal patch is both efficient and the preferred approach for treating hypertension.

Keywords: Hypertension, Nitrendipine, Formulation & development, Transdermal patch, Antihypertensive drug

INTRODUCTION

High blood pressure (HBP), sometimes referred to as hypertension (HTN or HT), is a chronic medical condition in which the blood pressure in the arteries is consistently increased. Symptoms of high blood pressure are uncommon. High blood pressure, however, is a significant risk factor for dementia, atrial fibrillation, peripheral arterial disease, vision loss, chronic renal disease, coronary artery disease, and heart failure. Around the world, hypertension is a key factor in premature death. In India, 57% of deaths from stroke and 24% from coronary heart disease are directly attributable to hypertension. A compilation of epidemiological studies conducted in India reveals that 25% of urban and 10% of rural respondents have hypertension. Therefore, there is a critical need for low-cost methods to effectively control blood pressure in Indians (Kearney *et al.*, 2004; Abboud, 1982; Lackland and Weber, 2015).

Transdermal drug delivery systems are drugs that are applied topically and come in the form of patches that release the medication

through the skin at a predetermined and controlled rate. In order to improve the therapeutic efficacy of the treatment and lessen its negative effects, transdermal patches distribute the drug via the skin in a controlled and predetermined manner. Transdermal drug delivery systems (TDDS), which may transfer the medication via the skin portal to systemic circulation at a predetermined rate over a longer period of time, can accomplish controlled drug release. The ability of the medicine to penetrate the skin and easily reach the target site is necessary for an efficient transdermal drug delivery system. TDDS improves patient adherence and reduces load as compared to oral route (Arunachalam *et al*., 2010; Kadam *et al*., 2014; Prisant *et al*., 1992).

Nitrendipine is an inhibitor of calcium channels is act by relaxing the blood arteries and lowering the strain on them, it controls blood pressure by facilitating the heart's ability to pump more blood throughout the body. It helps people with high blood pressure normalise their blood pressure in this way (Moser *et al*., 1984; Goa and Sorkin;1987). Thus, this study aims at formulation & evaluation of transdermal patch of Nitrendipine to treat hypertension.

MATERIALS AND METHODS

Chemicals

HPMC, RLPO RSPO Ethyl cellulose were obtained from Loba chemie pvt ltd Mumbai. All chemicals used were of laboratory grade.

Development of transdermal patches

Transdermal patches composed of different polymers HPMC, Ethyl Cellulose, Eudragit RLPO and Eudragit RSPO (Madishetti *et al.,* 2010). 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 (20 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.

Evaluation parameters

The prepared transdermal patch was evaluated for the following parameters:

Microscopic evaluation

An optical microscope (Olympus-Cover-018) with a camera attachment (Minolta) was used to observe the shape of the prepared Transdermal patch for all formulation.

Thickness

The thickness of patch 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 (Tanwar *et al.,* 2007).

Folding endurance

This was determined by repeatedly folding one film at the same place until it broken. The number of times the film could be folded at the same place without breaking / cracking gave the value of folding endurance (Shivaraj *et al.,* 2010).

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 starts 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 (Alka *et al.*, 2012).

Percentage of moisture content

The prepared patches were weighed individually and kept in desiccators containing activated silica at room temperature for 24 hrs (Amish *et al.*, 2012). Individual patch were weighed. The percentage of moisture content was calculated as the difference between final and initial weight with respect to initial weight.

Percentage of moisture uptake

Firstly weighed the patches and then kept in a desiccators at room temperature for 24 hrs and then its 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.

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 222 nm (Teja *et al.*, 2012).

***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 7.4. The Transdermal patch was firmly pressed onto the centre of the egg membrane and then the membrane was mounted on the donor compartment (Vidyavati and Jithan, 2010). 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.

Table No. 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 6000 (ml)	Permeation Enhancer % w/w of total polymer (Methanol, chloroform) ml
F1	240	350	50	-	100	500	0.5	10
F2	240	400	50	-	50	500	0.5	10
F3	240	450	50	-	0	500	0.5	10
F4	240	350	-	50	100	500	0.5	10
F5	240	400	-	50	50	500	0.5	10
F6	240	450	-	50	0	500	0.5	10

Dose calculations

- Width of the plate = 5cm
- Length of the plate = 12cm
- No. of 2.5 x 2.5 cm^2 wafers present whole plate = 12
- Each wafers contains 10 mg of drug.
- 12 no. of wafers contains mg of drug = 20×12 = 240mg
- The amount of drug added in each plate was approximately equal to 240mg.

Table No. 2: Thicknesses and folding endurance of different formulations

S. No.	Formulation Code	Thickness* (µm)	Folding Endurance* (Times)
1.	**F1**	85±4	174±5
2.	**F2**	89±2	165±3
3.	**F3**	92±4	195±4
4.	**F4**	82±3	149±7
5.	**F5**	87±2	152±8
6.	**F6**	89±3	163±5

Table No. 2: % Moisture content and moisture uptake of different formulations

S. No.	Formulation Code	% Moisture content*	% Moisture uptake*
1.	F1	6.65±0.32	3.45±0.15
2.	F2	6.23±0.15	3.12±0.25
3.	F3	5.11±0.28	2.15±0.11
4.	F4	5.85±0.47	3.22±0.25
5.	F5	5.41±0.36	2.85±0.36
6.	F6	5.88±0.15	2.75±0.10

Table No. 3: Tensile strength of different formulation

S. No.	Formulation code	Tensile strength (kg/cm^2)
1	F1	0.65±0.05
2	F2	0.72±0.03
3	F3	0.68±0.04
4	F4	0.71±0.06
5	F5	0.73±0.03
6	F6	0.69±0.02

.

Table No. 4: Percentage drug content of all the formulations

S. No	Formulation Code	% Drug content
1	**F1**	97.85±0.32
2	**F2**	98.52±0.15
3	**F3**	99.12±0.25
4	**F4**	98.65±0.21
5	**F5**	97.12±0.15
6	**F6**	98.52±0.32

Table No. 5: *In vitro* % permeation profile of Nitrendipine in formulation F1-F6

Time	% of Drug Release						
(hr)	F1	F2	F3	F4	F5	F6	Pure Drug
0.5	28.85	33.65	23.32	30.25	25.65	23.36	45.65
1	45.65	42.25	39.98	46.65	38.85	36.65	69.98
2	66.58	59.98	49.74	55.58	49.52	45.58	97.74
4	79.98	73.32	55.56	69.95	65.58	59.98	-
6	88.56	75.65	69.92	86.65	83.32	76.65	-
8	97.85	98.85	76.65	98.85	96.65	88.74	-
10	98.12	99.12	88.85	99.12	99.12	93.32	-
12	98.45	99.47	99.17	99.65	99.85	95.65	-

Table No. 6: *In-vitro* drug release data for optimized formulation F3

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	23.32	1.368	76.68	1.885
1	1	0	39.98	1.602	60.02	1.778
2	1.414	0.301	49.74	1.697	50.26	1.701
4	2	0.602	55.56	1.745	44.44	1.648
6	2.449	0.778	69.92	1.845	30.08	1.478
8	2.828	0.903	76.65	1.885	23.35	1.368
10	3.162	1	88.85	1.949	11.15	1.047
12	3.464	1.079	99.17	1.996	0.83	-0.081

Table No. 7: Regression analysis data of Nitrendipine transdermal patches

Batch	Zero Order	First Order
	R^2	
F3	0.957	0.775

RESULTS AND DISCUSSION

For F3 formulation the maximum thickness was found to be 92±4 µm & folding endurance was noticed as 195±4. The % moisture content & uptake for F3 was found to be 5.11±0.28 % and 2.15±0.11% respectively. Tensile strength for F3 was observed as 0.68±0.04 kg/cm$^{2.}$ The % drug content for F3 was also highest which is 99.12±0.25. The *In vitro* % permeation profile observed maximum for F5 which is 99.85 for 12hr. In-vitro drug release data for optimized formulation F3 revealed that Nitrendipine transdermal patches follow zero order kinetics which is evident from R^2 value 0.957.

CONCLUSION

The chosen transdermal patch (F3) has demonstrated good promising results for physical appearance, thickness, weight homogeneity, folding durability, surface pH, tensile strength, percentage moisture content and uptake, and drug content. Conclusion: Moderate concentrations of HPMC, EC, and chitosan are appropriate for creating transdermal patches with sustained release of matrix. The formulation (F3) has been effectively developed to provide a cast that is both efficient and the preferred approach for treating hypertension.

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

REFERENCES

- Kearney, P.M., Whelton, M., Reynolds, K., Whelton, P.K. & He, J. (2004) Worldwide prevalence of hypertension: A systematic review. *Journal of Hypertension*, 22, 11–19.
- Abboud, F.M. (1982) The sympathetic system in hypertension. State-of-the-art review. *Hypertension*, 4(3_pt_2), 208–225.
- Lackland, D.T. & Weber, M.A. (2015) Global burden of cardiovascular disease and stroke: Hypertension at the core. *Canadian Journal of Cardiology*, 31, 569–571.
- Arunachalam, A.A., Karthikeyan, M.K., Kumar, D.V.K., Prathap, M., Sethuraman, S.S., Ashutoshkumar, S.A. & Manidipa, S.M. (2010) Transdermal drug delivery system: A review. *Journal of Current Pharma Research*, 1, 70–81.
- Kadam, A.S., Ratnaparkhi, M.P. & Chaudhary, S.P. (2014). *Transdermal Drug Delivery: An Overview.*
- Prisant, L.M., Bottini, B., DiPiro, J.T. & Carr, A.A. (1992) Novel drug-delivery systems for hypertension. *American Journal of Medicine*, 93, 45–55.
- Moser, M., Lunn, J., Nash, D.T., Burris, J.F., Winer, N., Simon, G. & Vlachakis, N.D. (1984) Nitrendipine in the treatment of mild to moderate hypertension. *Journal of Cardiovascular Pharmacology*, 6 (Supplement 7), S1090.
- Goa, K.L. & Sorkin, E.M. (1987) Nitrendipine: A review of its pharmacodynamic and pharmacokinetic properties, and therapeutic efficacy in the treatment of hypertension. *Drugs*, 33, 123–155.
- Madishetti, S.K., Palem, C.R., Gannu, R., Thatipamula, R.P., Panakanti, P.K. & Yamsani, M.R. (2010)

Development of domperidone bilayered matrix type transdermal patches: Physicochemical, in vitro and ex vivo characterization. *Daru*, 18, 221–229.

- Tanwar, Y.S., Chauhan, C.S. & Sharma, A. (2007) Development and evaluation of carvedilol transdermal patches. *Acta Pharmaceutica*, 57, 151–159.
- Shivaraj, A., Selvam, R.P., Mani, T.T. & Sivakumar, T. (2010) Design and evaluation of transdermal drug delivery of ketotifen fumarate. *International Journal of Pharmaceutical and Biomedical Research*, 1, 42–47.
- Alka, V., Bhupesh, V., Sunil, P. & Kishu, T. (2012) Formulation and evaluation of transdermal therapeutic system of matrix type clonidine hydrochloride. *Pharmacia Lettre*, 4, 1137–1142.
- Amish AD, Zankhana, P.S. & Janki, J. (2012) Formulation and evaluation of transdermal ondansetron hydrochloride matrix patch: *In-vitro* skin permeation and irritation study. *International Journal of Pharmaceutical Research and Allied Sciences*, 2, 26–34.
- Teja, A.R., Hemant, K.S., Swetha, S. & Prasad, M.S. (2012) Preparation and evaluation of transdermal patches of metformin hydrochloride using natural polymer for sustained release. *International Journal of Pharmacy and Pharmaceutical Sciences*, 4, 297–302.
- Vidyavati, S. & Jithan, A. (2010) Development and evaluation of zero order sustained release matrix type transdermal films of ibuprofen. *Journal of Global Pharma Technology*, 2, 51–58.