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FORMULATION AND EVALUATION OF TRANSDERMAL PATCHES CONTAINING NIFEDIPINE

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ABSTRACT

The purpose of the research work was to develop and evaluate the transdermal therapeutic system containing drug nifedipine with different ratios of three polymers by the solvent casting technique. The physicochemical parameters such as Thickness, weight variation, drug content, folding endurance, tensile strength, In vitro drug release. In vitro skin permeation studies of formulation were performed by using Franz diffusion cells. Tween 80 was selected for solubility enhances &plasticizer during shelf life period. Nifedipine transdermal patches were successfully prepared with HPMC K15M, HPMC K100M &HPMC K200M. It was concluded that formulations F-5 was found to be satisfactory batch and was optimized for the desirable properties.

INTRODUCTION

Conventional systems of medication that require multi dose therapy are having many problems. The controlled drug delivery is a newer approach is to deliver drug in to systemic circulation at a predetermined rate. Our system should duplicate continuous intravenous infusion, which not only by passes hepatic 'first pass' elimination but also maintains a constant, prolonged and therapeutically effective drug level in the body.

Transdermal drug delivery offers the following potential advantages 1, 2, 3

1. Avoid the risks and inconveniences of intravenous therapy and of varied conditions of absorption and metabolism associated with the oral therapy.
2. Continuity of drug administration in TDDS permits the use of a drug with short biological half-life.

Disadvantages of transdermal drug delivery system:

1. The limitation of transdermal drug delivery is principally associated with skins Barrier function, which severely constrains the absolute amount of drug that can be absorbed across reasonable area of skin during the dosing period. Thus, the major disadvantage of the method is that it islimited to potent drug molecule typically those requiring a daily dose on the order of20 mg or less. Nifedipine has been formulated as both a long- and short-acting 1,4-dihydropyridine calcium channel blocker. It acts primarily on vascular smooth muscle cells by stabilizing voltage-gated L-type calcium channels in their inactive conformation. Byinhibiting the influx of calcium in smooth muscle cells, nifedipine prevents calcium- dependent myocyte contraction and vasoconstriction. A second proposed mechanism for the drug's vasodilatory effects involves pH-dependent inhibition of calcium influx via inhibition of smooth muscle carbonic anhydrase. Nifedipine is used to treat hypertension and chronic stable angina.

Materials and Methods

1.Calibration curve of Nifedipine in7.4pH phosphate buffer:

a) Preparation of 7.4pH phosphate buffer: 50ml of 0.2M potassium dihydrogen orthophosphate solution was taken in a 200ml of volumetric flask, to which 22.4ml of 0.2M sodium hydroxide solution was added. Then volume was madeup to the mark with distilled water and pH was adjusted to 7.4 with dilute sodium hydroxide solution [64].

b) Preparation of Nifedipine standard stock solution (100µg/ml) in 7.4 pH phosphate buffer solution: A standard stock solution of Nifedipine was prepared by dissolving accurately weighed 10mg of Nifedipine in 7.4pH phosphate buffer solution in a 100ml volumetric flask and the volume was made up to 100ml by using 7.4pH phosphate buffer solution to obtain a stock solution of 100µg/ml.

c) Determination of λ max of Nifedipine: From the standard stock solution, 1 ml was taken into 10ml volumetric flask. The volume was made up to 10ml with 7.4pH phosphate buffer solution. The resulting solution containing 10µg/ml was scanned between 200 and 400nm. The λ max was found to be 229nm and was used as analytical wavelength.

d) Calibration curve of Nifedipine in 7.4pH phosphate buffer solution: From stock solution, appropriate aliquots were pipette into different volumetric flasks and volumes were made up to 10 ml with 7.4pH phosphate buffer solution so as to get drug concentrations of 1,2,3,4 and 5µg/ml. The absorbencies of these drug solutions were estimated at λ max 229nm against a blank of 7.4pH phosphate buffer solution.

Evaluation of Transdermal patches:

1. Thickness
2. Weight variation
3. Drug contents
4. Folding endurance
5. Tensile strength
6. *In vitro* skin permeation studies

Thickness: The thickness of patches was measured at three different places using a micro meter and mean values were calculated.

Weight variation: The patches were subjected to mass variation by individually weighing randomly selected patches. Such determinations were carried out for each formulation.

Drug content: Patches of specified area ($1cm^2$) were dissolved in 5 mL of dichloromethane and the volume was made up to 10 mL with phosphate buffer pH 7.4; dichloromethane was evaporated using a rotary vacuum evaporator at 45 °C. A blank was prepared using a drug-free patch treated similarly. The solutions were filteredthrough a 0.45 µ m membrane, diluted suitably and absorbance was read at 274 nm in a double beam UV-Vis spectrophotometer. **.**

Folding endurance: Determined by repeatedly folding one film at the same place till it broke. The number of times the film could be folded at the same place without breaking/cracking gave the value of folding endurance

Tensile strength: In order to determine the elongation as a tensile strength, the polymeric patch was pulled by means of a pulley system; weights were gradually added to the pan to increase the pulling force till the patch was broken. The elongation i.e. the distance travelled by the pointer before break of the patch was noted with the help of magnifying glass on the graph paper, the tensile strength was calculated as kg cm-2.**6.In-vitro skin permeation studies:** *In- vitro* skin permeation studies were performed by using a Franz diffusion cell with a receptor compartment capacity of 22.5 ml. The excised rat abdominal skin (Wistar albino) was mounted between the donor and receptor compartment of the diffusion cell. The formulated patches were placed over the skin and covered with paraffin film. The receptor compartment ofthe diffusion cell was filled with phosphatebuffer pH 7.4.

RESULTS AND DISCUSSION

Calibration curve of Nifedipine in 7.4pH phosphate buffer solution: Standard calibration curve of Nifedipine was drawn by plotting absorbance versus concentration. The λ max of Nifedipine in 7.4pH phosphate buffer solution was foundto be 229nm.

The compatibility of the drug with polymer was evaluated by performing FTIR analysis of standard drug and bestformulation.

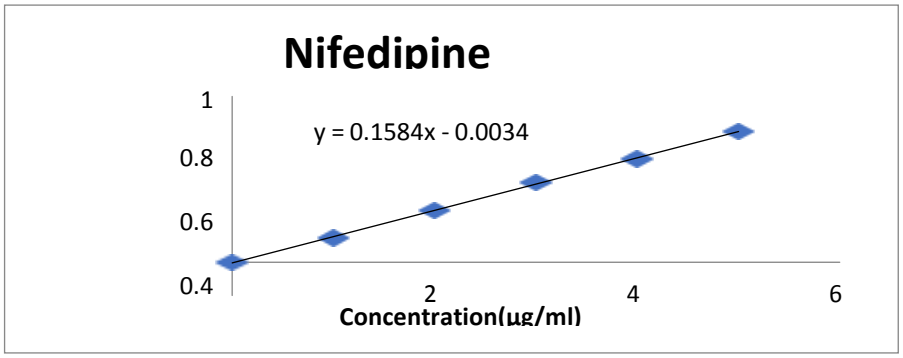

Fig no :1 Nifedipine in 7.4pH phosphatebuffer solution

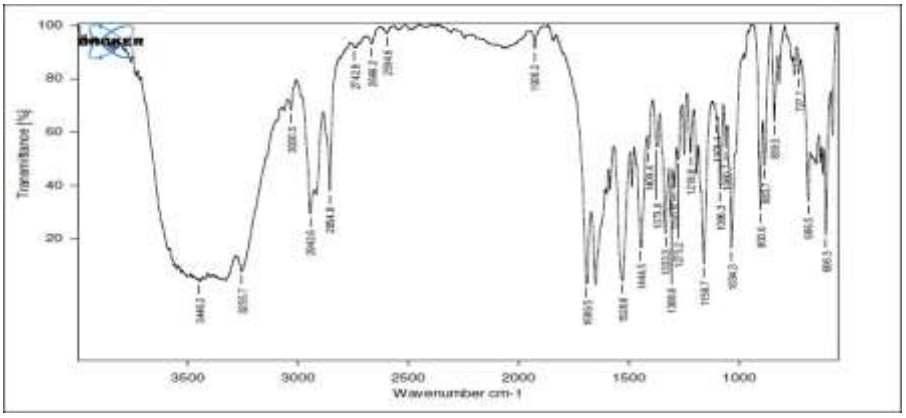

Figure 2 : FTIR graph of Nifedipine pure drug

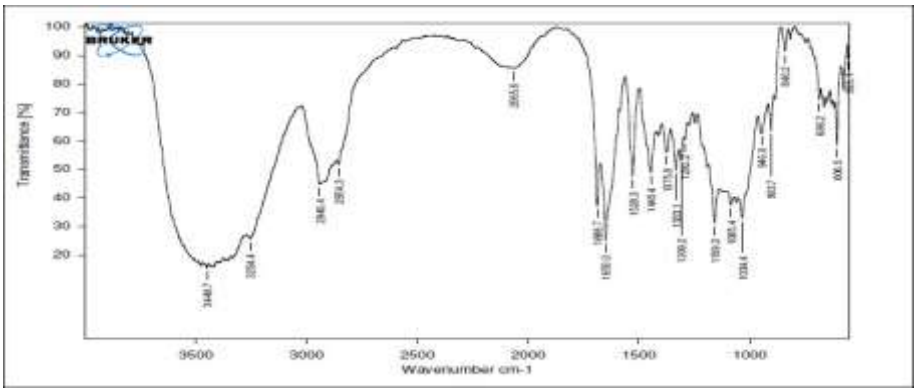

Figure 3: FTIR graph of Nifedipine best formulation

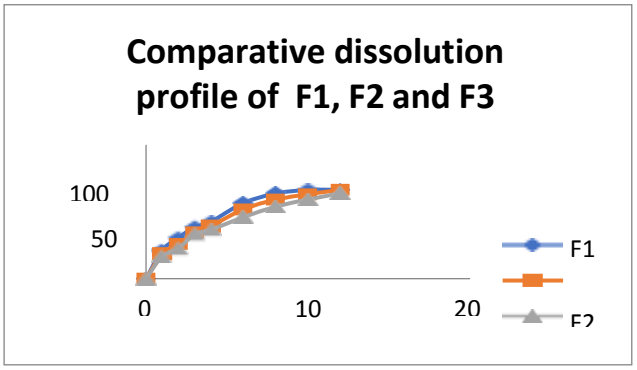

Figure 4: Comparative Dissolution profile for F1, F2 and F3 formulations

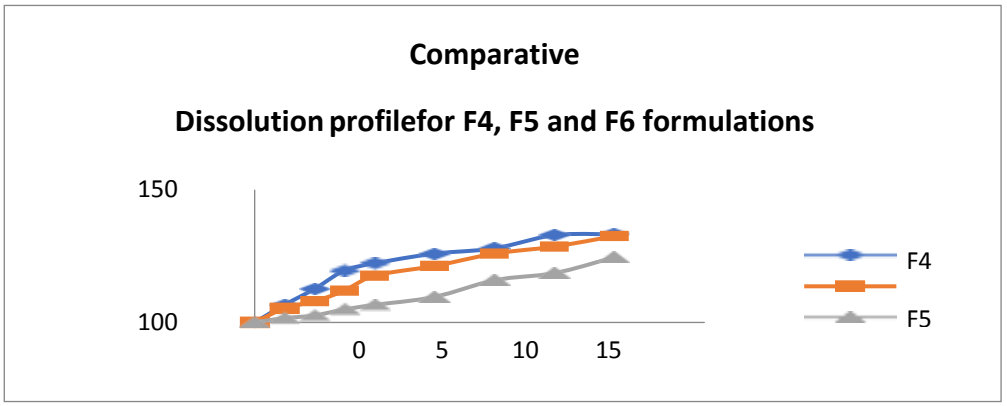

Figure 5: Comparative Dissolutionprofile for F4, F5 and F6 formulations

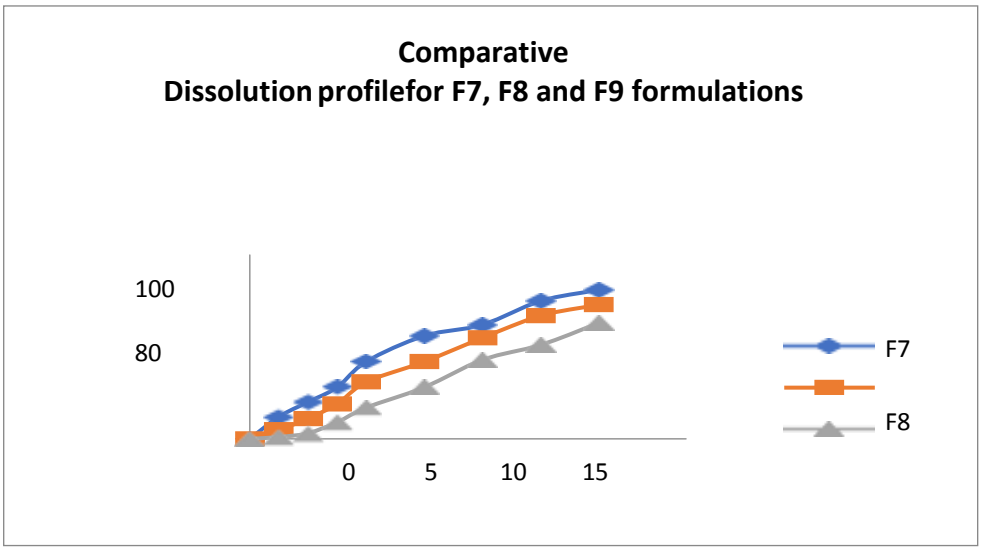

Figure 6: Comaparative dissolution profile for F7,F8,and F9 formulations

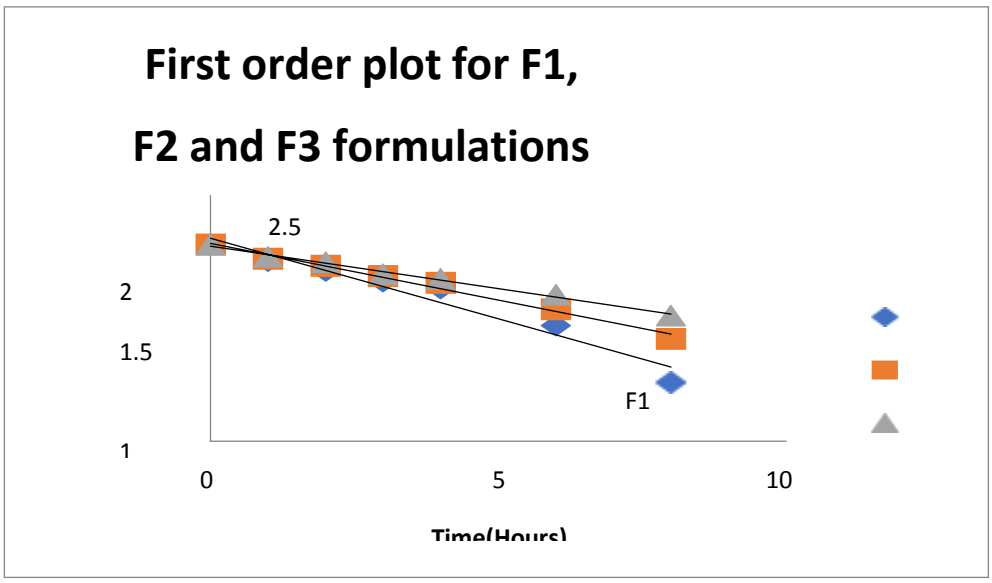

Figure 7: First order plot for F1, F2 andF3 formulations

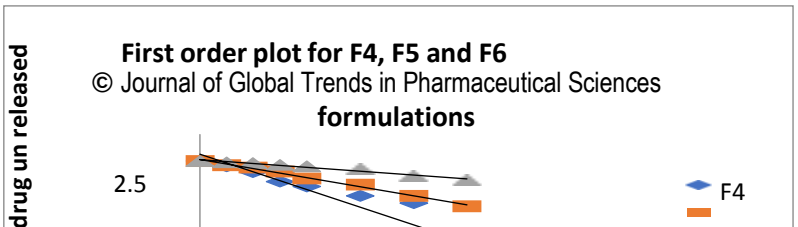

Figure 8: First order plot for F4, F5 andF6 formulations

Figure 9: First order plot for F7, F8 andF9 formulations

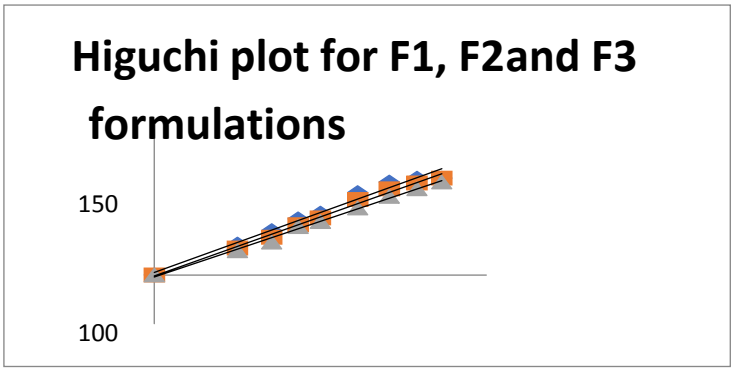

Figure 10: Higuchi plot for F1, F2 andF3 formulations

Figure 11:Higuchi plot for F4,F5 and F6 formulations

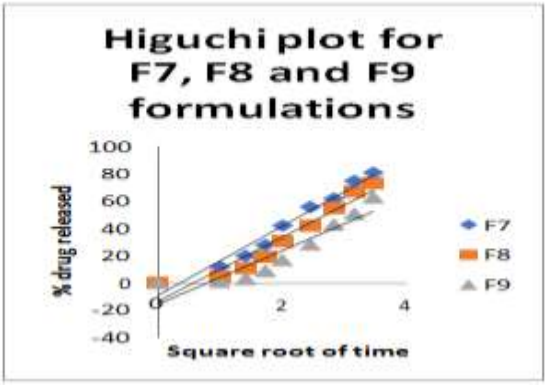

Figure 12:Higuchi plot for F7,F8 and F9 formulations

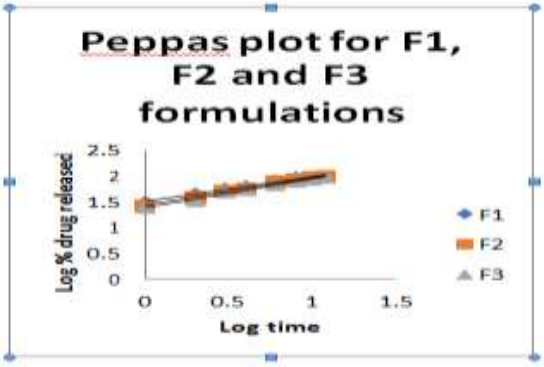

Figure 13: Peppas plot for F1, F2 andF3 formulations

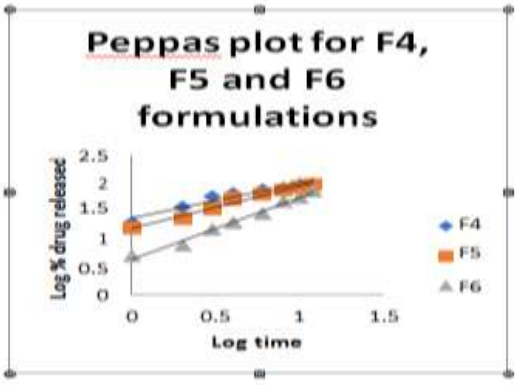

Figure 14: Peppas plot for F4, F5 andF6 formulations

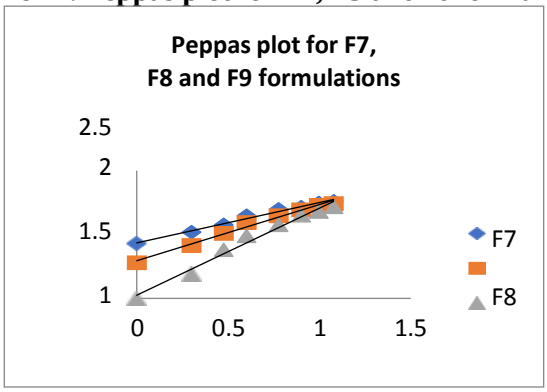

Figure 15: Peppas plot for F7, F8 andF9 formulation

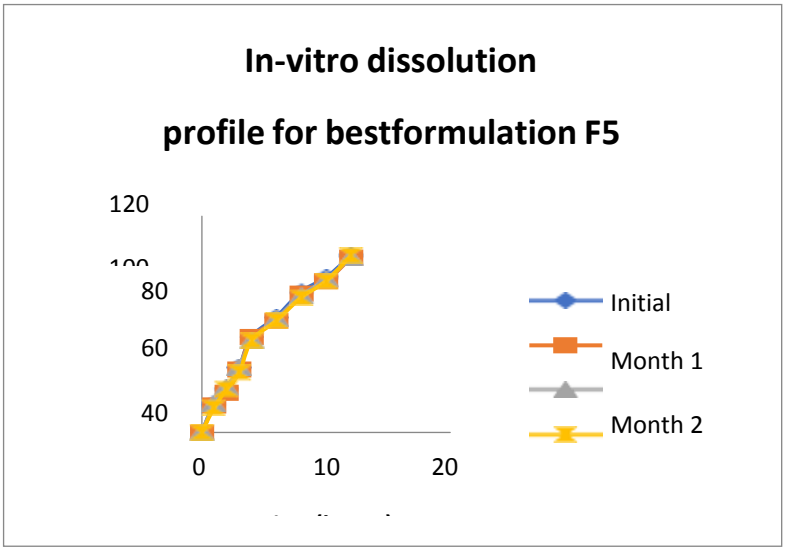

Fig. 16: *In-vitro* release profile of F9 duringStability studies (40°C ± 2°C / 75% ± 5% RH)

Table 1: Formulation of Nifedipine Transdermal patches

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Nifedipine	10	10	10	10	10	10	10	10	10
HPMC K15M	40	40	40	-	-	-	-	-	-
HPMC K100M	-	-	-	40	40	40	-	-	-
HPMC K200M	-	-	-	-	-	-	40	40	40
PVP K30	20	40	60	20	40	60	20	40	60
Tween-80	10	10	10	10	10	10	10	10	10
sorbitol	60	40	20	60	40	20	60	40	20

Table 2: Calibration data of Nifedipine in 7.4pH phosphate buffer at 229nm

Concentration (µg/ml)	Absorbance
0	0
1	0.147
2	0.314
3	0.481
4	0.624
5	0.789

Table 3:Evaluation parameters of Nifedipine Transdermal patches

Formulation code	Thickness	Weight variation	Drug content	Folding endurance	Tensil strength
F1	162	Pass	98.23	201	2.74
F2	158	Pass	99.14	199	2.96
F3	153	Pass	99.67	212	3.12
F4	160	Pass	98.83	219	3.04
F5	157	Pass	99.37	210	2.83
F6	152	Pass	99.95	206	2.92
F7	147	Pass	99.67	218	3.15
F8	138	Pass	99.82	237	2.86
F9	156	Pass	99.37	204	2.46

Table 4: *In-vitro* drug release data for Transdermal patches

Time (Hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	32	28	25	20	16	5	12	5	0
2	46	39	34	38	24	8	20	11	3
3	58	52	50	59	36	15	28	19	9
4	64	59	55	67	53	20	42	31	17
6	85	78	69	78	64	29	56	42	28
8	96	89	81	84	78	48	62	55	43
10	100	95	89	99	86	56	75	67	51
12	100	100	**96**	100	98	74	81	73	63

Table 5: R^2 and 'n' result table

Formulation code	R^2 Values				N Value
	Zero order	First order	Higuchi	Peppas	
F1	0.852	0.951	0.98	0.982	0.483
F2	0.9	0.986	0.992	0.991	0.535
F3	0.918	0.992	0.995	0.99	0.556
F4	0.869	0.84	0.973	0.94	0.624
F5	0.96	0.991	0.971	0.984	0.753
F6	0.988	0.964	0.867	0.989	1.113
F5	0.963	0.992	0.966	0.987	0.793
F6	0.987	0.99	0.926	0.986	1.103
F7	0.987	0.969	0.858	0.979	1.709

CONCLUSION:

Nifedipine transdermal patches were successfully prepared with HPMC K15Mand HPMC K100M and HPMC K 200 M.The amount of plasticiser tween 80 was critical for patch formation and separation properties.Tween 80 was selected for solubility enhancer and plasticizer during shelf life period.It was concluded that formulations F-5 was found to be satisfactory batch and was optimised for the desirable properties.

REFERENCES:

1. Bellantone N.H., Rim S., Rasadi B., Enhanced percutaneous absorption via Iontophoresis I. Evaluation of an in-vitro system & transport of model compound., Int. J. Pharm., 30, 1986, 63-72.
2. Gros L., Clark W.E., "The structure of skin" in " The tissue of the body" Le Gros & Clark W. E.(editors) edition VI, ELBS and Oxford University Press, London, 1980, 29-313.
3. Chien Y.W., "Systemic delivery of pharmacologically active molecules across skin" in "Targeted drug delivery" Radolph L., Juliano(Editor) Springer- Verlag, Berlin, 1991, 182-230.
4. Charro B.D., Guy R.H. "Transdermal drug delivery" in "Drug delivery & targeting" Hillery A. M., Lloyd A.W., Swarbrilk J. edition I., Published by Taylor & Francis. NY, US, 2001, 216-217.
5. Chen K., Schmidt C F., The action of ephedrine, the active principle of Chinese drug Ma Huang, J. Pharmacology. Exp. Ther., 24, 1925, 339-357.
6. Nelson H.S., Beta adrenergic Bronchodilator, Eng .J.Med.,33 3,1995,499-506.