ORIGINAL ARTICLE ET AL.

FUTURE JOURNAL OF PHARMACEUTICALS AND HEALTH SCIENCES

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Formulation and Evaluation of Transdermal Film of Nitroglycerin

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Article History:

Received on: 01 Mar 2021
Revised on: 13 Mar 2021
Accepted on: 15 Mar 2021

Keywords:

Nitroglycerin,
HPMC,
Ethyl Cellulose,
Cellulose Acetate Phthalate

ABSTRACT

The aim of the present study was to prepare and evaluate transdermal Films of Nitroglycerin using HPMC, Cellulose acetate phthalate, ethyl cellulose and Polypropylene glycol as a rate controlling membranes and HPMC, Cellulose acetate phthalate, ethyl cellulose as drug reservoir gels. Transdermal Films of Nitroglycerin with HPMC, Cellulose acetate phthalate, ethyl cellulose by varying the blend ratios were prepared by solvent casting method. The thickness medium range between 0.18 ± 0.02 mm to 0.22 ± 0.03mm whatever signifies that they're military uniform in thickness. The customized formulation NF1 acquires stability reports for one to three months and the general films were tested for drug content and *In-vitro* diffusion.

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eISSN: 2583-116X pISSN:

DOI: https://doi.org/10.26452/

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INTRODUCTION

In the present study, we aimed to deliver anti angina drug nitroglycerin for developing transdermal therapeutic systems for controlled release. Hence studies have been undertaken in the present investigation on membrane moderated therapeutic systems by employing HPMC, Cellulose acetate phthalate, ethyl cellulose and Polypropylene glycol as a rate controlling membranes and HPMC, Cellulose acetate phthalate, ethyl cellulose as drug reservoir gels [1]. The manner of biosmiliars is certain in order to avoid of chronic disorders specified hypertension, which need longer term dosing to take care of therapeutically drug concentration. Transdermal pitch of CVS drugs throw up individual advantages as warding off hepatic first pass metabolic process, asserting constant blood level for a long per period leading to a reduction of care for frequency [2].

MATERIALS AND METHODS

NItroglycerin used to be buying from Wockhardt Limited, Aurangabad. Hydroxy Propyl Methyl Cellulose, Cellulose acetate phthalate, Ethyl cellulose, Propylene glycol and dimethyl sulfoxide used to be frequent Pharmaceutics Private Limited, Mumbai and other ingredients victimised in with Analytical grade [Table 1].

Methodology

Compatibility studies

IR studies

In the preparation of drug and polymer might inter-

act as they will be in close displace every one, which might cause the instability of drug preformulation studies [3].

Procedure

Beaker that included 15 ml of purified water and 3 drops of glycerin was stirred up for 15 mints. The HPMC and PVP have been added slowly at unremitting soul-stirring for 30 mints [4]. Add Drug & Propylene glycol to with the above preparation it was get an aspect poured into transdermal mold & squelch a hot air oven for 15 minutes at 50^{o}C subsequent to remove the Films restrain in desiccators [Table 5].

Evaluation of Transdermal Films

Physical Appearance

All entire formulated Films have been visually inspected for colour, flexibility, homogeneity and smoothness [5].

Thickness

The Films was performed by screw gauge (micrometer) [6].

Weight Variation

For each one Patch used to be weighed individually along with average weight of films used to be determined [7].

Moisture Content

The Films (n =3) were weighed individually and kept in a desiccator containing calcium chloride at 37°C for 24 hrs [8]. Calculate the difference between initial and final weight of films.

Flatness

Then variation within the length as a result of non-uniformity in flatness was sounded [9]. It was planned by measuring narrowing of strips.

Tensile Strength

To be able to determine the stretching as a tensile strength, the polymeric patch drift in weights had been slowly added to the pan to increase the pulling work force till the patch was broken [10].

Folding Endurance

This was 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 gave the value of folding endurance [11].

Water Vapour Transmission Rate

The film was fixed over the brim of a glass vial, containing 3 g of fused calcium chloride as desiccant, with an adhesive tape. The vial was weighed and kept in desiccators containing saturated solution of potassium chloride to provide relative humidity of 84%. The vial was taken out and weighed at every 24 hrs interval for a period of 72 hrs. [12].

Drug Content

The Films at 1cm2 were cut and added to a beaker containing 100ml of Phosphate buffered solution of pH 7.4. The medium was stirred with a Teflon coated magnetic bead for 5hrs [5].

In vitro drug Permeation studies

In vitro release studies can be performed in a modified Franz diffusion cell over a period of time 12 hours. At specific time intervals, aliquots of samples containing the released drug are taken from the acceptor compartment and are quantified using a suitable method of determination [13].

Release Order Kinetics

The data obtained of the *in vitro* dissolution studies acquire kinetic track record analysis [14].

Zero-order kinetics: $Q_t = Q_o + K_o t$

First-order kinetics: $Q_t = \log Q_o + K_1 t/2.303$

Higuchi model: $Q_t = K_H \cdot t^{1/2}$; Korsmeyer-Peppas release model: $Mt / M_\infty = K \cdot t^n$

Stability Conditions

Stability study of Nitroglycerin transdermal films was carried out at tracking temperatures for 40^{o}C/75% RH one and three months the parameters estimated *In-vitro* diffusion [15].

RESULTS AND DISCUSSION

Compatibility Studies

The spectrum of the pure Nitroglycerin sample recorded by FTIR is shown in Figures 1, 2, 3, 4 and 5.

Evaluation of Nitroglycerin Transdermal Films

Physicochemical

The planned out formulations of Films used to be thin, flexible, elastic, smooth and transparent/ translucent [Table 2].

Thickness

The variability between 0.18 ± 0.02 mm to 0.22 ± 0.03mm which signifies homogenous in thickness [Table 2].

Weight Variation

The variability between 150 ± 2.2mg to 221 ± 2.6mg, Whichever signifies that assorted batches patch weights were similar [Table 2].

Moisture Content

The variability between 2.432 ± 0.01 % to 3.354 ± 0.02 % [Table 2].

Table 1: Ingredients of Transdermal Films

Ingredients	NF1	NF2	NF3	NF4	NF5	NF6
Nitroglycerin (mg)	100	100	100	100	100	100
Hydroxy Propyl Methyl Cellulose (mg)	400	-	-	100	100	-
Cellulose acetate phthalate (mg)	-	400	-	200	-	100
Ethyl cellulose (mg)	-	-	400	-	200	200
Propylene glycol (w/v)	40 %	40 %	40 %	40 %	40 %	40 %
Alcohol (ml)	10	10	10	10	10	10
Dimethylsulfoxide	20%	20%	20%	40%	40%	40%

Table 2: Evaluation of Transdermal Films

Parameters	NF1	NF2	NF3	NF4	NF5	NF6
Physical Appearance	Satisfactory	Satisfactory	Satisfactory	Satisfactory	Satisfactory	Satisfactory
Thickness (mm)	0.20 ± 0.04	0.18 ± 0.02	0.19 ± 0.03	0.22 ± 0.03	0.20 ± 0.04	0.21 ± 0.05
Weight variation (mg)	210 ± 1.19	170 ± 2.20	150 ± 2.2	221 ± 2.6	202 ± 5.0	187 ± 2.2
Moisture content	3.113 ± 0.04	3.321 ± 0.31	3.354 ± 0.02	3.131 ± 0.03	2.432 ± 0.01	3.114 ± 0.23
Flatness (I)	98%	98%	98%	98%	98%	98%
Tensile strength (Nm^{-2})	11.12 ± 1.11	12.14 ± 1.31	11.89 ± 1.57	12.12 ± 1.31	12.23 ± 1.78	10.21 ± 3.00
Folding endurance (F)	170.1 ± 3.10	150 ± 2.34	160 ± 1.10	134 ± 5.3	143.2 ± 4.5	100 ± 2.43
WVTR (g/m^2)	3.110 ± 0.24	3.232 ± 0.32	3.121 ± 0.14	2.189 ± 0.04	2.51 ± 0.34	2.01 ± 0.21
Drug Content (%)	98.2 ± 0.2	97.1 ± 0.1	96.9 ± 0.2	97.8 ± 0.3	96.3 ± 0.2	97.2 ± 0.3

Table 3: Cumulative % drug releases of Nitroglycerin Transdermal Films

Time (Mints)	% of Drug release					
	NF1	NF2	NF3	NF4	NF5	NF6
5	1.54	4.06	5.96	11.68	5.58	13.14
10	9.62	10.96	11.24	22.36	19.42	26.98
15	15.96	21.46	23.59	34.64	28.32	33.16
20	20.68	31.58	44.64	49.32	33.16	43.94
25	31.58	45.42	59.32	53.16	47.06	56.31
30	45.42	57.06	60.90	65.32	57.08	68.64
35	57.06	64.80	74.80	78.64	79.42	70.98
40	80.90	82.48	81.00	84.90	82.64	81.10
45	97.34	83.22	92.12	95.86	91.26	93.56

Table 4: Release kinetics of Nitroglycerin Transdermal Films NF1-NF6

Model	NF1		NF2		NF3		NF4		NF5		NF6	
	r^2	m	r^2	m	r^2	m	r^2	m	r^2	m	r^2	m
Zero order	0.655	69.4	0.655	69.4	0.939	1123	0.007	15.93	0.202	72.88	0.928	1414
First order	0.494	0.061	0.494	0.061	0.540	0.067	0.257	0.038	0.352	0.044	0.438	0.062
Higuchi's Matrix	0.516	4508	0.516	4508	0.767	7420	0.023	212.0	0.189	515.5	0.803	9618
Korsmeyer-Peppar	0.835	2.354	0.835	2.354	0.884	2.545	0.572	1.709	0.663	1.813	0.806	2.517

Table 5: Stability studies of the optimized formulation NF1

Time in (Mints)	Cumulative % Drug Release		
	Standard	After 1 Month	After 3 Month
5	1.54	1.59	2.59
10	9.62	9.79	10.79
15	15.96	16.00	17.00
20	20.68	22.68	23.68
25	31.58	33.58	34.58
30	45.42	46.42	47.42
35	57.06	58.06	59.06
40	80.90	81.90	82.90
45	97.34	97.37	98.37

Table 6: Stability studies of the Drug Content of optimized formulation NF1

Drug Content (%)	After 1 Month	After 3 Month
98.2 ± 0.2	98.3 ± 0.1	99.5 ± 0.3

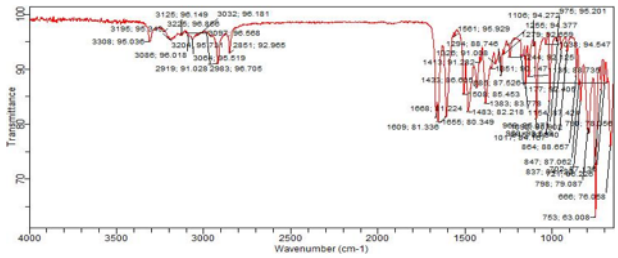

Figure 1: FTIR Spectrum of Nitroglycerin

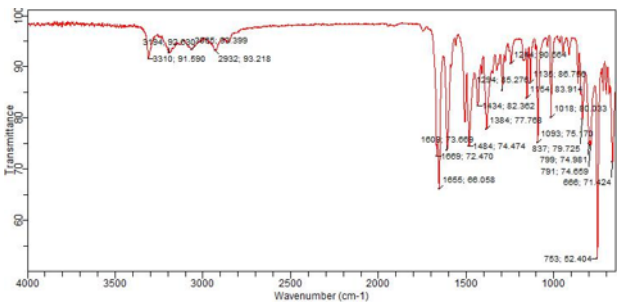

Figure 2: FTIR Spectrum of Hydroxy Propyl Methyl Cellulose

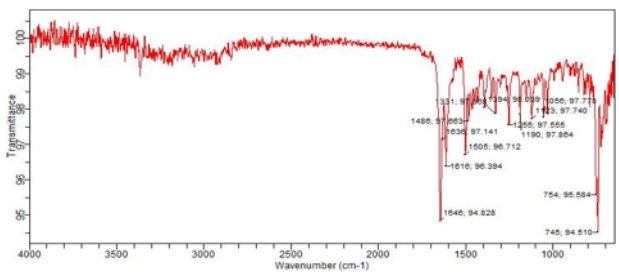

Figure 3: FTIR Spectrum of Cellulose acetate phthalate

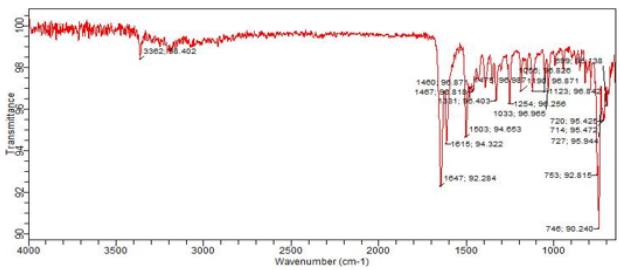

Figure 4: FTIR Spectrum of Ethylcellulose

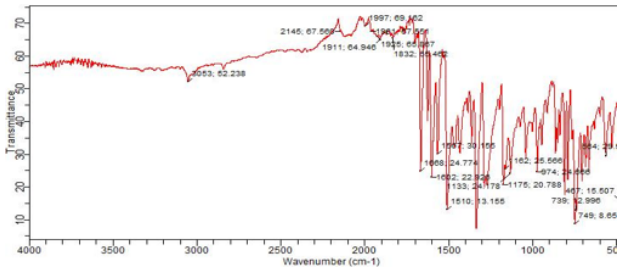

Figure 5: FTIR Spectrum of Mixture of compounds

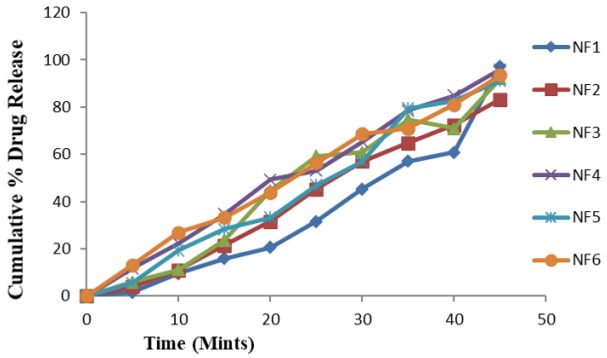

Figure 6: *In Vitro* diffusion Studies Nitroglycerin Transdermal Films

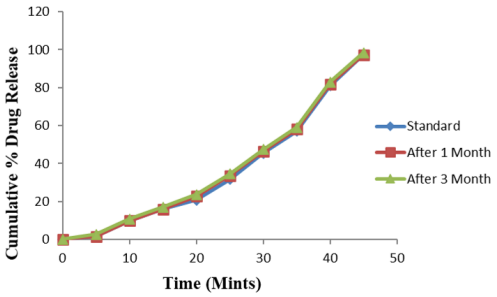

Figure 7: Stability studies of Optimized Formulation of NF1

Flatness

The flatness report displayed to that each one the formulation indicating 98% flatness [Table 2].

Tensile Strength

The NF1 to NF6 shows the 11.12 ± 1.11 to 12.23 ±1.31 shows the comprehensive viscosity [Table 2].

Folding Endurance

The NF1 to NF6 shows the 100 ± 2.43 to 170.1 ± 3.10 [Table 2].

Water Vapour Transmission Rate

The WVTR in NF1 to NF6 shows the 2.01 ± 0.21 to 3.232 ± 0.32 [Table 2].

Drug Content

The total amount of drug is present in the Films was found to be 98.2 ± 0.2 to 96.3 ± 0.2 % [Table 6].

In-vitro Drug Permeation studies

NF1 presented preeminent 97.34 % of drug release [Figure 6 and Table 3].

In vitro drug release kinetics

The *in vitro* drug diffusion data acquired was suited to various analytical models [Table 4].

Stability Study

The NF1 was subjected to stability studies for 1 to 3 months and the films were tested for Drug content & *In-vitro* diffusion [Table 5 and Figures 6 and 7].

CONCLUSION

Finally, I over for which drug release during the films of Nitroglycerin obeys First order kinetics. Customized formulation NF1 obtained stability reports for 1 to 3 months and also the films were proven for drug content as well as *In-vitro* diffusion. The finding of fact of the current effect revealed that the problems of Nitroglycerin on oral like dissolution rate limited absorption and gastric unwanted effects can be sweep over by using Nitroglycerin locally in the form of transdermal films.

ACKNOWLEDGEMENT

I would like to thank Dr. G. H. Srinivaasa Rao Sir (Founder and Manager), Saastra College of Pharmaceutical Education & Research, Near Varigonda Jwalamuhi Temple, Muthukur Raod, Kakupalli, Nellore-524311, Andhra Pradesh, India.

Funding Support

The authors declare that they have no funding support for this study.

Conflict of Interest

The authors declare that there is no conflict of interest.

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Cite this article: Arava Vidyadhari, Guduru Rajeswari, Dodda Chinni Krishna Reddy, Gangala Sudarsana, Gundala Mamatha, Kuramutla Sisindri, Podili Swarna Latha, Ramakkagari Sandhya Rani, Shaik Shajiya Taslim. Formulation and Evaluation of Transdermal Film of Nitroglycerin. Future J. Pharm. Health. Sci. 2021; 1(1): 37-42.