IJPAR |Volume 2 | Issue 4 | Oct - Dec - 2013 **ISSN: 2320-2831**

INTERNATIONAL JOURNAL OF PHARMACY AND ANALYTICAL RESEARCH

Available Online at: www.ijpar.com

[Research article]

Formulation, characterization and Evaluation of Transdermal Film Containing Naproxen

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ABSTRACT

Transdermal drug delivery system has numerous advantages over the more traditional drug delivery systems. This includes high bioavailability, steady drug plasma concentration, absence of first pass hepatic metabolism effect. Transdermal film is an adhesive film that has a coating of a drug that is placed on the skin to deliver a specific dose of the drug into the bloodstream over a period. The aim of present study an attempt was made to design the transdermal drug delivery system of naproxen with Ethyl Cellulose polymer in various concentrations. Transdermal films were prepared by solvent casting method by using Dibutylpthalate as plasticizer. The prepared films were characterized in physical appearance, thickness, drug content, weightvaration, Folding endurance, percentage moisture uptake and in-vitro release study.

Keywords: Transdermal Film, Naproxen, Ethylcellulose, Dibutylpthalate, Solvent casting method.

INTRODUCTION

Transdermal drug delivery system delivers the drug across the skin and into the systemic circulation is distinct from topical drug penetration, which targets local areas. Transdermal drug delivery takes advantage of the relative accessibility of the skin. Transdermal drug administration generally refers to topical application of agents to healthy intact skin either for localized treatment of the tissues underlying the skin or for systemic therapy[1]. For transdermal products the goal of dosage design is to maximize the flux through the skin into the systemic circulation and simultaneously minimize the retention and metabolism of the drug in the skin. Transdermal drug delivery has many advantages over the oral route of administration such as improving patient compliance in long term therapy, bypassing first-pass metabolism, sustaining drug delivery, maintaining a constant and prolonged drug level in plasma.[2,3] Naproxen is a nonsteroidal anti-inflammatory drug, which relieves pain and swelling. It is used to treat headaches, muscle aches, backaches, tendonitis, dental pain, menstrual cramps, arthritis, or gout. This drug works by blocking the enzyme that makes prostaglandins. Decreasing prostaglandins helps to reduce pain and swelling. The objective of the present study was to overcome the harmful side effects of naproxen a nonsteroidal anti-inflammatory drug [NSAID] which causes severe gastrointestinal bleeding while taken orally. [4] The usage of most of the NSAIDS by oral route associated with potential disadvantages such as peptic ulceration and gastric bleeding. This severe drawback creates a potential need for development of transdermal patches of NSAIDS. The major

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advantage of the transdermal delivery system is the ability to avoid first-pass metabolism and also to circumvent the hostile environment of the gastrointestinal tract.[5] In the present study an attempt was made to design the Transdermal patches of Naproxen with various proportions of Ethyl cellulose Polymer.

MATERIALS AND METHODS

Naproxen (Yarrow Chem products Pvt Ltd.), Ethyl cellulose, PEG 400, di-butylpthalate, Methanol, Glycerine. All the ingredients and reagents were used Analytical grade.

Preparation of transdermal film of naproxen by solvent casting method

Transdermal patches of Naproxen were prepared with the polymer Ethyl cellulose in Various concentrations. The matrix type patches were prepared by dispersing various Proportions of Ethyl cellulose in 30 ml of methanol. To this dispersion weighed quantity of Naproxen (5%w/w based on total polymer weight) is dissolved. This mixture was stirred Continuously by magnetic stirrer. After 1 hour of stirring 10% w/w (based on total polymer Weight) of dibutylphthalate as plasticizer was added to the above mixture as plasticizer. The Stirring was continued for another 1 hour. Then 5 ml of the sample was withdrawn by using A pipette and slowly poured over a glass plate covered with aluminium foil (5 x 5 cm). Car Was taken to avoid formation of air bubbles during the addition of sample on the glass plate. The solvent was allowed to evaporate at a controlled rate by placing an inverted glass Funnel over the glass plate. After 24 hours of drying at room temperature, the film was Removed and stored in a desiccator.[6]

Preparation of blank patches

Polymers of single or in combination were accurately weighed and dissolved in Respective solvent and then cast in a Petri-dish with mercury as the plain surface. The films were allowed to dry overnight at room temperature.

RESULTS

Drug content

The uniformity of drug content of the Transdermal film was determined, based on dry weight of drugs and polymers used by means of a UV Spectrophotometer method. Different Formulations were cut into pieces dissolved separately in 10 ml of Phosphate buffer pH 7.4and stirred for 30 minutes. Appropriate dilutions were made with methanol. The resulting solutions were filtered with whatmman filter paper and analyzed for content at 230nm in UV spectrophotometer. The average reading of the three films was taken as the content of the drug in one formulation.[7]

Weight variation

Uniformity of weight was determined by weighing five matrices of each formulation. After each film unit was weighed individually on a digital balance, the average weight of the film was taken as the weight of the film.[8]

Thickness of film

The thickness of the patch was determined by measuring the thickness at five sites on three films of each formulation using digital verniercalipher (Ocean premium) and the average was calculated. [9]

Folding endurance

The folding endurance is expressed as the number of folds (Number of times the film folded at the same place). Either to break the specimen or to develop visible cracks. This test is performed to check the suitability of sample to withstand folding and brittleness. Three patches of each formulation of size were cut by using a sharp blade. Folding endurance was determined by repeatedly folding one film at the same place till it breaks. The number of times the film could be folded at the same place without breaking gave the value of folding endurance.[10]

Percentage of moisture uptake

A weighed film kept in a desiccator at room temperature for 24 h was taken out and exposed to 84% relative humidity (a saturated solution of aluminium chloride) in a desiccator until a constant weight for the film was obtained. The percentage of moisture uptake was calculated as the difference between final and initial weight with respect to initial weight. [11]

Physical Appearance

All the transdermal systems were visually inspected for color, clarity, flexibility and Smoothness.

In-vitro Diffusion Study

The in-vitro diffusion study is carried out by using a Franz Diffusion Cell .Egg membrane is Taken as semipermeable membranes for diffusion. The Franz diffusion cell has receptorCompartment with an effective volume approximately 60ml and effective surface area of Permeation 3.14sq. Cms. The egg membrane is mounted between the donor and the Receptor compartment. A weighed amount of Transdermal patch is placed on one side of Membrane. The receptor medium is phosphate buffer pH 7.4. The receptor compartment is surrounded by a water jacket to maintain the temperature at 37 ± 0.5°C. Heat is provided Using a thermostatic hot plate with a magnetic stirrer. The receptor fluid is stirred by Teflon Coated magnetic bead which is placed in the diffusion cell .During each sampling interval Samples are withdrawn and replaced by equal volumes of fresh receptor fluid on each Occasion. The samples withdrawn are analysed spectrophotometrically at 230nm. The drug Release study was performed. [12]

DISCUSSION

FT-IR: FT-IR studies shown that there were no chemical interaction between drug and polymer.

Fig no: 1 FTIT Spectrum of pure Naproxen

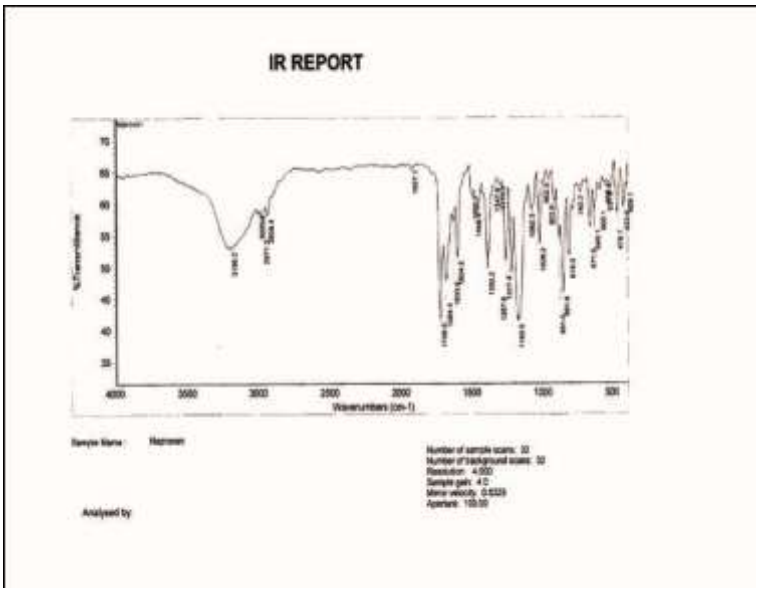

Fig no: 2 FTIT Spectrum of EC

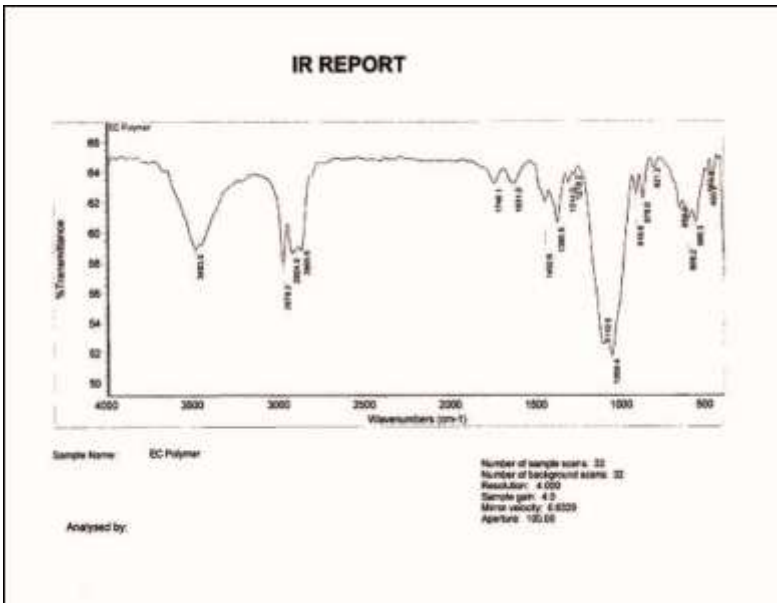

Fig no:3. FTIT Spectrum of EC+ Naproxen

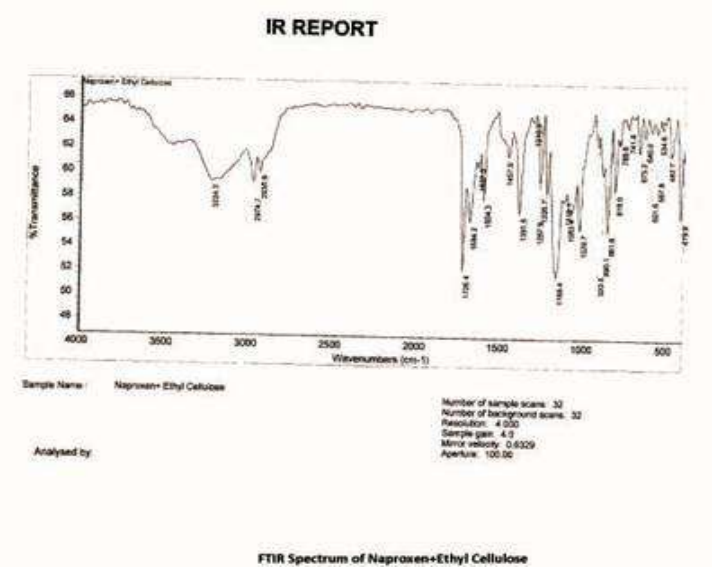

Fig no: 4 . percentage drug release of NXN1 & NXN2

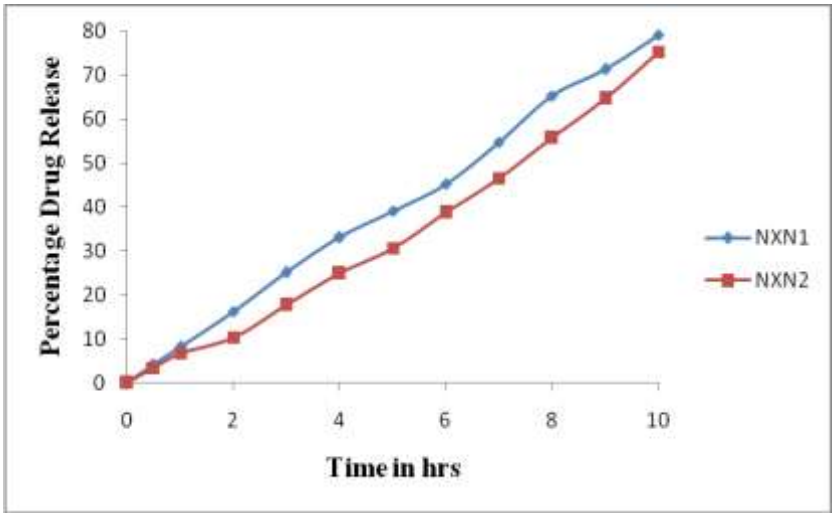

Table no: 1. Formulation design for naproxen transdermal film

S.No	Ingredients	NXN1	NXN2
1	Naproxen	500mg	500mg
2	Ethyl cellulose	500mg	1000mg
3	Polyethylene glycol	5ml	5ml
4	Methanol	10ml	10ml

Table no: 2. Evaluation of transdermal films

Formulation code	NXN1	NXN2
Drug content (%cm^{2})	89.6	92.8
Weight variation	0.07	0.05
Thickness of film (mm)	0.35	0.43
Folding endurance	75	82
% of moisture	2.65	3.82
Content		

Table no: 3 In-vitro released a profile of Naproxen transdermal film NXN1 & NXN2

S.no	Time (hours)	NXN1 (%drugrelease)	NXN2 (%drugrelease)
1	0.5	4.16	3.50
2	1	8.27	6.83
3	2	16.32	10.40
4	3	25.13	17.75
5	4	33.10	24.92
6	5	39.15	30.67
7	6	45.36	38.80
8	7	54.80	46.55
9	8	65.40	55.68
10	9	71.31	64.71
11	10	79.25	75.33

ACKNOWLEDGEMENTS: The authors are grateful to the Jyothismathi college of pharmacy, Thurkapally (v), Sharmeerpet (M), R.R-Dist. For providing research facilities.

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