RESEARCH ARTICLE

FORMULATION AND EVALUATION OF FEXOFENADINE HYDROCHLORIDE TRANSDERMAL PATCH

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ABSTRACT

To treat allergic disorders on long term therapy needs plasma concentration of drug in better manner. This was achieved by formulating the drug in controlled release pattern. Fexofenadine hydrochloride is almost completely absorbed from the gastro-intestinal tract following oral administration,but bioavailability is reported to be only about 45% due to hepatic first-pass metabolism. The present study aims to prepare Transdermal patch of Fexofenadine hydrochloride. Preparation of transdermal patches of Fexofenadine hydrochloride using polymers: Hydroxypropyl methyl cellulose, Ethyl cellulose plasticized with Glycerol. The patches were evaluated for various parameters like Thickness, Water-Vapor Permeability, Tensile Strength, Drug Content,Diffusion and Dissolution studies. Prepared patches exhibited Zero Order Kinetics and the permeation profile was matrix diffusion type.*In-vitro*release study of Fexofenadine hydrochloride transdermal patch shown release of drug 79 % at 24 h and also follows zero order kinetics release pattern.

Keywords: Fexofenadine Hydrochloride, Ethyl cellulose, Hydroxypropyl methyl cellulose, *In-vitro*.

INTRODUCTION

Transdermal drug delivery system is a therapeutic system designed to transfer drugs through intact skin for systemic treatment. It offers controlled drug release pattern by a simple application to the skin's surface, eliminating the vagaries influencing the gastrointestinal absorption associated with oral administration and providing for more efficient drug utilization.It offers various advantages such as:avoidance the risk and inconvenience of intravenous therapy (noninvasive), avoidance of first pass hepatic metabolism (avoiding the deactivation by digestive and liver enzymes) thus increasing bioavailability and efficacy of drugs, no gastrointestinal degradation (pH, enzymatic activity, drug interaction with food, drink and other orally administered drugs) andsubstitute for oral administration of medication when that route is unsuitable as with vomiting and diarrohea[1-3]. A list of current FDA-approved transdermal drug delivery systems is given in Table 1[4-7]. Extended therapy avoiding frequent dose administration.Fexofenadine,α,α - Dimethyl – 4 - [1-hydroxy – 4 - [4 - (hydroxydiphenyl-methyl) – 1 - piperidinyl]butyl]- benzene acetic acid is the active carboxylic acid metabolite of terfenadine, and is a non-sedating selective histamine H1 receptor antagonist. Unlike its precursor, fexofenadine lacks the cardiotoxic potential, since it does not block the potassium channel involved in repolarization of cardiac cells. Fexofenadine is effective in the management of allergic rhinitis and chronic idiopathic urticaria for which it is a suitable option for first-line therapy. It is taken by mouth twice a daily with food. The pharmacokinetics of Fexofenadine hydrochloride has been studied. It is completely absorbed from the gastro-intestinal tract following oral administration, but bioavailability is reported to be only about 45% due to hepatic first pass metabolism. Most of the drug is eliminated in liver as metabolites and only 1% of the intact drug is excreted from the kidney. Therefore, Fexofenadine hydrochloride might be designed as a suitable delivery system with long term effect and bypass the liver, such as transdermal delivery system, the delivery system may have constant drug delivery rate to the circulation system and convenient use for children[8-11].

Table 1: Currently Approved TDDS

Year	Generic (Brand) Names	Indication
1979	Scopolamine (Transderm Scop®)	Motion Sickness
1984	Clonidine (Catapres TTS®)	Hypertension
1986	Estradiol (Estraderm®)	Menopausal Symptoms
1990	Fentanyl (Duragesic®)	Chronic Pain
1991	Nicotine (Nicoderm®, Habitrol®, Prostep®)	Smoking Cessation
1993	Testosterone (Androderm®)	Testosterone Deficiency
1995	Lidocaine/epinephrine (Iontocaine®)	Local Dermal analgesia
1998	Estradiol/norethindrone (Combipatch®)	Menopausal Symptoms
1999	Lidocaine (Lidoderm®)	Post-herpetic neuralgia pain
2001	Ethinyl estradiol/norelgestromin (OrthoEvra®)	Contraception
2003	Estradiol/levonorgestrel (Climara Pro®)	Menopause
2003	Oxybutynin (Oxytrol®)	Overactive bladder

Table 1 Continue……..		
2004	Lidocaine/ultrasound (SonoPrep®)	Local Dermal anaesthesia
2005	Lidocaine/tetracaine (Synera®)	Local Dermal Analgesia
2006	Fentanyl/iontophoresis (Ionsys®)	Acute Postoperative pain
2006	Methylphenidate (Daytrana®)	ADHD
2007	Rivastigmine (Exelon®)	Parkinson's Disease
2008	Granisetron (Sancuso®)	Chemo- induced emesis
2009	Oxybutynin (Gelnique®)	Overactive bladder
2010	Buprenorphine (Butrans®)	Chronic pain

MATERIALS AND METHODS

Fexofenadine hydrochloride was obtained as gift sample from Ranbaxy Pvt Limited, Toansa. HPMC K-100M, HPMC K-4M, ETHYL CELLULOSE was purchased fromColorcon Asia Pvt Ltd, Goa, India. All other chemicals used were of analytical grade.

Preparation of matrix patches

Polymers of ethyl cellulose and hydroxyl propyl methyl cellulose were accurately weighed and dissolved individually in 5 ml of ethanol. The drug was then dispersed in the polymeric solution and then plasticizer of glycerol was added. The solution was stirred to attain semisolid like consistency and casted on a glass substrate containing 'o' ring, the rate of evaporation of solvent from polymeric solution was controlled by placed an inverted funnel at room temperature for a day. The formed films were separated. Formulation of Fexofenadine hydrochloride patches was given in Table: 2.

Table 2: Composition of Transdermal Patches

Sr.No	Formulation	Code	Composition (drug: polymer)	Plasticizer (Glycerol)	Casting solvent
1	HPMCK100M	A	1:1.4	0.1-0.5 ml	Ethanol: Dichloromethane
2	HPMCK100M	B	1:2	0.1-0.5 ml	Ethanol: Dichloromethane
3	HPMCK4M	C	1:1.4	0.1-0.5 ml	Ethanol: Dichloromethane
4	HPMCK4M	D	1:2	0.1-0.5 ml	Ethanol: Dichloromethane
5	ETHYL CELLULOSE	E	1:1.4	0.1-0.5 ml	Ethanol: Dichloromethane
6	ETHYL CELLULOSE	F	1:2	0.1-0.5 ml	Ethanol: Dichloromethane

Preparation of rate controllingmembrane

The transdermal patches of compositionlisted in Table 1 were prepared by solvent casting method. The polymer (HPMC K100M), (HPMC K4M) and (EC) were dissolved in Ethanol at room temperature. Glycerol was used as a plasticizer, with continuous mixing at lower rpm initially and later at a higher speed. The drug was incorporated with continuing agitation and the volume was made up. The films were cast onto a suitably designed and fabricated glass mould and then dried in oven at 40^{o}C for six hours in an oven. The films were removed by using sharp blade by inserting along the edges of the film[12]. The dried films were wrapped in butter paper and stored in a closed container away from light and in cool place.

Physical Appearance:

All the transdermal patches were visually inspected for color, clarity, flexibility and smoothness.

Measurement of Thickness:

Patch thickness was measured by a dial caliper. The average of the five observations was calculated[12]. Result was shown in Table 2.

Weight Uniformity:

The dried patches were weighed on digital balance. The average of five observations ofeach formulation was calculated[13]. Result was shown in Table 2.

Folding endurance:

The folding endurance is expressed as the number of folds (no. of times the film is folded at the same place) either to break the specimen or to develop visible cracks. This test is important to check the ability of sample to withstand folding. This also gives an indication of brittleness; less folding endurance indicates more brittleness. Folding endurance of the film was determined by repeatedly folding a small strip of film (2cm x 2cm) at the same place till it broke. The number of times, the film could be folded at the same place, without breaking gave the valve of folding endurance[14]. Result was shown in Table 3.

Table 3: Thickness, weight and folding endurance of the patches

Patch	Mean Thickness (mm) n=5	Mean Weight (gm.) (10-3) n=5	Mean Folding Endurance n=5
A	0.413 ± 0.015	0.20±0.020	>100
B	0.366 ± 0.011	0.203 ± 0.011	>100
C	0.383 ± 0.015	0.200 ± 0.017	>150
D	0.393 ± 0.015	0.196 ± 0.025	>100
E	0.380 ± 0.030	0.153 ± 0.115	>100
F	0.416 ± 0.015	0.206±0.011	>100

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Tensile strength and % Elongation

The films were taken in rectangular containers using proportionate quantity of the solution calculated on the basis of area. The films were cut into strips of 1cm width and 15cm length. The films were fixed onto the Tensile strength apparatus in such a way that the length of film between the jaws was initially 10 cm. The trials where the breakage occurred at the jaw were invalid and the result was repeated on another strip. The Tensile strength was calculated by the formula, Tensile strength = Break force [1 + change in length] / (width) (breadth) [initial length of the film].The percent elongation was determined by noting the length just before the break point and substituting the formula

% Elongation = [Final length - Initial length] /Initial length * 100[15-17].

***In-vitro* drug release**

The prepared Fexofenadine hydrochloride patch was evaluated for release pattern using commercially available semi permeable membrane. The membrane and patch were fitted between donor & receptor compartment of self-fabricated modified Franz diffusion cell. The donor compartment was empty & receptor compartment was containing 50 ml of phosphate buffer pH 7.4. The samples were collected at different time intervals for analyzing the drug content in the receptor compartment for release pattern of drug and replaced with equal volume of freshly prepared phosphate buffer pH 7.4. The drug content was analyzed at 259 nm using U.V double beam spectrophotometer (Table: 4). From the study best formulation was selected for further studies[18-20].

Table 4: *In-vitro* Release of Fexofenadine hydrochloride Transdermal patches

Formulation code	Cumulative percentage of release	Time of release
A	78.2%	24hr
B	69.0%	24hr
C	61.2%	24hr
D	59.4%	24hr
E	70.2%	24hr
F	65.3%	24hr

RESULTS AND DISCUSSION

The prepared films were smooth, flexible and uniform. Total twenty four formulations were formulated using HPMCK100M, HPMCK4M and ETHYL CELLULOSE in different ratios. The composition of various formulations is shown in Table 1.

Weight variation test was performed by weighing three patches and average value was taken as the weight of the film. All the formulations exhibited uniform weight with low standard deviation values indicating the uniformity of the films prepared by solvent casting method. The weight of the films varied between 0.20±0.020 to 0.206±0.011 mg. Thickness of transdermal patches was measured by screw gauge. The thickness of the patches varies between 0.413±0.015 to 0.416±0.015 mm. Low standard deviation values in the film thickness measurements ensure uniformity of the patches prepared by solvent casting technique. The area of the patch was found to be 2.5 cm^2.

The folding endurance of transdermal patches was measured manually. The folding endurance of the patches is shown in Table 2. Folding endurance test results indicated that the patches would not break and would maintain their integrity with general skin folding when applied.

The drug content uniformity was determined for all formulations by UV spectrophotometer method. The results of drug content vary between 18.04±0.047 to 20.88±0.07 mg as shown in Table 4.7. The results indicated that the process employed to prepare patches in this study was capable of producing patches with uniform drug content and minimal patch variability.

The results of *in vitro* drug permeation from different formulations are depicted in Table 3. The corresponding value of cumulative percentage drug permeated from the formulations A, B, C, D, E and F after 24 hrs were 78.2%, 69%, 61.2%, 59.4%, 70.2% and 65.3% respectively. From the *in vitro* skin permeation study it was confirmed that release of formulations A and E after 24 hrs was found to be higher than other formulations (B, C, D and F). The kinetic studydata also proves that which follows zero order kinetics for controlled release ofdrug to maintain drug concentration in better manner

CONCLUSION

The drug selected of fexofenadinehydrochloride for transdermal therapeutic system of anti-histaminic study shown appropriate release in *in-vitro* studies. This confirms that the formulation A and F may control the allergic disorder in better manner by achieving drug concentration in steady manner for over a day.

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