An Elsevier Indexed Journal ISSN-2230-7346

Journal of Global Trends in Pharmaceutical Sciences

DEVELOPMENT AND EVALUATION OF TRANSDERMAL PATCHES FOR IMPROVED *IN-VITRO* PERMEATIONOF FESOTERODINE

Krishna Mohan Chinnala*,HemalathaPendkar andSree Giri Prasad Beri

Department of Pharmaceutics, School of Pharmacy, Nalla Narasimha Reddy Education Society's Group of Institutions, Hyderabad, Telangana, INDIA-500088.

ARTICLEINFO

Keywords:

RP-HPLC,
Duloxetine,
Mecobalamin,
Method development,
Validation

ABSTRACT

The present investigation was taken up to prepare and evaluate a transdermal drug delivery system of Fesoterodine to increase its bioavailability. The matrix type patches were prepared using polymers such as HPC, Hydroxyl Propyl Methyl Cellulose (HPMC E15CPS, HPMC E50CPS) by solvent casting method and to study the effect of polymer composition, plasticizer and permeation enhancer on the physico-mechanical and *in-vitro* drug release characteristics of the film. Propylene glycol and DMSO were used as plasticizer and permeation enhancer respectively. Incorporation of Propylene glycol improved the flexibility, folding endurance and handling properties of the patches. Increasing the concentration of plasticizer and the presence of DMSO were found to increase the *in vitro* drug release of the patches. The presence of DMSO produced significant increase in the flux and permeability constant. The formulation with HPC, DMSO as permeation enhancer and propylene glycol as plasticizer showed the best results which exhibited the cumulative percentage of drug release of 95% in 8 hrs. Drug-excipients interaction studies were carried out using IR technique; patches indicated no chemical interaction between drug and excipients. The results of the skin irritation studies showed no noticeable irritancy on rabbit skin indicating the skin compatibility of the drug as well as polymer.

Key words: Fesoterodine, Transdermal patches, Permeation Enhancer, *In-vitro* Permeation Study, HPC and HPMC

INTRODUCTION:

Transdermal delivery of drugs provides many advantages over conventional administration including enhanced efficacy, increased safety, greater convenience, and improved patient compliance. This can avoid the "peak and valley" effect of oral or injectable therapy and can enable more effective treatment by delivering drugs at a steady rate into blood- stream over an extended period of time. It also reduces the dosage-related side effects because the amount of drug delivered into the biological system takes place in a controlled fashion and also avoids first-pass metabolism (1 & 2). This route of administration may be particularly significant in infants and children because of their greater surface area to weight ratio (3). The system designed for transdermal patches include matrix, microreservoir, reservoir, adhesive, and membrane-matrix hybrid. Matrix type

transdermal patches remain the most popular as they are easy to manufacture (4). Fesoterodine is an antimuscarinic agent used treat overactive bladder syndrome. It is a prodrug, *In-vivo* it is broken down into its active metabolite, 5-hydroxymethyl tolterodine (5-HMT), by plasma esterases. The 5-hydroxymethyl metabolite exhibits the antimuscarinic activity. Both urinary bladder contraction and salivation are mediated via cholinergic muscarinic receptors. Therefore, acting as a competitive muscarinic receptor antagonist, Fesoterodine ultimately acts to decrease the detrusor pressure by its muscarinic antagonism, thereby decreasing bladder contraction and consequently, the urge to urinate. The half-life of fesoterodine is about 7–8 hrs and its bioavailability has been reported to be about 52%. Fesoterodine is administered perorally and its physicochemical and pharmacokinetics characteristics like lower molecular weight, lipid solubility and low melting point are in agreement with the ideal properties of molecules for the effective penetration of the stratum corneum. Hydroxypropyl Methylcellulose (HPMC) is a semisynthetic, inert, non toxic, non allergic and nonirritating viscoelastic polymer that has good film forming properties for controlled-delivery of oral drug products (7 & 8).

MATERIALS AND METHODS:

Materials

Fesoterodine was from Natco Pharma Pvt. Ltd., Hyderabad, India, and Hydroxy Propylmethyl Cellulose of different grades are obtained from Aurobindo Pharma Ltd., Hyderabad, India. Propylene Glycol and Dimethyl Sulfoxide (DMSO) were purchased from S. D. Fine Chem. Ltd., Mumbai, India. Di-n-butyl phthalate was purchased from Central Drug House Pvt. Ltd., Mumbai. All other reagents were of analytical grade.

Method

Preparation of Transdermal Film

Solution of HPMC E15cps, HPMC E50cps and HPC were prepared by dissolving 2gm of polymer in 100ml of 1.0% acetic acid solution. To the above prepared polymer solution, 20%, 30% W/W (dry weight of polymer) of Propylene glycol followed by 20%W/W (dry weight of polymer) of Fesoterodine was added and stirred for half an hour. Drug containing polymer solution (25ml) were poured into petridish, precoated with polyurethane and kept in oven at 40^{o}C for complete drying. The dried patches were cut with a circular metallic die of 2.1 cm^2 and stored in airtight desiccators under ambient conditions prior to use(4-6).

Evaluation of Transdermal Patches

The transdermal patches prepared were evaluated for the following parameters:

Physical Appearance

All the prepared patches were visually inspected for color, clarity, flexibility and smoothness (9-18).

Thickness

The thickness of film is measured using micrometer screw gauge. A micrometer with a least count of 0.001 cm was employed. The thickness was measured at five different points on the film and average of five readings was taken and standard deviation was calculated (9-18).

Weight Variation

Weight variation was determined by cutting the transdermal Patch into 1cm^2 using mold, weighing three patches individually, from each batch and then average weight was calculated (9-18).

Folding Endurance

A modified USP tablet disintegrate tester was used to determine the folding endurance of the membrane. It consisted of fixed and movable jaws that could be moved up and down at the rate of 30 stokes per minute. The distances between two jaws at their farthest and closest were 6 centimeter and 0.5 centimeter respectively. The membrane (6cm length) was clamped between the jaws in such a way that the jaws were at their closest , the membrane beats across its middle and when at their farthest, the membrane was in a stretched condition Thus for every stock of the movable jaw the membrane went through one cycle of bending and stretching. The folding endurance is expressed as the number of strokes required to either break or develop visible cracks on the membrane. The test was conducted for 20min equating 600 strokes (9-18).

Swelling Index

The transdermal film membrane was cutted into 3 cm^2. It was initially weighed and later immersed in 50 ml of phosphate buffer pH 7.4. The films were taken out carefully at 5,10,30,60 minute intervals blotted with filter paper to remove the water present on their sur-

face and weighed accurately to calculate swelling index using formula (9-18).

$$\text{Swelling Index} = \frac{\text{Wet weight - Initial weight}}{\text{Wet weight}} X100$$

Water Vapor Transmission (WVT) Study

The water vapor transmission is defined as the quantity of moisture transmission through the unit area of a patch in unit time. The water vapor transmission data through the transdermal patches are important to knowing the permeation characteristics. Glass vials of equal diameter were used as transmission cells. These transmissions were washed thoroughly and dried to constant weight in an oven. About 1gm of fused calcium chloride as a desiccant was taken in the vial and the polymeric films were fixed over the brim with the help of an adhesive tape. These pre weighed vials were placed in a closed desiccators containing saturated solution of potassium chloride. The cells were removed and weighed every day for seven days of storage (9-18).

WVT = WL /S

Where, W = Weight of water vapor transmitted in gm,L = Thickness of film in cm^2

S = Exposed surface area in cm^2

Percentage of Moisture Content

The membrane of size 3 cm^2 were weighed individually and stored in dessicator consists of fused calcium chloride at room temperature for 24h. Individual membranes were weighed repeatedly until they showed a constant weight. The percentage of moisture content was calculated until they showed a constant weight. The percentage of moisture content was calculated as difference between initial and final weight with respect to final weight (9-18).

$$\%\text{Moisture Content} = \frac{\text{Initial weight - final weight}}{\text{final weight}} X100$$

Percentage of Moisture Uptake

A weighed membrane of size 3 cm^2 stored in a desiccator at room temperature for 24hr was taken out and exposed to 74.9%, 52% and 98% relative humidity (RH) using sodium chloride (NaCl), sodium bisulphate ($NaHSO_4.H_2O$) and potassium dichromate ($K_2Cr_2O_7$) respectively in their saturated solution at room temperature. These specimens were checked periodically until no further increase in weight was recorded. The percentage of moisture uptake was calculated as the difference between final and initial weight with respect to initial weight (9-18).

Bursting Strength

The bursting strength of all the films were evaluated by using standard burst strength tester the result obtained in terms of Kg/ cm^2 (19).

Tensile Strength and Extension

Tensile strength of the films was determined by using house field universal testing machine. The sensitivity of the machine was 1mg-500mg. It consists of two load cell jaws. The upper one is movable and lower one is fixed. The films of specific size (4x1cms) were fixed between these grips and upper jaw was moved at speed of 100 mm/min (ISI STD speed) applying force gradually till the films break. The tensile strength of the films was taken directly from the dialed reading in kilograms and extension of film in mm (9-18).

Drug Content

A film of 2.1 cm^2 area were cut into small pieces and transfer to 100ml volumetric flask. Finally the volume was adjusted with phosphate buffer pH 7.4 to the desired volume. The solution was filtered and the drug content was determined spectroscopically at 275 nm (21).

***In-vitro* Drug Permeation Study:**

This is done by using Modified Franz Diffusion Cells. A cell is composed of two compartments, donor and receptor. The receptor compartment has a volume of 5-12ml and effective surface area of 1-5 cm^2. The diffusion buffer is continuously stirred at 50rpm by a magnetic bar. The temperature in the bulk of the solution is maintained by circulating water through a thermostatic water jacket that surrounds the receptor compartment. The apparatus was equilibrated at 37 ± 0.5^0C and operated at 50 rpm. 5ml of samples were withdrawn at appropriate regular time intervals and the aliquots were analyzed in UV spectrophotometer at 275 nm (21).

Statistical Analysis of Data:

The results were analyzed by one-way analysis of variance (ANOVA) with Tukey post't' test using Graph Pad Prism software 5.0 version (Graph Pad software Inc., San Diego, CA, USA) (21).

Fourier Transform Infrared Spectroscopy (FTIR) Technique: In order to check the integrity (Compatibility) of drug in the formulation, FTIR spectra of the formulation along with the

drug and other excipients were obtained and compared using Shimadzu-8400 spectrophotometer.

In the present study, Potassium Bromide (KBr) pellet method was employed. The samples were thoroughly blended with dry powdered potassium bromide crystals. The mixture was compressed to form a disc. The disc was placed in the spectrophotometer and the spectrum was recorded.

The FTIR spectra of the formulations were compared with the FTIR spectra of the pure drug and the polymers. The FTIR spectra of Pure Drug, Polymer and in combination are presented in Figs: 2 - 4.

RESULTS AND DISCUSSION:

When all the dried films were subjected to physical examination, films appeared to be translucent suggesting that the drug was not completely solubilized rather dispersed/ suspended in the matrix.

Table - 1: Formulation of Transdermal Patches of Fesoterodine

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Fesoterodine*	4	4	4	4	4	4	4	4	4
HPMC E15 cps*	32	40	48	----	----	----	----	-----	----
HPMC E50 cps*	----	----	----	32	40	48	-----	----	-----
HPC*	----	----	----	----	----	----	32	40	48
Propylene Glycol#	6.4	8	9.6	8	6.4	8	9.6	8	6.4
DMSO*	1%	1%	1%	1%	1%	1%	1%	1%	1%
DCM#	10ml	10ml	10ml	10ml	10ml	10ml	10ml	10ml	10ml
METHANOL#	10ml	10ml	10ml	10ml	10ml	10ml	10ml	10ml	10ml

*** - indicates all ingredients are taken in % w/w and # - indicates all ingredients were taken in %w/v**

Table - 2:Physico- Chemical Evaluation of Formulated Patches of Fesoterodine

S. no	Formulation Code	Thickness (mm) (n=3, ± SD)	Weight Uniformity (n=3, ± SD)	Folding Endurance (n=3, ± SD)
1	F1	0.222±0.02	25.66±1.527	No visible cracks
2	F2	0.234±0.013	29.10±1.732	No visible cracks
3	F3	0.198±0.022	17.33 ±1.52	No visible cracks
4	F4	0.206±0.023	27.66±0.577	No visible cracks
5	F5	0.238±0.073	18.33±1.52	No visible cracks
6	F6	0.214±0.032	22.11±102	No visible cracks
7	F7	0.226±0.024	29.33±1.15	No visible cracks
8	F8	0.228±0.066	24.33 ± 2.08	No visible cracks
9	F9	0.222±0.014	20.14±1.14	No visible cracks

S.D – indicates the Standard Deviation

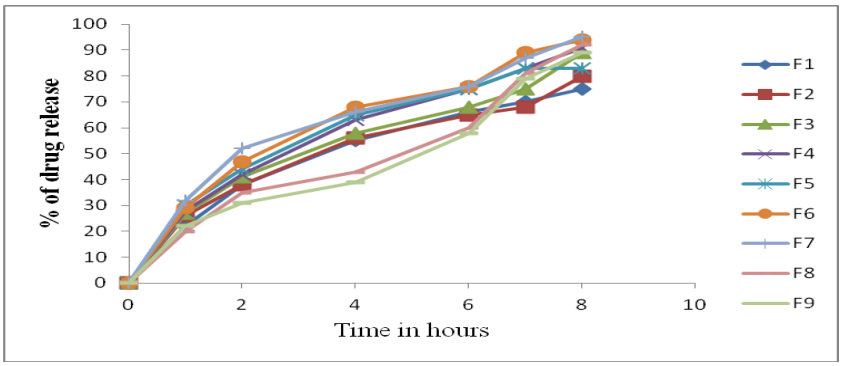

Figure - 1: Cumulative *In-vitro* percent Drug Release of formulations F1 to F9.

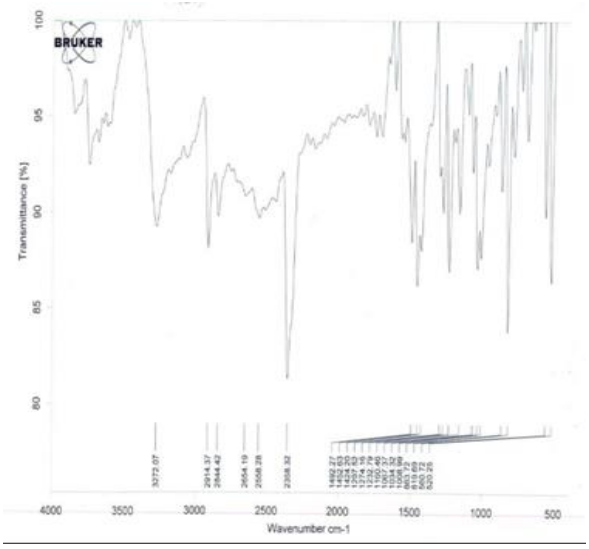

Fig – 2: FTIR Spectra of Fesoterodine

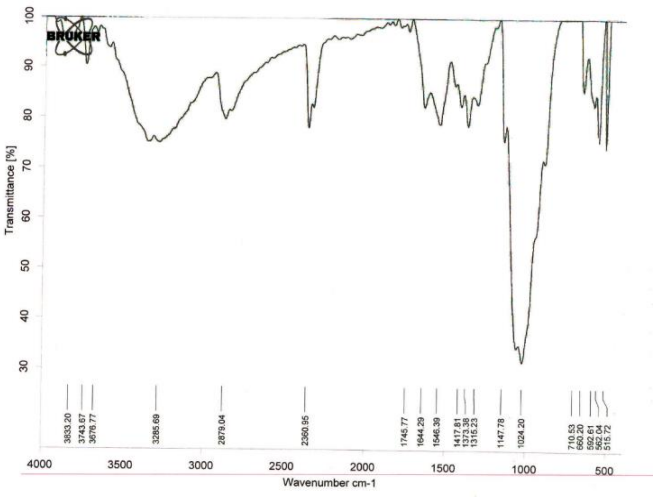

Fig – 3: FTIR Spectra of Fesoterodine with HPC

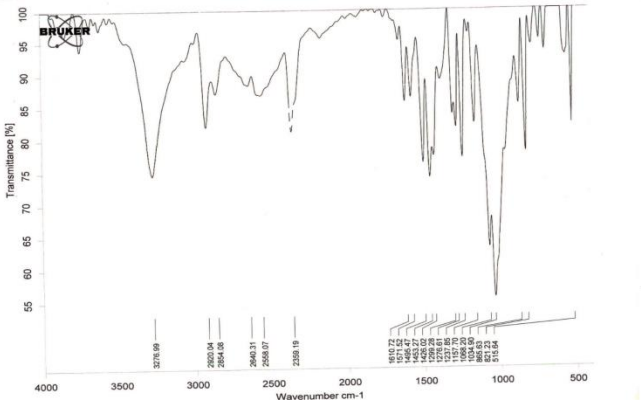

Fig – 4: FTIR Spectra of Fesoterodine with HPMC

Table - 3: Swelling Index and Water Vapor Transmission Rate of Different Formulations

S.no	Formulation Code	Swelling Index				Water Vapor Transmission Rate(gm/hr/cm^2) (n = 3, ± SD)
		5min	10min	30min	60min	
1	F1	51.315	53.147	57.295	64.885	7.7 × 10-3
2	F2	47.706	49.157	50.392	57.459	11.9 × 10-3
3	F3	39.494	41.819	43.514	45.529	16.2 × 10-3
4	F4	31.402	33.916	35.804	37.554	13.6 × 10-3
5	F5	24.135	27.642	31.53	34.172	19.9 × 10-3
6	F6	22.491	26.034	29.422	31.242	17.3 × 10-3
7	F7	41.438	43.775	46.428	47.998	12.1 × 10-3
8	F8	44.183	48.227	53.553	55.374	14.7 × 10-3
9	F9	24.421	28.254	39.42	41.042	15.6 × 10-3

Table - 4: % Moisture Uptake & Moisture Content of Different Formulations

Sl. No	Formulation Code	% Moisture Uptake(n = 3, ± SD)			% Moisture Content (mm) (n = 3, ± SD)
		52% RH	74.9% RH	98% RH	
1	F1	9.786	11.989	16.561	16.444 ± 2.35
2	F2	13.201	15.181	22.86	9.275 ± 2.733
3	F3	11.262	16.952	20.824	22.80 ± 2.32
4	F4	15.591	18.316	22.034	14.016 ± 1.74
5	F5	8.776	12.393	17.205	27.039 ± 1.93
6	F6	13.987	16.238	21.943	34.090 ± 2.35
7	F7	12.809	19.501	24.961	14.819 ± 2.73
8	F8	15.714	23.06	27.925	21.393 ± 3.12
9	F9	14.276	18.345	22.315	16.444 ± 2.35

Table - 5: Bursting Strength, Drug Content, Tensile Strength and Extension of Transdermal Patches

S.No	Formulation Code	Bursting Strength (Kg/cm^2) n=3, ± S.D	Tensile Strength (Kg/cm^2) n=3, ± S.D	Extension (Kg/cm^2) n =3,± S.D	Drug Content (mg) n=3, ± S.D
1	F1	4.36 ± 0.37	0.755 ± 0.04	0.206 ± 0.07	96.67±4.570
2	F2	4.4 ± 0.2	0.796 ± 0.04	0.232 ± 0.10	94.36±6.33
3	F3	2.66 ± 0.11	0.583 ±0.038	0.169 ± 0.04	99.32±2.45
4	F4	3.2 ± 0.4	0.654 ± 0.074	0.178 ± 0.09	101.78±6.27
5	F5	2.23 ± 0.15	0.553 ±0.065	0.191 ±0.01	95.77±12.26
6	F6	2.4 ± 0.2	0.632 ± 0.052	0.197± 0.07	98.66±6.97
7	F7	3.66 ± 0.15	0.786 ± 0.087	0.229 ±0.10	94.59±10.31
8	F8	4.03 ± 0.05	0.815 ± 0.055	0.231 ±0.100	97.98±12.10
9	F9	3.2 ± 0.02	0.582 ± 0.049	0.217± 0.12	97.52±3.48

Table - 6: Kinetics and Mechanism of Drug Release of Fesoterodine

Formulation	Zero Order	First Order	Korsmeyer et al	
	R^2	R^2	R^2	n
F_1	0.9323	0.9634	0.9812	0.89
F_2	0.9754	0.9412	0.9854	0.89
F_3	0.9564	0.9852	0.9393	0.82
F_4	0.8654	0.8139	0.8668	0.61
F_5	0.8773	0.8798	0.8927	0.77
F_6	0.8645	0.8867	0.8881	0.64
F_7	0.8363	0.8881	0.9934	0.49
F_8	0.8537	0.8436	0.8948	0.61
F_9	0.8227	0.8554	0.8954	0.62

In preliminary studies, the HPMC E15 cps films were found to be brittle and di-n-butyl phthalate was used as plasticizer to reduce the brittleness of the films. The studies revealed that addition of di-n-butyl phthalate at 15% w/w of polymer produces smooth, uniform, and flexible films. Hence, further studies were carried out using plasticizer at 15% w/w level in the films.

Thickness Uniformity

Thickness of various Fesoterodine transdermal patches were shown in Table - 2, which is varied from 0.198 ± 0.022 to 0.238 ± 0.073mm. Low standard deviation values in the film thickness measurements en-

sures uniformity of the patches which indicates that the formulation variables did not produce any significant changes ($p>0.05$) on the thickness of film.

Weight Uniformity: For each formulation, three randomly selected patches were used. The 3 films from each batch were weighed individually and the average weight was calculated. Table - 2 shows weights of various Fesoterodine patches which ranged between 17.33 ± 1.52 mg and 29.33 ± 1.15 mg. The results indicates weight of the patches of different batches were relatively similar.

Folding Endurance: The test results indicated that the patches have no visible cracks and maintain their integrity indicating that they were sufficiently flexible with general skin folding when applied. Table - 2shows folding endurance of various Fesoterodine patches.

Swelling Studies: The water uptake capacity of the patch was measured by the swelling index (SI). All the films show increase in weight with time. The swelling ratios of different polymers were given in the Table - 3. Formulation F_1 show highest swelling index of 64.88%. This result suggests that the patch is more permeable to the drug. This may be due to the porosity generated in the reminants of the patches after dissolution of drug. Whereas F_6 shows lowest swelling index of 31.42%. The Films made by using HPC showed low swelling index as compared to that of films HPMC E50 cps.

Water Vapor Transmission Rate Study:
Water vapor transmission studies indicated that all the membranes prepared were permeable to water vapor. Formulation F_1 shows lowest WVTR 7.7 × 10-3 gm/cm/day whereas formulation F_5shows highest WVTR 19.9× 10-3 gm/cm/day. The results are shown in Table - 3.

PercentageMoisture Content: Moisture content and moisture uptake studies provide information regarding stability of the formulation. The results revealed that the moisture content and moisture uptake were found to increase with increasing concentration of hydrophilic polymer. The presence of penetration enhancer DMSO did not show any major changes in moisture content and moisture uptake values. But, a slight increment in both parameters was observed. This may be due to the water affinity of DMSO. Thesmallmoisturecontentintheformulationhelpsthemto remainstableandfrombeingacompletelydriedandbrittle-films.Physicochemicalstudiesconductedondifferentpolymericfilmscontainingdrugforpreparation of transdersal films. Table – 4 shows the results of Moisture Content.

Percentage Moisture Uptake: The prepared formulations also demonstrated low moisture absorption, which may protect the formulations from microbial contamination and bulkiness of the patches. The study of the hydration of polymers used in sustained release applications has been an area of interest because it is believed that it affects drug release from controlled release matrix. The consequence of water uptake could be the formation of empty spaces within the patch that could make its structure less resistant to mechanical stresses. Formulation F6 shows highest moisture content 34.090 ± 2.35 and F2 shows low 9.275 ± 2.733. Moisture uptake of films was carried out at different RH. All films showed an increase in moisture uptake with an increase in relative humidity. The increase in moisture uptake may be attributed to the hygroscopic nature of polymer-plasticizer of films. Table – 4 also shows the results of Moisture Uptake.

Bursting strength: The bursting strength show linear correlation with increase in concentration of plasticizer. Bursting Strength of formulation F2 was found to be highest 4.4±0.2 kg/cm^2 whereas bursting formulation F5 showed lowest bursting strength (2.23±0.15 kg/cm^2). Table –5shows the results of bursting Strength of Transdermal patches.

Tensile Strength and Extension: Formulation F8 shows highest tensile strength of 0.815 ± 0.055. Formulations F2, F9 show highest extension whereas F3 show low extension. The results reveal that the membranes have reasonable tensile strength and moderate extension capability. Table – 5alsoshows the results of Tensile Strength of Transdermal patches.

Drug Content Analysis: The drug content of patches (1 cm^2)were measured by cutting the strips of patches that were later kept in a beaker containing 100 ml of distilled water and kept aside until it get dissolved. Finally the solutions were filtered using whatman filter paper and the filtrate was examined for the drug content at 275 nm spectrophotometrically**.** Table – 5 shows drug Content results of various Transdermal patches. The drug content of all the formulations was ≥1.43 mg/cm^2 with a low standard deviation (≤0.07). The results of drug content analysis have shown that the method employed to prepare films in this study was capable of giving films with uniform drug dis-

tribution with an insignificant batch variability ($p>0.001$).

***In-vitro* Drug Permeation Studies:**

In-vitro drug permeation studies were performed by using a modified Franz diffusion cells. The formulated patches were cut into size of 2.1 cm^2 and placed over the synthetic filter membrane which was mounted between the donor and receptor compartment that was filled with phosphate buffer P^H 7.4.The whole assembly was fixed on a magnetic stirrer, and the solution in the receptor compartment was constantly and continuously stirred using magnetic beads at 50 rpm. The temperature of the buffer solution in the receiver compartment was maintained at 37 ± 0.5^0C. Aliquots of 5 ml were withdrawn at regular time intervals and the collected samples were analyzed for drug release spectrophotometrically at 275 nm. The receptor phase was continously replenished with an equal volume of phosphate buffer pH 7.4 at each time of sample withdrawal to maintain sink conditions. The cumulative amounts of drug permeated per square centimeter of patches were plotted against time.

Release Kinetics and Mechanism of Drug Release

Different kinetic models (Zero-Order, First Order, and Korsmeyer's equation) were applied to interpret the drug release kinetics and to know the mechanism of drug release from these matrix systems with the help of equation 1-4.

$$M_t = M_0 + K_0 t \quad (1)$$

$$\text{Ln } M_t = \text{Ln } M_0 + K_1 t \quad (2)$$

$$M_t/M_0 = K_k t^n \quad (3)$$

In these equations, M_t is the cumulative amount of drug released at any specified time point and M_α is the dose of the drug incorporated in the delivery system. k_0, k_1 and k_k are rate constants for zero order, first order and Korsmeyer's model respectively and n is the diffusion release exponent indicative of the operating release mechanism. The correlation coefficient values (R^2) are presented in Table – 6.

The *in-vitro* drug permeation profile of all formulations were plotted by taking cumulative amount of drug permeated against time. Figure–1shows drug permeation profile of trasdermal patches, showing initial faster (burst) release followed by slower release. The initial faster release may be attributed to the rapid diffusion of the drug immediate to the surface of the film. Thus, rapid depletion of the surface drug caused a consequent increase in mean diffusion path length that might have caused further slower release. In addition, latter slower release of the drug from the formulations (except F_7) can also be accounted for the increase in diffusion path length due to the swelling of hydrated HPC. The hypothesis was further confirmed by the increase ($p<0.01$) in thickness of the films after the permeation study. This assumption was further confirmed by the fitting the release data into Eq.3. Table-6 shows the drug release kinetics of all transdermal patches that were ranged between zero order (R^2=0.9323 to 0.9754) and first order (R^2=0.9412 to 0.9852). Hence, the *in-vitro*permeation data neither fit into zero order kinetics nor first order kinetics respectively. Formulation F_7 among all formulations showed strong linearity with R^2 value 0.9934 with 'n' value of 0.49. It indicates that diffusion is the mechanism of drug release from the formulation F_7. It was observed that as the concentration of hydrophilic polymer (HPC) increased in the formulations, the mean cumulative amounts of drug permeated decreased substantially. Thus, based on above observations, it is concluded that the polymer matrix has a strong influence on the diffusivity of active molecule. The alteration of structural arrangement of polymers by using different polymers makes possible to enhance the permeation of the drug across the membrane. Formulation (F7) was optimized as it indicates that drug release was leaning toward diffusion and swelling coupled mechanism – so called anomalous diffusion, which might be responsible for the controlled drug release that follows more than one process. Presence of swellable polymer (HPC) in the matrix has controlled drug release which was extended up to 8hrs.

CONCLUSION:

Fesoterodinetransdermal films using HPMC E15 cps, HPMC E50 cps and HPC. Fesoterodine were prepared for treatment of overactive bladder syndrome. The films were prepared by solvent-evaporation method using dimethyl sulfoxide as penetration enhancer and propylene glycol as plasticizer. Transdermal films prepared by using different varities of hydrophilic water swellable polymers enhanced the release of the drug and also were responsible for the coupled diffusion of drug release. Finally, we conclude that the formulation (F7) was optimized as it indicates that drug release was leaning toward diffusion and swelling cou-

pled mechanism – so called anomalous diffusion.

ACKNOWLEDGMENT:

Authors are thankful to Natco Pharma Pvt. Ltd, Hyderabad and Aurobindo Pharma Pvt. Ltd Hyderabad for providing necessary ingredients as gift samples.

BIBLIOGRAPHY

1. Geeta A, Dr. Sanju D. Development, Fabrication and evaluation of transdermal drug delivery system - A Review. *Pharmainfo.net*: 2009; 7.
2. Baker RW, Heller J. Material selection for transdermal delivery systems; cited in: Hadgraft J, Guys RH, editors. Transdermal drug delivery: development issues and research initiatives. New York, Marcel Dekker Inc. 1989; 293-311.
3. Walters KA. Transdermal drug delivery systems In: Swarbick K, Boylan JC, Encyclopedia of pharmaceutical technology. New York, Marcel Dekker Inc. 1997; 253-293.
4. Chandra A, Pramod Kumar S, IrchhiayaR. Microemulsion-based hydrogel formulation for transdermal delivery of dexamethasone. *Asian. J. Pharm*. 2009; 3(1): 30-8.
5. Agrawal SS, Munjal P: Permeation studies of atenolol and metoprolol tartrate from three different polymer matrices for transdermal delivery. *Ind. J. Pharm. Sci*. 2007; 69: 535-39.
6. Chein YW, Novel drug delivery systems. 2nd ed. New York: Marcel Dekker Inc; 1992. Vol.50,338-44
7. www.drugbank.ca/drug/DB06702
8. www.wikipedia.org/wiki/Fesoterodine
9. Delgadillo , Transdermal iontophoresis of dexamethasone sodium phosphate in vitro and in vivo: effect of experimental parameters and skin type on drug stability and transport kinetics. Eur. J. Pharm. Biopharm. 2010; 75: 173-78.
10. Sanap GS, . Preparation of transdermal monolithic systems of indepamide by solvent casting method and the use of vegetable oils as permeation enhancer. Int. J. Green Pharm. 2008; 129-33.
11. Manish K Abheshek KR, Design and evalution of pectin based metrics for transdermal patches of meloxicam. JPRHS 2 (3); 244-47.
12. Debjit B, Recent advances in transdermal drug delivery sytem:Int. J. Pharm. Tech Res: 1(2): 2010; 68-77.
13. Kaza R, Pitchaimani R. Formulation of transdermal drug delivery system: Matrix type, and selection of polymer, their evaluation. Current drug discovery technologies. 2006; 3:279-85.
14. Tanu Bhargava, Current trends in NDDS with the special rFdaeferences to NSAIDS: Int.J. Pharm. Biosci: 2(1):2011: 92-114.
15. Guy RH. Current status and future prospects of transdermal drug delivery, Pharm Res 1996: 13; 1765-69.
16. Ubaidulla U, Transdermal therapeutic system of carvedilol: Effect of hydrophilic and hydrophobic matrix on *in vitro* and *in vivo* characteristics. AAPS PharmSciTech 2006; 7(1): Article 2.
17. Lopez FV, Collet JH, Vitoria M, Bentley LB. Influence of cyclodextrin complexation on the *invitro* permeation and skin metabolism of dexamethasone. Int. J. Pharm.2000; 200: 127-32.
18. Gondaliya, Studies in formulation and pharmaco technical evaluation of controlled release transdermal delivery system of bupropion, AAPS SciTech 2003; 285-86.
19. James EF Reynolds. Martindale the extra pharmacopoeia. 28th ed. London: The pharmaceutical press.1982.
20. Goodman, Gilman. The pharmacological basis of therapeutics. McGraw Hill companies. 11th ed.2006; 285-86.
21. Sanap, Preparation of transdermal monolithic systems of indepamide by solvent casting method and the use of vegetable oils as permeation enhancer. *Int. J. Green Pharm.* 2008; 129-33