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FORMULATION DESIGN AND CHARACTERIZATION OF TRANSDERMAL PATCH OF ATENOLOL

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Abstract:
The present study was carried out to develop the transdermal patches Containing Atenolol with different polymers of HPMC, PVPK30 and EC was added in the formulation Propylene glycol used as a plasticizer, DMSO, ethanol and eugenol is used as penetration enhancers by solvent casting method. Solvent Casting method was used for the formulation of patches. The patches showed satisfactory folding endurance and tensile strength. And it indicated good physical stability. The drug-excipients compatibility studies were performed by Fourier Transform Infrared spectrophotometer (FTIR). Formulated transdermal patches were evaluated with regard to physicochemical characteristics and It was found that all the formulations follow the first order kinetics.

Keywords: *Trasdermal patches, Atenolol, Permeation enhancer, In-vitro permeation study.*

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INTRODUCTION:

Transdermal delivery provides an improved approach to the administration of drugs by maintaining a therapeutic constant concentration of drug in the blood for desired period of time, usually between one and seven days. Transdermal drug delivery enables avoidance of gastrointestinal absorption, which is associated with pitfalls of enzymatic and pH associated deactivation. This method also allows for reduced pharmacological dosing due to the shortened metabolic pathway of the Transdermal route versus the gastrointestinal pathway. Transdermal drug delivery system releases its active ingredient through the patient's skin providing a uniform blood level. In addition since the active ingredient moves with the blood stream directly into the targeted organ, the effective dose can be lower than that in the traditional drug type. The transfollicular pathway in which the drug travels through cells and across them is the shortest way that most likely provides relatively large for diffusion of a molecule. The intracellular pathway avoids the cell contents, but aqueous considerably more tortuous. The transfollicular pathway involves passage or diffusion of drug molecule through the hair shaft openings, which presumably are filled with sebum. This route offers substantially lower diffusion resistance to the most of the drugs that are generally not permitted fairly through other routes.[3] However the path length is relatively long and the density of hair follicles in human skin quite low. The Transdermal permeation of most neutral molecules is recognized to be primarily a process of passive diffusion across the intact stratum corneum through the transfollicular region.

Hypertension is defined conventionally as a sustained increase in blood pressure and is responsible for 57% of all stroke deaths and 24% of all coronary heart disease deaths in India. It is one of the main causes of heart diseases in recent years and an important risk factor for cardiovascular mortality and morbidity. It is defined to be 140 mmhg systolic and 90mmhg diastolic, though risk appears to increase even above 120/80 mmhg.

MATERIALS AND METHODS:

Atenolol was obtained as a gift sample from Mac Mohan Pvt. Ltd., Hyderabad, India. HPMC, EC, PVP K30, Span 80, Propylene glycol gift sample from K.P Labs, Hyderabad.

Identification of Drug through Fourier Transform Infrared (FTIR)

Sample drug is identified by FTIR. FTIR spectra of sample drug are compared with the FTIR spectra of standard drug.

Compatibility Study of Drug with Polymers

Fourier transform infrared (Perkin Elmer, India) spectroscopy is used to study the compatibility between Atenolol and polymers used in preparation of transdermal patch. The IR spectrum was recorded using an FTIR by KBr pellet method and Nuzol method. The spectra were recorded in the wavelength region between 4000 and 400 cm^{-1}.

Preparation of Calibration Curve of Atenolol

From the stock solution, were prepared by dissolving 50mg of each standard drug samples in 50ml volumetric flask separately and the volume was made up with distilled water to get a concentration of 1mg/ml. From this, suitable dilutions were made in distilled water to get the working standard solution of 0.1-1.0µg/ml for atenolol spectra were measured at 275nm atenolol. The absorbances of the 3 replicate analyses were carried out. Absorbance Vs Concentration were plotted to obtain the calibration graph.

Preparation of Transdermal Patch:

Transdermal patch of atenolol was prepared by solvent evaporation technique in a petridish. Six types of polymer patches were prepared. First three formulations were prepared by using HPMC, EC and PVPK-30 alone having drug and polymer ratio 1:4, 1:6, 1:8 using distilled water as a solvent and one more formulation is formulated using HPMC with permeation enhancer Span 80. Formulations were prepared by using HPMC and EC in combination having drug and polymer by using permeation enhancer and using methanol and chloroform as solvent (1:1) ratio and the remaining formulation is formulated with HPMC, EC and Propylene glycol used as a plasticizer.

Table 1: Preparation of Atenolol Transdermal Patch

S.No	Ingredient	Formulation Code				
		F1	F2	F3	F4	F5
1	Atenelol (mg)	10	10	10	10	10
2	HPMC	40	-	-	20	20
3	EC	-	60	-	-	40
4	PVPK-30	-	-	80	-	-
5	Span 80%	-	-	-	2%	2%
6	Propylene Glycol	2%	2%	2%	2%	2%

Evaluation of TDDS [8- 12]

Thickness of the patch:-

The thickness of patches was measured by using a micrometer and mean value in mm is used to measure the thickness of the patch.

Percentage (%) of Moisture Absorbed:-

Checking the physical stability of the film in high humidity conditions, film that are accurately weighted were placed in a desiccators containing saturated aluminium chloride solution 79.5%RH for 3 days. The films were re-weighed and the percentage moisture absorption was calculated using the formula.

$$\text{Percentage (\%) Moisture Absorbed} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

Percentage (%) of moisture lost:-

In order to check the extent of moisture lose from freshly prepared film, the accurately weighed film are placed in a desiccators containing fused anhydrous calcium chloride for 72hrs, After 72hrs films were re-weighed percentage moisture is calculated using by the following formula

$$\text{Percentage (\%) moisture lost} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Drug Content Uniformity:-

By cutting a patch into pieces and put in dissolution of 100 ml or diffusion medium is used respectively and stirred continuously using a mechanical stirrer and after the ends of 3hrs the sample is withdrawn the drug content to be determined spectrophotometrically at 275 nm.

***In-vitro* Diffusion Study:-**

The study of *in-vitro* diffusion is carried out by using Franz Diffusion Cell. Egg membrane is used the purpose of semi-permeable membrane for diffusion. Franz diffusion cell has a receptor compartment with an effective volume approximately 60 ml and effective surface area of permeation 3.14cm^2.

Using Franz diffusion cell *In-vitro* release studies were carried out results were shown in table 7 .

Drug Release Kinetic Study

The mechanism of drug release from the transdermal patches is analyzed by fitting the release data to following equations

Zero – Order Equation:

$$Q = k_0 t$$

Where, Q is the amount of drug released at time t

k_0 is the zero – order release rate.

First – order equation:

$$\ln (100 - Q) = \ln 100 - k_1 t$$

Where, Q is the percent of drug release at time t

k_1 is the first – order release rate constant.

Higuchi's Equation:

$$Q = k_2 \sqrt{t}$$

Where, Q is the percent of drug release at time t

k_2 is the diffusion rate constant.

Mathematical Model for TDDS:-

The drug release mechanism and kinetics are two important characters of delivery system for the drug dissolution profile.

RESULTS AND DISCUSSION:

Table 2: Data for Calibration Curve of Atenolol

S. No.	Concentration (µg/ml)	Absorbance
1	0	0
2	1	0.0200
3	2	0.0470
4	4	0.1410
5	6	0.1983
6	8	0.2622
7	10	0.3423

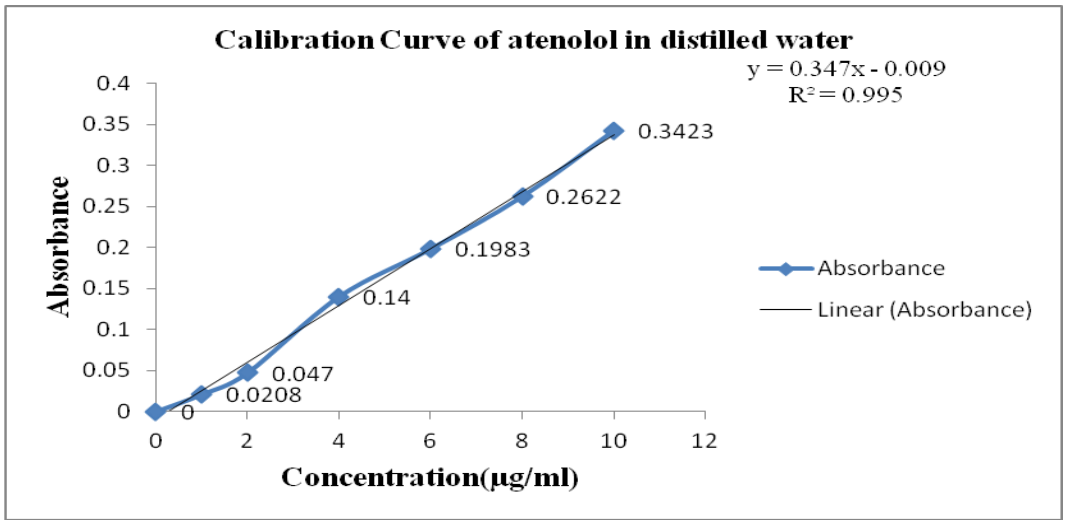

Fig 1: Calibration Curve of Atenolol λ_{max}: 275 nm

FT-IR:

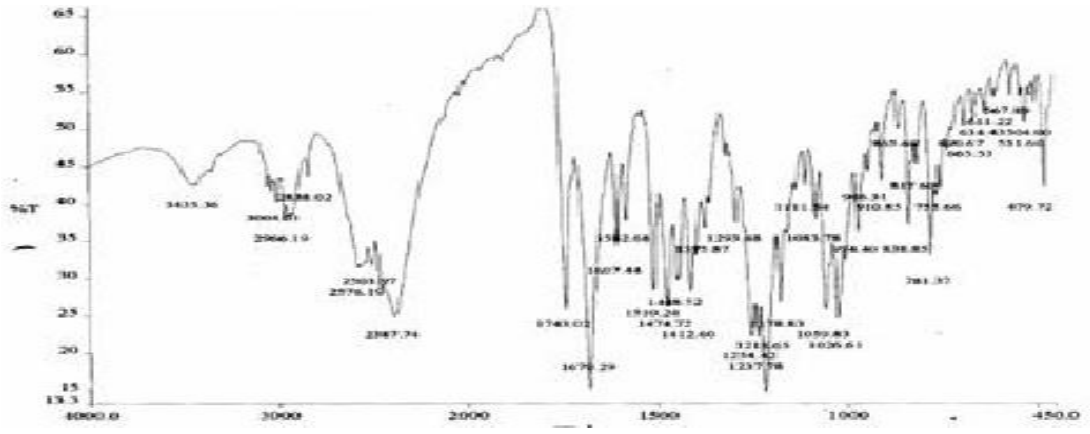

Fig 2: Identification of Sample Atenolol through FTIR

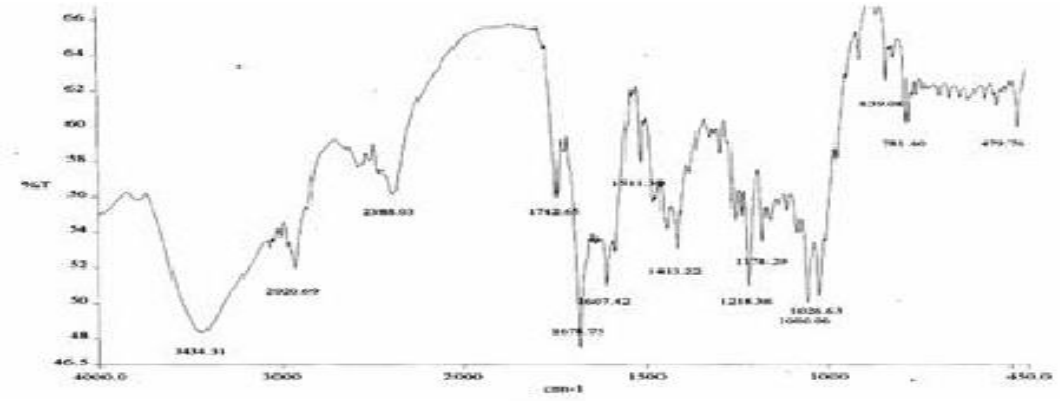

Fig 3: Physical Mixture of Atenolol and polymers

Table 3: Evaluation Parameters of Transdermal Patches of Atenolol

S.No	Formulation Code	Thickness(mm)	Folding endurance	% Moisture absorbed	% Moisture lost
1	**F1**	0.25±0.002	62	2.96±0.012	1.26±0.01
2	**F2**	0.26±0.004	69	2.48±0.034	1.23±0.04
3	**F3**	0.24±0.006	74	3.68±0.086	1.95±0.43
4	**F4**	0.29±0.004	88	2.74±0.054	1.35±0.02
5	**F5**	0.32±0.005	92	2.15±0.015	1.27±0.06

Mean ± SD (n=3)

Table 4: Drug Content Uniformity

Formulation	% of drug in 3.14 sq.cm			
	1st	2nd	3rd	Mean
F1	93.30	93.76	93.54	93.53
F2	91.23	91.30	91.29	91.94
F3	90.21	90.38	90.38	90.66
F4	95.16	95.08	95.24	95.49
F5	96.48	96.25	96.12	96.28

Table 5: *In-Vitro* Permeation Profile of Atenolol Formulation

S.No	Time(hrs)	% Cumulative drug release				
		F1	F2	F3	F4	F5
1.	0	0	0	0	0	0
2.	1	8.31	8.08	6.56	11.02	13.36
3.	2	17.46	16.23	12.78	22.32	23.48
4.	4	25.04	18.54	17.32	26.65	32.43
5.	6	28.19	22.38	21.18	31.61	35.84
6.	8	35.27	25.58	23.67	35.98	39.52
7.	10	38.66	26.35	27657	42.63	47.46
8.	12	43.38	32.95	31.35	47.13	52.25

Table 6: Model Fitting Release Profile of Formulation F1 to F6

Formulation code	Regression coefficient (R^2)			Korsmeyer-Peppas	
	Zero order	First order	Higuchi model	R^2	n
F1	0.924	0.964	0.983	0.959	0.601
F2	0.912	0.932	0.993	0.981	0.523
F3	0.927	0.958	0.990	0.975	0.525
F4	0.914	0.963	0.966	0.979	0.515
F5	0.916	0.961	0.995	0.992	0.487

The calibration curve of pure Atenolol was plotted with distilled water to get a concentration of 1mg/ml. From this, suitable dilutions were made in distilled water to get the working standard solution of 0.1-1.0µg/ml for atenolol spectra were measured at 275nm atenolol. The absorbances of the 3 replicate analyses were carried out. Absorbance Vs Concentration were plotted to obtain the calibration graph shown in figure 1 and table 2. The compatibility between Drug and polymer was studied by using FTIR absorption spectra showing in figures 2 & 3. The preliminary study conducted on compatibility between Atenolol with HPMC EC and PVPK 30 revealed that there is no interaction between the drug and polymer as from FTIR spectra. The polymers are the backbone for Transdermal delivery. Span 80 having drug polymer ratio 1:4. Next formulations were prepared by using HPMC and EC in combination having drug and polymer by using permeation enhancer Span 80 and using methanol and chloroform as solvent and the remaining formulation is formulated with HPMC, EC and PVP, Propylene glycol used as a plasticizer.

Hence, it is commonly employed in formulation of patch. The physico-chemical characteristics such as thickness of the patch, folding endurance, percentage of moisture absorbed, percentage of moisture lost, and drug content analysis were found to be within the acceptable limits. The patches were found to be stable to withstand the stress. In vitro Diffusion studies of Transdermal patches: The study of *in-vitro* diffusion is carried out by using Franz Diffusion Cell. Egg membrane is used the purpose of semi-permeable membrane for diffusion. Franz diffusion cell has a receptor compartment with an effective volume approximately 60 ml and effective surface area of permeation 3.14cm^2. Using Franz diffusion cell *In-vitro* release studies were carried out. F1, F2, F3, F4and F5 was 43.38%, 32.95%, 31.35%, 47.13%, 52.25% respectively in 12 hrs.

CONCLUSION:

Atenolol is a multiple-action cardiovascular drug that is used for the treatment of hypertension now approved in many countries. Administration of atenolol by oral route caused various disadvantages and has some limitations, so the transdermal drug delivery approach is used to deliver these agents, which maintain relatively consistent plasma level for long term therapy and overcome various disadvantages associated with oral administration. TDDS have great potential being able to use for both hydrophobic and hydrophilic active substances.

Transdermal patch of atenolol contain HPMC, EC and PVP as polymer, PG as plasticizer and Span 80 as permeation enhancer for control release of the drug over an extended period of 8 hrs. Greater understanding of the different polymers and different mechanism of biological interactions are required to optimize this drug delivery system.

REFERENCES:

1. Richard., H. Guy, Jonathan Hadgraft., Transdermal Drug Delivery, Second edition, Revised and Expanded, India special edition, 2010;(123):1-143 & 361-367.
2. Dheeraj., T. Baviskar, Dinesh K. Jain. Novel Drug Delivery Systems., Nirali prakashan publications, first edition 2012; 6.1-6.34.
3. N. K. Jain., Controlled and Novel Drug Delivery, CBS publishers, first edition, 1997; 100-127.
4. Goodman and Gilman., The Pharmacological Basis of Therapeutics, twelth edition, Me graw-Hill companies publications, 2006; 327.
5.M. E. Aulton., Pharmaceutics, The Science of Dosage Form Design, Churchill Livingstone,2004; 2: 499-533.
6.Indian Pharmacopoeia., 2007, vol (I & II); 144-747.
Manikandan et al., Am. J. Pharm Health Res 2015;3(1):223

7.S. Ramkanth and C. Madhusudhanachetty., Development and Evaluation of Trandermal Drug Delivery System of Atenolol, International Journal of Research in Pharmaceutical Science, 2012; 2(4):692-697.
8. P. Eswaramma and M. Karthikeyan , Formulation and Evaluation of Transdermal Patch of Atenolol, International Journal of Comprehensive Pharmacy, 2010;110.
9.D. M. Brahmankar & S. B. Jaiswal., Bio pharmaceutics and Pharmacokinetics, Vallabh Prakashan, Delhi, 2009; 495-501.
10. Yie. W. Chien., Novel Drug Delivery System, second edition, 2005; 301:378.
11.Shobha Rani. R. Heirmath., Text Book of Industrial Pharmacy, 2008; 27-49.
12.Banker G S and Rhodes C T., Modern Pharmaceutics, third edition, Marcel Dekkar, 1990.