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Formulationand Evaluation of Amitriptyline Transdermal Patches for Adults

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ABSTRACT:
The idea of transdermal patches has attracted significant attention in the pharmaceutics community in recent decades. Transdermal patch medication administration provides a number of benefits, including extending the dose's residence duration at the application site. The main aim of the study is to formulate and evaluate amitriptyline transdermal patches by using HPMCK15 as rate controlling polymer and poly vinyl pyrollidone as an adhesive agent. Transdermal patches where prepared by using solvent casting method. The drug and drug-polymer compatibility was studied using FTIR studies. The results represents that the amitriptyline transdermal patches bypasses first-pass metabolism and reduce desirable side effects with desired adhesive properties. These patches are proposed for the use of transdermal anti depressant properties.

I. INTRODUCTION:

Drug delivery refers to the approaches, formulation, technologies and system for transporting therapeutics into the body as that improve its safety and efficacy by controlling the rate, time, and place of release of drug into the body to achieve their desired therapeutic effect. It is the method or process of administering pharmaceutical compound to achieve a therapeutic effect in human and animals.

Transdermal drug delivery system is also known as patches, are dosage form designed to deliver a therapeutically effective amount of drug across a patients skin.

TDDS is a painless method of delivering drugs systematically by applying a drug formulation onto intact and healthy skin. The drug initially penetrates through the deeper epidermis and dermis without drug accumulation in dermal layer. When drug reaches the dermal layer, it becomes available for systemic absorption via the dermal microcirculation.

MECHANISM OF TRANSDERMAL PATCHES:

The mechanism of action involves the following steps:

1. **Skin penetration:**

The patch adheres to the skin, and the medication begins to penetrate through the outermost layer of the skin, the stratum corneum. This layer acts as a barrier but is permeable to certain substances.

2. **Diffusion:**

The medication moves through the layers of the skin, aided by factors such as concentration gradients, the properties of the drug, and the design of the patch. Some patches use enhancers or permeation enhancers to facilitate drug penetration.

3. **Absorption:**

Once through the skin, the medication enters the blood vessels in the underlying dermis layer. From here, it enters the bloodstream and is distributed throughout the body.

4. **Continuous delivery:**

The patch maintains a steady and controlled release of the drug over a specified period. This sustained delivery helps in maintaining consistent therapeutic levels of the medication in the bloodstream.

II. MATERIALS AND METHODS:

HPMCK15 was obtained as gift sample from colorcon asia pvt.ltd. Goa, Poly vinyl pyrollidone was brought from Bangalore fine chemicals, Poly ethylene glycol was brought from Bangalore fine chemicals, Ethylcellulose, Glycerol, Propylene glycol were brought from isochem laboratories.

FORMULATION OF AMITRIPTYLINE TRANSDERMAL PATCHES BY SOLVENT CASTING METHOD:

Solvent casting method is the most widely used method for the preparation of transdermal patches The steps involved are as follows

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• Hydrophilic polymers are dissolved in water to form a homogenous viscous solution.
• API and other lipophillic excipients are dissolved in suitable solvent to form a clear viscous solution.
• Both the solutions are mixed to form a clear homogenous mixture.
• The plate is lubricated evenly with glycerin and the mixture is poured in it.
• Then the resulting solution is allowed to dry and once it is dried the patches are cut into needed size.

Formulation	Ingredients								
	Amitriptyline (mg)	HPMC K_{15} (mg)	PVP (mg)	PEG (mg)	Ethyl cellulose (mg)	Propylene glycol (ml)	Ethanol	Menthol	Sucrose
F_1	25	100	75	50	50	4	q.s	q.s	q.s
F_2	25	75	50	50	60	4			
F_3	25	50	100	50	30	4			

Table No. 3: Formulations profile

EVALUATION OF AMITRIPTYLINE PATCHES

a. THICKNESS

The thickness of the film is determined by travelling microscope, dial gauge, screw gauge or micrometer at different points of the film.

b. PHYSICAL APPERANCE

Colour, non transparency, softness, elasticity of the formulated films were formulated.

c. WEIGHT VARIATION TEST

Weight variation is studied by individually weighing three selected films and calculating the average weight. The individual weight should not deviate from the average weight

d. FLATNESS

For flatness determination, one strip is cut from the centre and two from each side of the patches. The length of each strip is measured and various in length is measured by determining percent constriction. Zero percent constriction is equivalent to 100 percent flatness.

% constriction = $L1-L2\ L2 \times 100$

Where,

L1= initial length of the film

L2=final length of the film

e. MOISTURE LOSS

The films are weighed individually and kept in desiccators containing calcium chloride at room temperature of 24hrs. The films are weighed after specific interval until they show constant weight. The percentage moisture was calculated as the difference between the initial and final weights in relation to the initial weight.

% Moisture content = $initial\ weight-final\ weight\ final\ weight \times 100$

f. MOISTURE UPTAKE

Weighed films are kept in the desiccators at room temperature for 24hr. These are then taken out and exposed to 84% of relative humidity using standard solution of potassium chloride in a desiccators until constant weight is achieved, % moisture uptake is calculated as

% moisture uptake = $final\ weight-initial\ weight\ innitial\ weight \times 100$

g. FTIR SPECTRAL ANALYSIS

FTIR study was carried out to check identity of drug, infrared spectrum of Amitriptyline hcl was determined by Fourier transform infrared spectrophotometer using kBr dispersion method. The base line correction was done using dried potassium bromide. Then the dried mixture of drug and potassium bromide was run followed by using FTIR spectrophotometer. It was employed for compound identification.

h. DETERMINATION OF UV ABSORPTION MAXIMA

The identification of drug was done by uv spectrophotometric method. The absorption maximum obtained with the substance being examined corresponds in position and relative intensity to those in the reference spectrum. The absorption maximum of the standard solution was

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scanned between 200- 400 regions on double beam uv- visible spectrophotometer.

III. RESULTS AND DISCUSSION:

a. Determination of Melting Point:

The melting point of the drug was done by capillary method. According to IP melting point of amitriptylin is

SI.No.	MELTING POINT	CONCORDANT VALUE
1.	198℃	198℃
2.	195℃	
3.	197℃	

TABLE NO. 1

b. Solubility Studies

Solubility of AMT HCl

SOLVENT	Solubility status	Parts of solvent required per part of solute	Parts per solute as per IP
Chloroform	Slightly soluble	400 parts	100-1000 parts
Methanol	Freely soluble	3 parts	1-10 parts
Ethanol	Freely soluble	3 parts	1-10 parts
Water	Sparingly soluble	50 paarts	30-100 parts
HCl	Freely soluble	3 parts	1-10 parts

TABLE NO. 2

c. THICKNESS

Formulation	Thickness
F1	0.55±0.047
F2	0.57±0.042
F3	0.52 ±0.007

TABLE NO. 3

d. WEIGHT VARIATION

Formulation	Weight (mg)
F1	356 ±1.56
F2	342 ±1.65
F3	345 ±2.58

TABLE NO. 4

e. MOISTURE LOSS AND MOISTURE UPTAKE

FORMULATION	MA	ML
F1	4.58 ±1.12	1.68±0.51
F2	3.21 ±1.59	0.96±0.41
F3	4.15 ±0.98	0.86±0.42

TABLE NO. 5

f. ANALYTICAL METHODS

- **Determination of λ max by using 0.1N HCL:**

The maximum absorption for Amitriptyline hydrochloride in 0.1N HCL was found to be 239nm and it is shown in the figure

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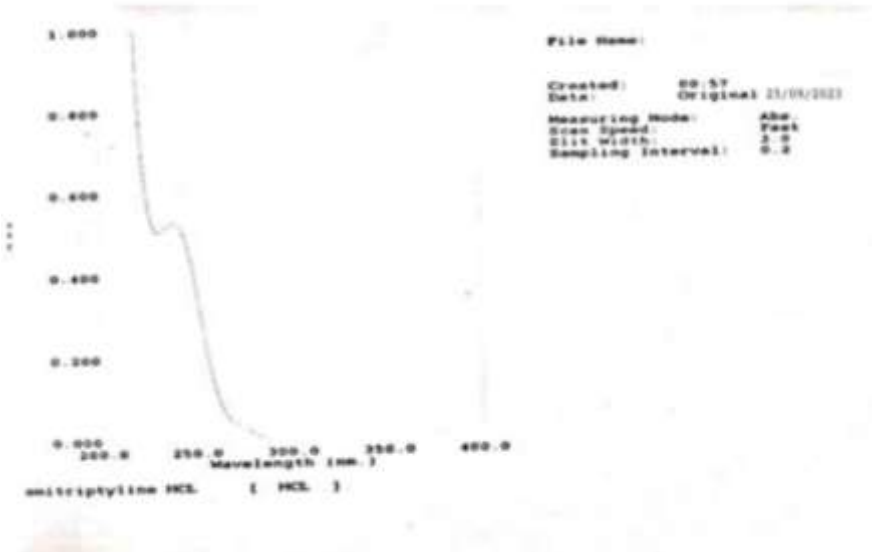

Fig. No.1: λ max observed for Amitriptyline hydrochloride in 0.1 HCl

- **Preparation of standard curve of Amitriptyline HCL 0.1N HCL:**

UV absorption spectrum of Amitriptyline hydrochloride in 0.1N HCL showed λ max at 239nm. Absorbance obtained for various concentration of AMT HCL in 0.1N HCL are given in the table. The graph of absorbance vs concentration for ATM HCL was found to be a linear in the concentration range of 20-10 g/ml.

S.no	Concentration(g/ml)	Absorbance (nm)
1	2	0.092
2	4	0.173
3	6	0.258
4	8	0.345
5	10	0.430

Table No. 6: Data of absorbance vs. concentration for AMT HCL

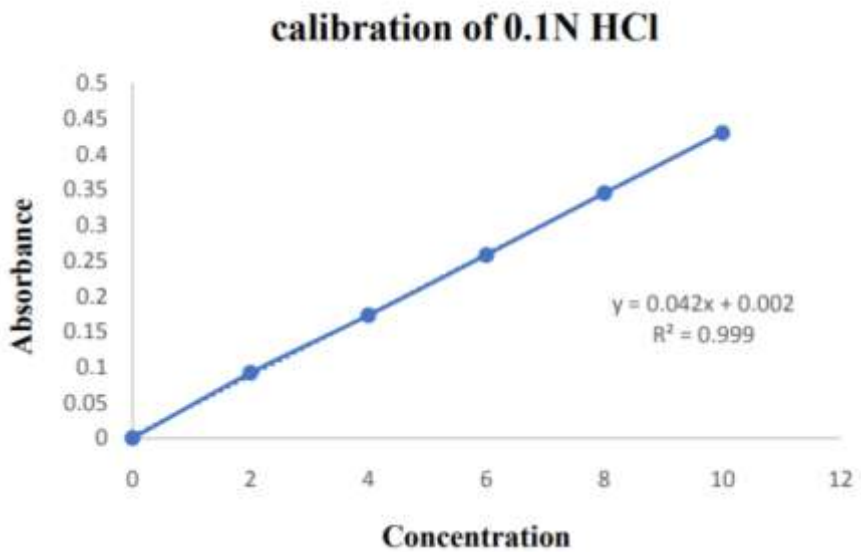

Fig. No. 2: Standard graph of AMT HCl in 0.1N HCl

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- **Preparation of standard curve of AMT HCL pH 7.4 phosphate buffer:**

The absorption spectrum of AMT HCL in Ph 7.4 phosphate buffer showed λ max at 239nm. Absorbance obtained as various concentration of AMT HCL in pH 7.4 phosphate buffer are given I the table. The graph of absorbance vs. concentration of ATM HCL was found to be linear in the concentration range of 2-10μg/ml. the drug obeys Beer –Lambert law in the range of 2-10μg/ml.

- **Preparation of phosphate buffer (pH7.4)**

50ml of 0.2M potassium phosphate and 39.1ml of 0.2m NaOH is mixed and volume made up to 200ml with distilled water.

- **0.2M potassium dihydrogen phosphate:**

27.218 gram of potassium dihydrogen phosphate is dissolved in few ml of distilled water and volume is made up to 1000ml with distilled water.

- **0.2M NaOH**:

8g of NaOH is dissolved in few ml of distilled water, mixed well and volume upto 1000ml with distilled water.

S.no	concentration(μg/ml)	Absorbance (nm)
1	0	0
2	2	0.084
3	4	0.152
4	6	0.226
5	8	0.305
6	10	0.386

Table No. 7: Data of absorbance vs. concentration of ATM HCL in pH 7.4 phosphate buffer

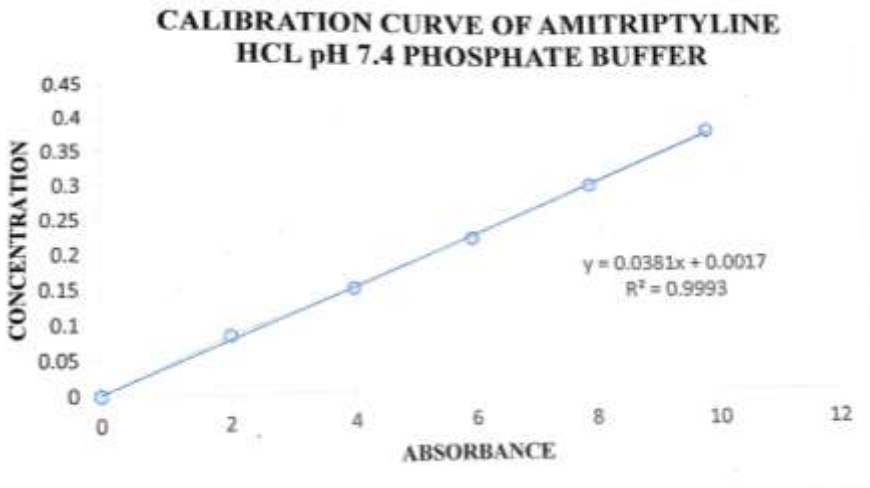

Fig No. 3: Standard graph of AMT HCl in pH 7.4 Phosphate buffer

FTIR Spectral Analysis:
IDENTIFICATION OF AMITRIPTYLINE BY FTIR SPECTROSCOPY:

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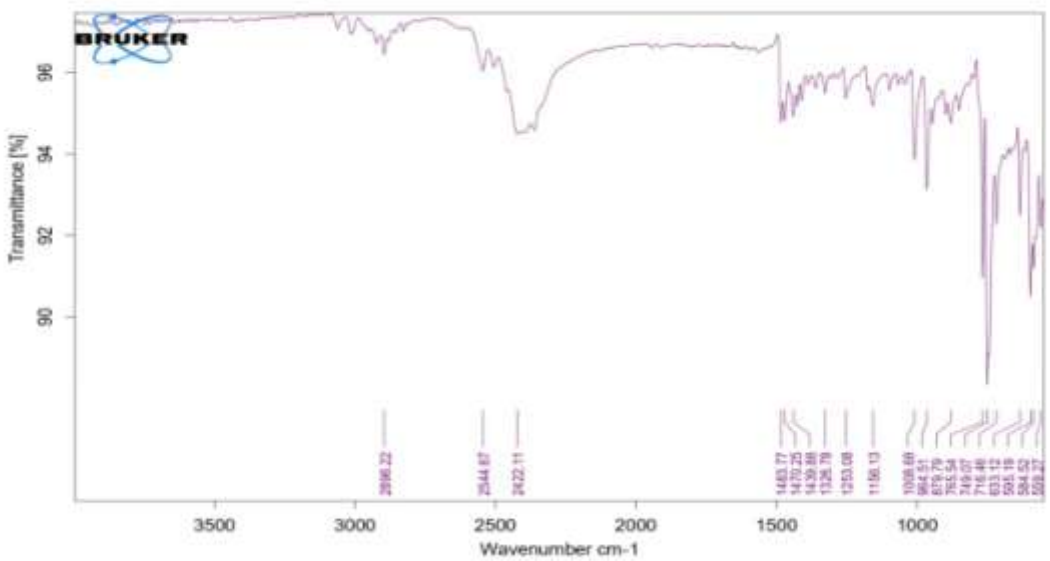

Fig. No. 4: FTIR spectrum of pure drug Amitriptyline

DRUG EXCIPIENT COMPATABILITY STUDIES

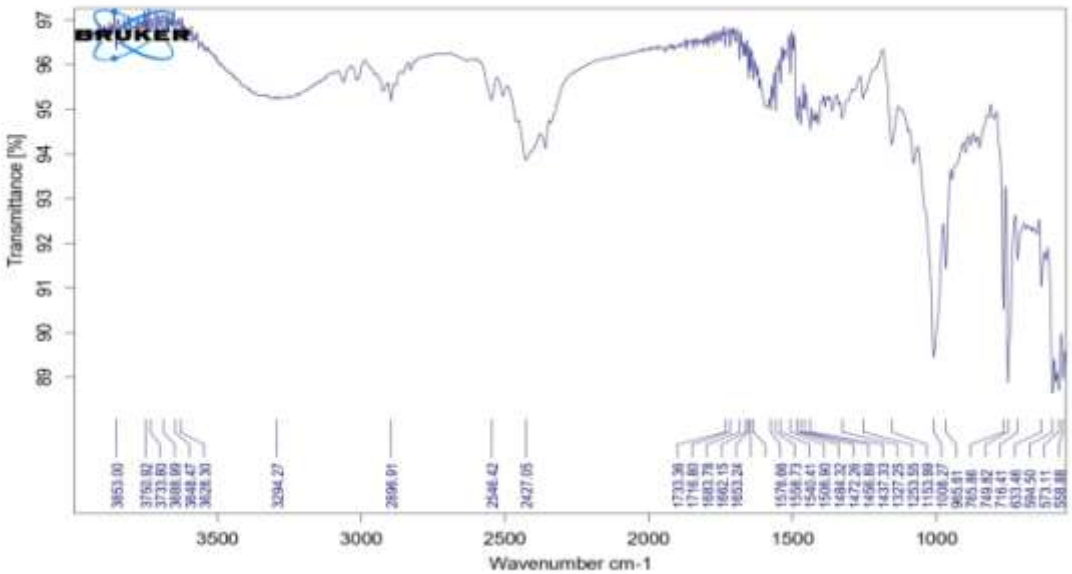

Fig. No. 5: FTIR SPECTRUM of pure drug Amitriptyline and Ethyl cellulose

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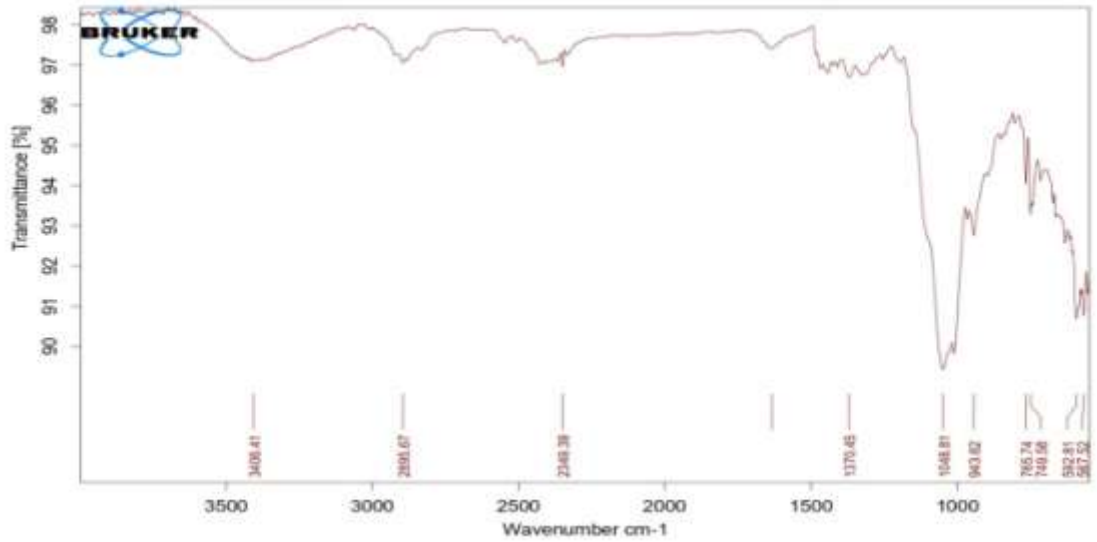

Fig. No. 6: FTIR spectrum of pure drug Amitriptyline and HPMC K-15

IV. CONCLUSION

Amitriptiline HCl transdermal patches are prepared from blends of HPMC, PVP and ethyl cellulose using propylene glycol as plasticizer. And it was thin, flexible, smooth. The patch shows satisfactory physicochemical properties. F1 shows better action when compared to F2 and F3.