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CHARACTERIZATION AND DRUG RELEASE OF HPMC & PVA ETHOSOMAL PATCH

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ABSTRACT

Characterization were performed for the optimizing the phospholipid and ethanol concentration, after the optimization of ethosome formulation, it was incorporated in the transdermal patch of PVA and HPMC. The present investigation attempted to prepare and evaluate the finasteride ethosomes for transdermal drug delivery. The ethosomal formulations were developed using different concentrations of ethanol (20-60%) and soya lecithin (1-5%). *In-vitro* release studies of formulation containing 30% ethanol and 3% soya lecithin showed highest % drug release (82.66%) with highest transdermal flux.The entrapment efficiency and drug content of optimized formulation were found to be 85.32% and 99.5% respectively.

From both the ethosomal patch it was found that PVA patch shows low moisture content, high weight variation, tensile strength and folding endurance and it also shows the maximum release of drug in 72 hr and treats the hypertension effectively in the rats. Consequently, current study assume that the prepared ethosomal patch safely assist the targeted delivery of drug losartan potassium and help in treating the hypertension. This type of work helps the industry to develop and scale up the novel formulation, further to bring this work in its clinical recognition more research work is still needed.

Key Word-: *HPMC, PVA, Ethanol, propylene glycol*

INTRODUCTION

Hypertension also known as high blood pressure, it is the condition in which arteries blood pressure was increased to more than 120 mmHg (Naish et al., 2014). Because of the increased blood pressure, the heart has to work harder i.e. to pump harder. The elevated blood pressure is directly related to the chances of cardiovascular morbidity and mortality. Hypertension gave rise to many other diseases like dementia, heart failure, kidney disease and vision loss (Hernandorena et al., 2017; Mendis et al., 2011;Lackland et al., 2015). Various reports and survey shows that approximately one fourth of world'spopulation suffered from hypertension in which 1 out of every 5 adults are unaware about their situation (Farley TA et al., 2010). About three-fourth hypersensitive people are belonging to 70 or more than 70 year age group (Burt et al.;

1995). The rapid growth of hypertension leads to death of many individuals. Epidemiological studies reveal that in India, 31.5 million hypersensitive people in rural and 34 million hypersensitive people were reported in urban area. Not only in India, since the last three decades many cases of hypertension have been reported from all over the world(Gu et al., 2002; Mbanya et al., 1998; Mohammadi et al., 2002; Unwin et al., 2001)which is been a major concern as it is a serious health problem. Expectancy of longer and healthy life prevail the treatment which reduces more than 50% heart failure and 20% chances of heart attack by lowering down the blood pressure. Because HTN is the major cause of arteries hardening, eye damage, kidney stone formation, stroke (Cubillos-Garzon et al., 2004) and physical inactivity (Cooper et al., 1976). For the treatment of hypertension, many drugs are employed which are angiotensin-receptor blocker (ARB) used either alone or along with other agents and angiotensin converting enzyme inhibitors. Eposartan, Irbesartan, valsartan and losartan are the class of ARBs. Angiotensin-converting enzyme (ACE) inhibitors have unfavourable effects like cold cough which wasn't shown by ARBs. Other than hypertension, this drug also used to cure systolic dysfunction, coronary artery disease, diabetic nephropathy and heart failure. On the oral administration of losartan potassium it shows wide first pass metabolism and short half- life due to which it entails a high dose frequency; this reason makes the transdermal drug delivery system an ideal candidate to deliver the drug in the skin.

Material and Method

Materials

Losartan Potassium was obtained as a gift sample Mepro Pharmaceutical Ltd Ahmedabad, India. Phospholipon 90-G was obtained as a gift sample from the Lipoid Germany, India. Ethanol, Tween80 and propylene glycol were purchased from Sigma Aldrich Chemie, USA, HPMC and PVA was obtained as a gift sample from Evonik industries, India. Methocell K 100M was obtained as a gift sample from Colorcon Goa, India. All other reagents and solvents were of Analytical grade. Distilled water was used throughout the study.

Characterization of ethosomal patch

Weight variation

Inconsistency in weight was determined by accurately weighing the three patches separately from each batch on digital balance and calculate the average weight (Mamatha et al., 2009)

Thickness

With the aid of micrometer the thickness of patch was measured from three different places and the average thickness was noted **(**Ramarao et al., 2000).

Folding endurance

Uniformly cut the strip of film which is 2x2 cm in size and fold it from the same place again and again until the film broke. Value of folding endurance was given by the number of times the folding of film done without breaking at the same place (Wade Hull, 2002; Barry, 2001).

Tensile strength

Tensile strength employed to determine the mechanical properties of polymeric patches (Samanta et al., 2003) and it was determined with the help of tensile instrument. Attach the transdermal patch to the assembly and attach the down weight needed to break the patch and calculate the average of three readings to calculate tensile strength. Calculation of the tensile strength of the patch was done by the given formula-

Tensile strength (kg/cm sq) = Force at break (kg) / Cross sectional area of the sample (cm sq)

Percentage moisture content

Cut the 2 x 2 cm strip from ethosomal patch and measure its weight. After weighing place the prepared film individually in the desiccator containing calcium chloride, for 24 hours at room temperature for determination of percentage moisture content. After incubation of 1 day, weigh the film again and again until a constant weight was achieved (Bhatia et al., 2012) and then calculate the percentage of moisture content with the help of given formula:

$$\% \text{ of Moisture content} = \frac{\text{Initial weight} - \text{final weight}}{\text{final weight}} \times 100$$

In-vitro drug release of ethosomal patch

In-vitro permeation study of HPMC and PVA patch loaded with ethosomal losartan potassium was accomplished by utilizing diffusion cell (Keshary et al., 1984). For this purpose, fabricated diffusion cell and cellulose acetate membrane were used. Cellulose acetate membrane which acts as a semi permeable membrane was allowed to soak in phosphate buffer overnight before conducting the experiment. Fix the membrane to the one end of hollow diffusion tube made up of glass. The diameter of diffusion tube is 2 cm and it forms the donor compartment of the diffusion cell in which ethosomal transdermal patch was placed. As an elution medium pour the 100 ml phosphate buffer of pH 7.4 in receptor compartment. Receptor and donor compartment of diffusion cell were place in such a manner that surface releasing drug should face towards receptor compartment. For the even distribution of the releasing drug place the assembly consists of elution medium on magnetic stirrer at 100 rpm speed with 37 oC temperature. 1ml sample was withdrawn from the compartment and is exchanged by same volume of phosphate buffer.Amount of drug diffuse was investigated by UV/Visible spectrophotometer by taking an absorbance at 242 nm. The % cumulative drug release was calculated from the drug concentration (Pisipati et al, 2013; Sarkara et al, 2014).

RESULTS AND DISCUSSION

Thickness and Weight variation

Thickness of the patch taken from the three point of the same patch was found to be 0.24 ±0.008 mm for PVA and 0.16±0.002 mm for HPMC. The results of thickness and weight variation were shown . The weight of the prepared patch was found to be 18.3±1.2 for PVA and 14.63± 0.8 for HPMC.

Folding endurance and tensile strength

The results of folding endurance and tensile strength were shown in **Table 16**. Folding endurance of the PVA was found to be 48.2±0.4 and 40.6±0.3 for HPMC.The transdermal ethosomal patch prepared with PVA polymer shows a high strength as compared with the HPMC patch because of high folding endurance of the PVA patch. With the help of tensile instrument, tensile strength was determined and it was found to be 30.2±0.8 for PVA patch and 26.4±0.2 for HPMC patch. With the help of tensile strength the mechanical property of the patch was studied and the high tensile strength shows that on any stress or pressure condition, the patch will not break. From the results it was observed that PVA patch shows high tensile strength and it will remain stable and maintain its integrity as compared with the HPMC patch.

Table 16: Characterization of ethosomal transdermal patch

S.NO.	Characterization	PVA	HPMC
1	Weight variation	18.3±1.2	14.63± 0.8
2	Thickness (mm)	0.24 ±0.008	0.16±0.002
3	Folding endurance	48.2±0.4	40.6±0.3
4	Tensile strength	30.2±0.8	26.4±0.2
5	% Moisture content	2.65±0.07	3.15±0.04

% Moisture content

The percent moisture content for the PVA patch was found to be 2.65±0.07 and 3.15±0.04 for HMPC patch as shown in **Table 16**. From the study, it was observed that PVA patch will remain stable for longer duration and also show brittleness as compared with HPMC patch because of the low moisture content of the PVA patch.

In-vitro drug release of ethosomal patch

With the help of Franz diffusion cell, the in-vitro release of drug from the ethosomal patch was studied. The drug release study was performed for both the patches for 72 hr and it was found that the PVA patch shows the release of 91.56±2.03% and HPMC patch show 80.45±1.49% drug release. The result of the study was shown in **Figure 34**. The PVA patch provide maximum release of drug as it resist the crystallization of drug which causes easy perforation of drug inside the patch hence it shows better permeation activity when compared to HPMC patch.

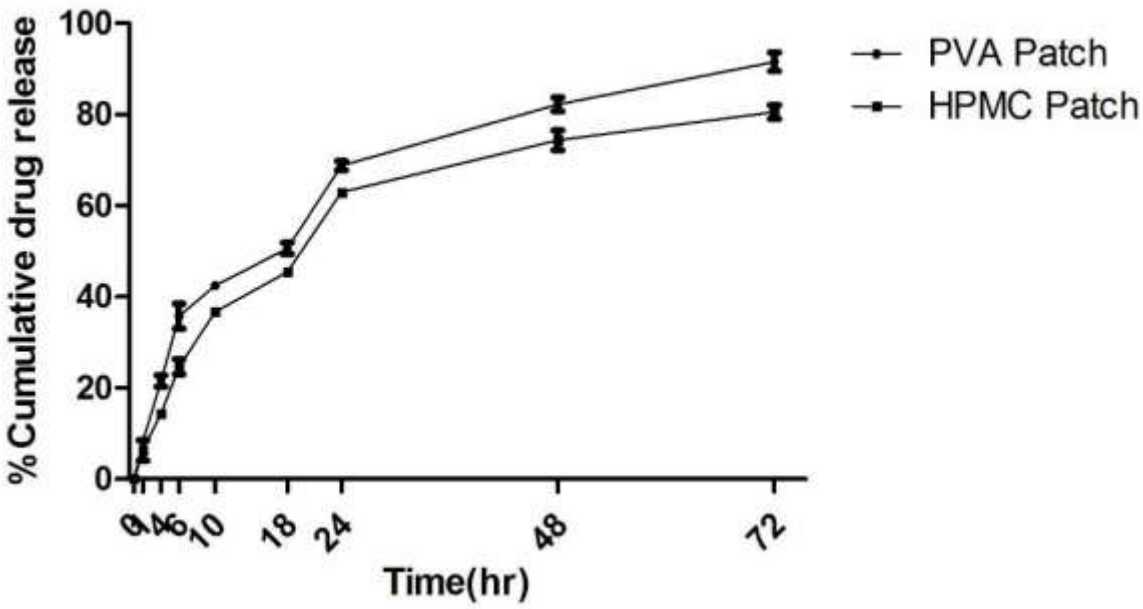

Figure 34: In-vitro drug release of PVA patch and HPMC patch ethosomal patch

CONCLUSSION

The present investigation attempted to prepare and evaluate the finasteride ethosomes for transdermal drug delivery. The ethosomal formulations were developed using different concentrations of ethanol (20-60%) and soya lecithin (1-5%). *In-vitro* release studies of formulation containing 30% ethanol and 3% soya lecithin showed highest % drug release (82.66%) with highest transdermal flux. Characterization were performed for the optimizing the phospholipid and ethanol concentration, after the optimization of ethosome formulation, it was incorporated in the transdermal patch of PVA and HPMC. The entrapment efficiency and drug content of optimized formulation were found to be 85.32% and 99.5% respectively.

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