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FORMULATION & EVALUATION OF TRANSDERMAL PATCH OF ACETOHEXAMIDE

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ABSTRACT

The aim of the present investigation was to prepare acetohexamide transdermal patches by solvent casting technique using the HPMC and PVP. The systems were evaluated for various *in- vitro* parameters (Thickness, Folding endurance, Moisture content, Moisture uptake, Flatness, Water vapor transmission rate etc). *In- vitro* permeation studies were performed by using Franz diffusion cells. Variations in drug permeation profile were observed among various formulations. From all the formulations, formulation P3 was selected as the best formulation and formulation was stable for period of 90 days stability study.

KEYWORDS: Transdermal drug delivery, Matrix patch, Membrane controlled Patch, acetohexamide, HPMC, PVP, *In vitro* skin permeation studies.

INTRODUCTION

A transdermal patch is a medicated adhesive patch that is placed on the skin to deliver a specific dose of medication through the skin and into the bloodstream. Often, this promotes healing to an injured area of the body. An advantage of a transdermal drug delivery route over other types of medication delivery such as oral, topical, intravenous, intramuscular, etc. is that the patch provides a controlled release of the medication into the patient, usually through either a porous membrane covering a reservoir of medication or through body heat melting thin layers of medication embedded in the adhesive. The main disadvantage to transdermal delivery systems stems from the fact that the skin is a very effective barrier; as a result, only medications whose molecules are small enough to penetrate the skin can be delivered by this method. A wide variety of pharmaceuticals are now available in transdermal patch form. The first commercially available prescription patch was approved by the U.S. Food and Drug Administration in December 1979. These patches administered scopolamine for motion sickness.[1,2]

One way to study these patches is through the use of Franz Diffusion Cell systems. This system is used to study the effects of temperature on the permeated amount of a specific drug on a certain type of membrane, which in this case would be the membrane that is used in the patches. A Franz Diffusion Cell system is composed of a receptor and a donor cell. In many of these research studies the following procedure is used. The donor cell is set at a specific temperature (the temperature of the environment), while the receptor cell is set at different one (temperature of the body). Different runs are performed using different temperatures to study the impact of temperature on the release of a certain medicament through a certain type of membrane. Although different concentrations of the medicament are used in this study, they do not affect the amount permeated through the membrane (the process is constant). From Chemical kinetics it is concluded that these studies are zero order, since the concentration plays no role in the permeated amount through the membrane.

Some pharmaceuticals must be combined with substances, such as alcohol, within the patch to increase their ability to penetrate the skin in order to be used in a transdermal patch. Others can overwhelm the body if applied in only one place and are often cut into sections and applied to different parts of the body to avoid this, such as nitroglycerin. Many molecules, however, such as insulin, are too large to pass through the skin without it being modified in some way. Several new technologies are being investigated to allow larger molecules to be delivered transdermally.[3]

MATERIALS AND METHOD

Materials:- Acetohexamide, HPMC, PVA, PEG, octanol, potassium chloride, calcium chloride, phosphate buffer, hexane.

Methods

Preparation of patch

The solvent-casting technique was used to formulate the acetohexamide patches containing different concentrations of HPMC keeping PVA constant &

polyethylene glycol (PEG 400) was used as a as plasticizer. The drug polymer solution was transferred into a glass petridish. The petridish was then kept in an air circulation drier and maintained at a temperature of 45-50^{o}C for 6 hours. A backing film (aluminium foil) was applied to TDDS.[4]

Solubility Measurement

The solubility of acetohexamide was determined by taking excess amount of drug and dissolving in a measured volume of distilled water in a glass vial to get a saturated solution. The solution was kept at room temperature for the attainment of equilibrium. The concentration of acetohexamide in the filtrate was determined spectrophotometrically by measuring at 250 nm after 24 hours.[5]

Physical appearance

All the transdermal patches were visually inspected for color, clarity, flexibility, and smoothness.[6,7]

Percentage moisture uptake

The weighed films were kept in a desiccator at room temperature for 24 hours and then exposed to 84% relative humidity using a saturated solution of potassium chloride. Finally, the films were weighed and the percent moisture uptake was calculated using the formula.[8]

Percentage moisture uptake = [Final weight -Initial weight/Initial weight] × 100

Percentage moisture content

The prepared films were weighed individually and kept in a desiccator containing fused calcium chloride at room temperature for 24 hours. The films were again weighed and the percentage moisture content was calculated using the formula:

Percentage moisture content = [Initial weight -Final weight/Final weight] × 100

Water vapor transmission

The film was fixed over the glass vial with an adhesive containing 3 g of fused calcium chloride as a desiccant. Then, the vial was placed in a desiccator containing saturated solution of potassium chloride (relative humidity 84%). The vial was taken out periodically and weighed.

Drug content

Transdermal system of specified area (2.9865 cm^2) was cut into small pieces and taken into a 50 ml volumetric flask and 25 ml of phosphate buffer pH 7.4 was added, gently heated to 45^{o}C for 15 minutes, and kept for 24 hours with occasional shaking. Then, the volume was made up to 50 ml with phosphate buffer of pH 7.4. Similarly, a blank was carried out using a drug-free patch. The solutions were filtered and the absorbance was measured at 250 nm.

***In vitro* drug release studies**

A Paddle over disc assembly (USP 23, Apparatus 2) was used for the assessment of release of drug. The TDDS patch was mounted on the disc and placed at the bottom of the dissolution vessel. The dissolution medium was 900 ml phosphate buffer of pH 7.4. The apparatus was equilibrated to 37 ± 0.5^{o}C and operated at 50 rpm. The samples (5 ml aliquots) were withdrawn at appropriate time intervals up to 8 hours and analyzed on a UV spectrophotometer at 250 nm.[9,10,11]

***In- vitro* skin permeation studies**

Fresh full-thickness (75-80 mm) goat skin was used for the study. The skin was immersed in water at 60^{o}C for a period of 5 minutes. The epidermis was peeled from the dermis. The isolated epidermis (25 ± 5 mm thick) was rapidly rinsed with hexane to remove surface lipids and then rinsed with water and used immediately. The i*n-vitro* skin permeation from the prepared polymeric patches across the goat skin barrier was studied using diffusion cell. Fifty-four milliliters of phosphate buffer of pH 7.4 was used as an elution medium. The patches to be studied were placed in between the donor and the receptor compartment in such a way that the drug releasing surface faced toward the receptor compartment. The elution medium was magnetically stirred for uniform drug distribution at a speed of 60 rpm. The temperature of the whole assembly was maintained at 37 ± 1^{o}C by thermostatic arrangements. An aliquot of 1 ml was withdrawn at a suitable interval and an equivalent volume of fresh buffer was replaced. The amount of drug permeated across the skin was determined on a UV spectrophotometer at 250 nm. The cumulative amount of drug permeated per cm^2 of skin values are tabulated in [Table1][12,13,14]

RESULT AND DISCUSSION

Table 1. Parameter evaluation

S.No	Parameter	P1	P2	P3	P4	P5	P6	P7	P8
		Ratio of HPMC							
		2%	3%	4%	5%	6%	7%	8%	9%
1.	Folding endurance	12.25±0.02	13.26±0.03	14.23±0.045	12.88±0.044	11.25±0.02	15.22±0.06	13.02±0.04	13.66±0.02
2.	Thickness of the films(mm)	0.022±0.03	0.023±0.04	0.0019±0.08	0.021±0.07	0.020±0.04	0.036±0.06	0.032±0.07	0.024±0.06
3.	Weight uniformity(g)	0.32±0.07	0.36±0.08	0.46±0.04	0.35±0.06	0.30±0.05	0.39±0.08	0.44±0.07	0.45±0.06
4.	Percentage moisture uptake	0.78±0.06	0.88±0.05	0.33±0.07	0.59±0.08	0.45±0.07	0.66±0.04	0.84±0.012	0.78±0.036
5.	Percentage moisture content	0.65±0.055	0.54±0.058	0.35±0.026	0.68±0.057	0.45±0.065	0.66±0.045	0.55±0.042	0.58±0.031
6.	Water vapor transmission(g/cm)	0.022±0.036	0.033±0.021	0.026±0.026	0.031±0.024	0.021±0.029	0.024±0.065	0.032±0.045	0.028±0.054
7.	Percentage Drug content	2.51±0.069	2.54±0.065	2.85±0.045	2.44±0.058	2.57±0.069	2.58±0.015	2.65±0.045	2.66±0.069
8.	*In-vitro Cumulative Percentage* drug release	75	96	35	55	88	90	91	93

All values are expressed as Mean±SD.

CONCLUSION

The acetohexamide patch was prepared using varying concentration of HPMC polymer and was evaluated using different parameters and amongst all eight patches P3 patch was found to be the best.

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