



FORMULATION & EVALUATION OF TRANSDERMAL PATCH OF TOLBUTAMIDE

Ganju Eisha*¹ and Ganju Kuldeep²

¹School of Pharmacy & Research, People's University, Bhopal, 462037.

²Sagar Institute of Pharmacy & Technology, SIPTec (SISTec), Bhopal, 462036.

Abstract: The aim of the present investigation was to prepare tolbutamide transdermal patches by solvent casting technique using the HPMC and PVP polymer in different ratios. The systems were evaluated for various *in-vitro* parameters like (Thickness, Folding endurance, Moisture content, Moisture uptake, etc). *In-vitro* permeation studies were performed by using Franz diffusion cell. Variations in drug permeation profile were observed among various formulations. From all the formulations, formulation P4 was selected as the best formulation and formulation was stable for period of 90 days stability study.

Keywords: Transdermal drug delivery, Matrix patch preparation, Membrane controlled Patch, tolbutamide, HPMC, PVP, *In-vitro* skin permeation studies.

Introduction: A transdermal patch is a medicated type of adhesive patch that is placed on the skin to deliver a specific dose of medication through the skin into the bloodstream. This promotes healing to an injured area of the body. An advantage of a transdermal drug delivery route over other types of medication delivery 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

For Correspondence:

eishaganju26@gmail.com.

Received on: January 2017

Accepted after revision: February 2017

Downloaded from: www.johronline.com

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 generally composed of a receptor cell 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). The impact of temperature on the release of a certain medicament through a certain type of membrane is studied and 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 follow zero order, since they are independent of concentration. 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, such as insulin, are too large to pass through the skin. Several new technologies are being developed to allow larger molecules to be delivered transdermally.^[3]

Tolbutamide is a first-generation potassium channel blocker and sulfonylurea oral hypoglycemic drug. This drug may be used in the management of type 2 diabetes if diet alone is not effective. Tolbutamide stimulates the secretion of insulin by the pancreas. Since the pancreas must synthesize insulin for this drug to work, it is not effective in the management of type 1 diabetes.

Materials and Method

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

Methods Preparation of patch: The solvent-casting technique was used to formulate the tolbutamide patches containing different

concentrations of HPMC keeping PVA constant & polyethylene glycol (PEG 400) was used as a 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°C for 6 hours. A backing film (aluminium foil) was applied to TDDS.^[4]

Solubility Measurement: The solubility of tolbutamide 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 to attain equilibrium. The concentration of tolbutamide in the filtrate was determined spectrophotometrically by measuring at 250 nm after 24 hours.^[5]

Physical appearance: 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 they were exposed to 84% relative humidity using a saturated solution of potassium chloride. Then 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 Transdermal film was fixed over a glass vial with an adhesive containing 3 g of fused calcium chloride used as a desiccant. Then, the vial was placed in a desiccator which had saturated solution of potassium chloride (relative humidity 84%). The vial was taken out

periodically and weighed again and again.

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°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 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 $37 \pm 0.5^\circ\text{C}$ and operated at 50 rpm. The samples of 5 ml aliquots were withdrawn at an appropriate time intervals up to 8 hours and analyzed then they were inspected 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

Result And Discussion:

the study. The skin was immersed in water at 60°C for a period of 5 minutes. The epidermis was peeled from the dermis. The isolated epidermis was instantly and quickly rinsed with hexane to remove surface lipids and then they were rinsed with water and used immediately. The *in-vitro* skin permeation from the prepared polymeric patches across the goat skin barrier were 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 stirred magnetically for uniform drug distribution. The temperature of the whole assembly was maintained at $37 \pm 1^\circ\text{C}$ by some 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 Table 1.^(12,13,14)

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	13.25±0.02	14.26±0.03	13.88±0.044	13.23±0.035	12.25±0.02	15.22±0.06	12.02±0.04	12.66±0.02
2.	Thickness of the films(mm)	0.025±0.03	0.063±0.04	0.011±0.07	0.0017±0.07	0.030±0.04	0.026±0.06	0.032±0.07	0.034±0.06
3.	Weight uniformity(g)	0.22±0.07	0.26±0.08	0.25±0.06	0.36±0.03	0.40±0.05	0.59±0.08	0.54±0.07	0.35±0.06
4.	Percentage moisture uptake	0.68±0.06	0.48±0.05	0.49±0.08	0.32±0.06	0.35±0.07	0.56±0.04	0.72±0.012	0.68±0.036
5.	Percentage moisture content	0.55±0.055	0.44±0.058	0.64±0.057	0.45±0.036	0.55±0.065	0.46±0.045	0.45±0.042	0.68±0.031
6.	Water vapor transmission(g/cm)	0.022±0.031	0.023±0.021	0.021±0.024	0.036±0.026	0.011±0.029	0.014±0.065	0.042±0.045	0.018±0.054
7.	Percentage Drug content	2.51±0.069	2.64±0.065	2.34±0.058	2.65±0.035	2.67±0.069	2.38±0.015	2.45±0.045	2.46±0.069
8.	<i>In-vitro</i> Cumulative Percentage drug release	71	88	58	34	77	88	86	74

All values are expressed as Mean±SD.

Conclusion: The tolbutamide patch was prepared using varying concentration of HPMC polymer and was evaluated using different parameters and amongst all eight patches P4 patch was found to be the best.

References

1. Segal, Marian. "Patches, Pumps and Timed Release: New Ways to Deliver Drugs". Food and Drug Administration. Archived from the original on 2007-02-10. Retrieved 2007-02-24.
2. "FDA approves scopolamine patch to prevent peri-operative nausea". Food and Drug Administration. 1997-11-10.
3. Prausnitz M, Langer R. Trans dermal drug delivery. Nature Biotechnology. Volume 26, Number 11, Pages 1261-1268, November 2008.
4. Shaila L, Pandey S and Udupa N. Design and evaluation of matrix type and membrane controlled transdermal delivery systems of nicotine suitable for use in smoking cessation. Indian J Pharm Sci., 2006; 68: 179-84.
5. Krishnaiah YS, Satyanarayana V and Bhaskar P. Influence of limonene on the bioavailability of nicardipine hydrochlorothiazide from membrane modulated transdermal therapeutic systems in human volunteers. Int J Pharm Krishnaiah, 2002; 247: 91-102.
6. Barry BW. Novel mechanism and devices to enable successful transdermal drug delivery. Eur J Pharm Sci., 2001; 14: 101-14.
7. Wade Hull MS. Heat-enhanced transdermal drug delivery: A survey paper. J Appl Res., 2002; 2: 1-9.
8. Chein YW. Transdermal drug delivery systems and delivery systems. 2nd. Marcel Dekker, Inc, 1992; 301.
9. Libermann and Lachman. Pharmaceutical dosage forms. 2nd ed. Lea and Febiger, 1990; 265.
10. Mohamed A, Yasmin S and Asgar A. Matrix type transdermal drug delivery systems of metoprolol tartarate: In vitro characterization. Acta Pharm., 2003; 53: 119-25.
11. Shukla AJ and Lee JC. Handbook of pharmaceutical excipients. 2nd ed. In: Wade A, Wellers PJ, editors. American Pharmaceutical Association and Royal Pharmaceutical society of Great Britain, 1994; 362-6.
12. Shah HS, Tojo K and Chien YW. Transdermal controlled delivery of verapamil: Characterization of in vitroskin permeation. Int J Pharm., 1992; 86: 167-73.
13. Squillante E, Needham T and Zia H. Solubility and in vitrotransdermal permeation of nifedipine. Int J Pharm., 1997; 159: 171-80.
14. Ghosh TK, Adir J, Xiang S and Onyilofur S. Transdermal delivery of Metoprolol II: In vitroskin permeation and bioavailability in hairless rats. J Pharm Sci., 1995; 84: 158-60.