



## FORMULATION DESIGN AND *IN VITRO* EVALUATION OF METFORMIN HYDROCHLORIDE TRANSDERMAL FILM USING HYDROPHILIC POLYMER

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The purpose of the experimental study was to design a sustained release film formulation of metformin hydrochloride. In this study a transdermal film has been prepared by incorporating hydrophilic polymers like HPMC and PVA in combination of different ratios. The prepared film were subjected for different evaluation parameters like swelling index study, surface pH, drug content analysis, thickness of film, folding endurance study, drug release study. Results of evaluation of all the film was found satisfactory. Again further study needs to be conducted to stabilize the formulations.

**Key words:** Transdermal film, Metformine hydrochloride, *in vitro* evaluation

### INTRODUCTION

Among the several lifestyle diseases, Non insulin dependent diabetes mellitus is very common. It may also leads other health related problems like high BP, lipid disorder, cardiac disease, nephritis, Retinopathy, muscle weakness & obesity<sup>1</sup>. It's a chronic metabolic disorder characterized by a high blood glucose concentration (hyperglycemia) caused due to deficiency insulin.<sup>2</sup> As per WHO around 347 million people worldwide having diabetes. In 2004, an estimated 3.4 million people died from consequences of fasting high blood sugar. A similar number of deaths have been estimated for 2010.<sup>3</sup> WHO projects that diabetes will be the 7th leading cause of death in 2030.<sup>4</sup>

Metformin is the only antidiabetic drug that has been conclusively shown to prevent the cardiovascular complications of diabetes. It helps to reduce LDL cholesterol and triglyceride levels, and is not associated with weight gain<sup>5</sup>. As of 2010, metformin is one of only two oral antidiabetics in the World Health Organization Model List of Essential Medicines<sup>7</sup>. Despite of the rationality in use, metformin reported to have several adverse effects like gastrointestinal upset, lactic acidosis, vomiting abdominal pain, anorexia, nausea, metallic taste and mild diarrhoea etc when administered orally<sup>6</sup>.

In the year 1979 Food and Drug Administration

approved the first transdermal drug delivery system. Transdermal Drug Delivery System is one which delivers the active ingredients by the means of skin. It's a most popular novel approach and consider as successful alternative to systemic drug delivery. Transdermal delivery systems have proved advantageous for delivery of selected drugs, such as estrogens, testosterone, clonidine, nitroglycerin, scopolamine, fentanyl, and nicotine. Compared with oral dosage forms, these systems offer not only improved patient compliance, but also superior uniformity of drug concentrations in plasma throughout their duration of use. Most transdermal patches are designed to release the active ingredient at a zero-order rate for a period of several hours to days following application to the skin. This kind of delivery systems especially advantageous for prophylactic treatment or maintenance therapy in chronic conditions where the patient is otherwise required to carry oral medications and remember to take them several times a day.

In consideration of above fact current study has been designed to develop transdermal film of the metformin hydrochloride. The film was fabricated using different combination of polymers namely HPMC and PVA.

### MATERIAL AND METHODS

Hydroxyl propyl methyl cellulose (HPMC), polyvinyl alcohol and glycerin were procured from S.D. Fine chem. Ltd. Mumbai. Metformin hydrochloride was received as generous gift sample from Sun

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Pharmaceuticals Ltd., Baroda, Gujarat. All other chemicals and solvents used were of analytical grade.

### PREPARATION OF TRANSDERMAL FILM

The transdermal film of metformin hydrochloride was prepared using different concentration of polymers like HPMC and PVA. The calculated amount of polymer was shocked in 20 ml of distilled water for 24 hours. Then drug (metformin hydrochloride 500 mg) was added in the polymeric solution with continues stirring. Desire quantity of glycerin was added in homogenized drug polymer solution and kept aside for some time at room temperature. The prepared formulation was then transferred into Petridis and kept for drying in room temperature and followed by dryer at around 45°C temperature. The dried film was then cut into desire pieces, wrapped in aluminum foil and was kept in desiccators until further use<sup>9</sup>. The formula of the prepared films is mention in table no. I

### EVALUATION OF TRANSDERMAL FILMS

#### Weight Uniformity

The prepared films are dried for 4 hours at 60°C before performing the test. A specific part of a definite dimension is cut from various parts of the patch and weighed on a digital balance. The average weight and standard deviation values are then calculated.

#### Thickness of the films

The thickness of the drug loaded film is determined at different points by using a digital micrometer.

#### Folding Endurance

Folding endurance of the 2x2cm films was determined by repeatedly folding one film at the same place till it broke or folded upto 300 times manually, which was considered satisfactory to reveal good film properties. The number of times of film could be folded at the same place without breaking gave the value of the folding endurance. This test was done on three individual films of each formulation batches.<sup>13</sup>

#### Surface pH of Film

For determination of surface pH three films of each formulation were selected randomly and are allowed to swell for 2 hours on the surface of previously prepared 1% agar plate. The surface pH was measured by using a pH paper placed on the surface of swollen film.<sup>14</sup>

#### Swelling Index

Films were weighed individually (designated as W1) and placed separately in 1% agar gel plates, incubated at 37°C ± 1°C, and examined for any physical changes. At regular 1hour time intervals until 3 hours, films were removed from the gel plates and excess surface water was removed carefully using the filter paper. The swollen patches were then reweighed (W2), and the swelling index (SI) was calculated using the following formula.<sup>10</sup>

$$SI = \frac{W2 - W1}{W1} \times 100$$

#### Content Uniformity

Drug content uniformity was determined by dissolving each 2x2cm films of different batches in 100mL distilled water. The whole content was then shake continuously 5 hours with the help of rotary shaker and then kept aside for 24 hours. Then the solution was filter with Whatman filter paper (0.45 µm). Form the filtrate 5ml solution was taken and suitably diluted with distilled water and analyzed using UV spectrophotometer.<sup>12</sup>

#### In vitro Drug Release Study

The *in vitro* release study was performed using Franz diffusion cell. A piece of film having definite size was used for this study. The dissolution media consist of 500ml of distilled water. The release study was performed in 500ml distilled water as dissolution medium and a rotation speed of 50 rpm and temperature of 37°C ± 1°C was maintained throughout the experiment. The study was carried out for 8 hours. After every 1hr interval 5ml of sample was withdrawn from receptor compartment and the same was replaced back

to donor compartment. Each withdrawn sample was filtered, diluted suitably and then analyzed spectrophotometrically<sup>11</sup>.

**Table No. I Formula of Different Formulation Batches**

S. No.	Ingredients	Formulation batch			
		F1	F2	F3	F4
1.	Metformin hydrochloride(g)	0.5	0.5	0.5	0.5
2.	HPMC (g)	2	1.66	1.33	2.4
3.	PVA (g)	2	1.33	1.66	1.6
4.	Glycerin(ml)	0.3	0.3	0.3	0.3
5.	Distill water(ml)	100	100	100	100

**Table No. II Different Physical Parameter of All the Prepared Films**

S. No	Batch code	Weight variation (mg)	Folding endurance	Swelling index (%)	Thickness (mm)	Surface Ph	Drug content
1.	F1	230	>300	350	0.62±0.03	6.5	48.02
2.	F2	260	>300	80	0.85±0.02	7	25.48
3.	F3	320	>300	200	0.73±0.04	7	35.77
4.	F4	210	>300	60	0.81±0.03	6	40.18

## RESULTS AND DISCUSSION

The main goal of this experimental work was to find out the in-vitro efficiency of the prepared dosage form to deliver metformin effectively. Four set (F1-F4) of transdermal film were prepared and evaluated accordingly. Formulas of prepared formulation are presented in Table I. And the Physical characteristics of all the prepared films are represented in Table II. The prepared films were of around 0.75 mm in thickness. The weight of films was found within the range from 210 to 320 mg. Folding endurance capacity of all the formulations were found > 300 that can be consider as a sign of good flexibility. The swelling behavior study was performed to determine the percentage of swelling and found within the satisfactory range. Based on the results of release study, as shown in (Fig-1) it can be state that, all the formulation showing first order followed by zero- order release profile. More than 80%

of drug gets release after 8 hrs time interval. It has been found that drug release from all the formulations were uniform and prolong, follows sustained release pattern.

## CONCLUSION

All the prepared formulations show satisfactory results in terms of the evaluated parameters. The outcomes of the current experiments advocate a rational guideline for formulating a sustained release transdermal therapeutic system of metformin hydrochloride for effective therapy. Further this experimental work shall be carried out for the estimation of several other important parameters before commercialization of product.

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