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Formulation and Evaluation of Transdermal Patch of Metformin Hydrochloride

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Abstract:- The main objective of the this study was to formulate, develop and evaluate a Transdermal drug delivery system containing Metformin hydrochloride to overcome the critical problems related with oral route. Transdermal patch of Metformin hydrochloride were prepared using solvent evaporation technique. Different trial of formulation were carried out by changing the polymer ratio. Transdermal Patch formulations were characterized for Thickness, weight variation, Percentage Moisture content, Folding endurance, Assay and In vitro drug release studies. I*n-vitro* drug release study and evaluation were carried out for formulation No. F1-F7. Separately Drug and physical mixture were characterized by using FTIR, the result showed that between drug and polymers compatability.

Keywords:- *Transdemal Delivery, Metformin Hydrochloride, Topical Drug Delivery.*

I. INTRODUCTION

Transdermal drug delivery system is a self-contained delivery use for topical application in the form of multi-laminated adhesive patch which gives a specific dose of drug at a predetermined rate and controlled the rate of drug release through skin[1]. This delivery provides the constant drug release but it also allows the short biological half life drug continuously and eliminates the pulsed entry into the blood circulation[2]. Transdermal drug delivery system provides more benefits than conventional system, such as sustained release delivery reduces the dosing frequency of the drug, it avoid the first pass metabolism, reduces side effect and improve the patient compliance.[3] The Transdermal drug delivery system designed by various methods such as transdermal patches includes matrix, micro reservoir, reservoir, adhesive, and membrane matrix hybrid. Matrix type transdermal patches are most popular as they are easy to costruct. The metformin hydrochloride transdermal patch in this paper also developed by using the Matrix type of transdermal drug delivery system. Metformin hydrochloride is the anti-diabetic agent having the low molecular weight water soluble drug. The daily dosage of transdermal delivered metformin in between 5 and 500 mg per day. Thus, the dose of metformin may be in the range from about 5-10 mg, or 10, 20, 30, 40, 50, 60, 70, 80, 90, 100,200, 300, 400 and 500 mg and increments there between.[4] Ethyl cellulose (EC) is nontoxic, non-allergic,and nonirritating material and has good film forming properties that form tougher films.

II. MATERIALS AND METHODS

A. Material

Metformin Hydrochloride was gifted from Medreich Limited, Karnataka (India), Ethyl cellulose received from the Research Lab, Hydroxy Propyl Methyl Cellulose received from Analab fine chemicals and ethanol and PEG 400 from Loba chemicals.

➢ *Physical Interaction Study:*

Pre-formulation study of drug and polymer carried out for determination of the comparability. The proportion of drug and excipient were kept in accelerated condition shown in Table 1. and evaluate physically.

Sr. No	Material	Drug polymer Ratio	40 °C/75%RH
1	Metformin Hydrochloride	1 :0	3 weeks
2	Metformin Hcl + HPMC	1:1	3 weeks
3	Metformin Hcl + Ethyl cellulose	1:1	3 weeks
4	Metformin Hcl + Ethyl cellulose+ HPMC	1:1:1	3 weeks

Table 1:- Drug polymer composition for interaction study

➢ *FTIR Interaction Study*

The drug and polymer are found to be compatible with one to produce a product that is stable formulation. The drug and excipients interaction produce effect on bioavailability and stability of the drug formulation. For new excipient which is not previously used in formulations, the compatibility is an important role in such formulation development. This study are taken out by Fourier transform infrared spectroscopy (FTIR). Drug and excipients interaction studies were carried out using FTIR. IR spectrum of drug, Ethyl cellulose, HPMC and the physical mixture of drug: Ethyl cellulose: HPMC in 1:1:1 ratios were characterized in between 400 to 4000 cm^{-1}.

➢ *XRD of Metformin hydrochloride*

X-ray diffraction scanning of Metformin hydrochloride were carried out for determination of the peak intensity of drug.

B. Methods

➢ *Calibration curve of Metformin Hydrochloride:*

Weight accurately 10 mg of the drug and dissolved into the phosphate buffer of pH 6.8 and make up the volume 100ml to form 100 microgram concentration of the solution and make a dilution 2, 4,6,8,10,12 micrograms per ml and carry out U.V. spectrophotometry

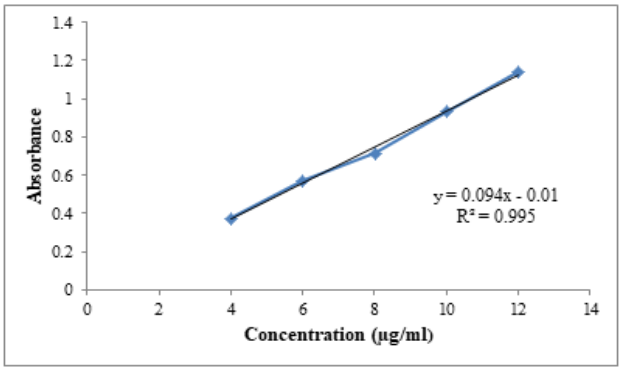

Fig 1:- Calibration curve of the Metformin hydrochloride

➢ *Preparation of Transdermal patch*

Transdermal patch of Metformin Hydrochloride was by using solvent casting method. Different polymers such as Methyl cellulose, ethyl cellulose, Hydroxy Propyl Methyl Cellulose are mainly used in the formulation of the patch. Different polymer with different ratio was used for the preparation of the patch. The required quantity of the drug and excipient were dissolve into the suitable solvent under stirring. To remove the entrapped air bubbles for 5 minutes sonication was carry out then the resultant clear solution transferred into the petri plate. Before transferring the solution in to the petri plate small quantity of glycerin were apply at the surface of plate which helps to easily remove the patch from the plate. The transdermal films were completely dried, and wrapped in aluminum foil and kept in desiccators.[5]

Formulation No.	DRUG (mg)	Ethyl cellulose :HPMC Ratio	PEG 400
1	20	1:3	1 ml
2	20	1:5	1ml
3	20	1:7	1 ml
4	20	1:9	1 ml
5	20	3:1	1 ml
6	20	5:1	1 ml
7	20	7:1	1 ml

Table 2:- Formulation chart of transdermal patch

➢ *Evaluation of Transdermal Patch:*

- *Thickness*

The thickness uniformity of the transdermal patch was recorded at three different places using vernier caliper and the average thickness was determined.[6]

- *Weight uniformity*

The manufactured patches are to be dried at 60°C for 4 h. and weighed in digital balance. The average weight and standard deviation values are calculated from the individual weights.[7]

- *Percentage Moisture content*

The specific area of the patch were and take its initial weight and keep patch in desiccator and take its weight after 24 hrs till constant weight will not found and calculate the moisture content using the following formula.[8]

$$\% \text{ Moisture content} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} X\ 100$$

➢ *Folding endurance:*

Folding endurance were measured by repeatedly film folding at the same place till it break. The small piece of transdermal film (2cm x 2cm) was cut and repeatedly folds it at the same place till it breaks. The number of fold at which film brakes or visible any crack on that folded film considered as a folding endurance.[9]

➢ *Drug Content:*

A measured area of transdermal patch was dissolved in a suitable solvent (phosphate buffer 7.2) in specific volume. Then filtered solution and Carry out the U.V. spectrophotometry and calculate the drug contain in that patch.[2,7,10]

$$\% \text{ Drug content} = \frac{\text{Actual weight of drug}}{\text{Therotical weight of drug}} \times 100$$

➢ *In vitro drug Release:*

In vitro drug release of prepared metformin hydrochloride patch was carried out with the dialysis membrane by using Franz diffusion cell. Which contains two parts, the top part called as the donor and the bottom part receptor compartment. During Over all experiment temperature was maintained at 37 ± 0.5°C and through receptor compartment sample was withdrawn after time interval points was provided with sampling port. phosphate buffer (pH 6.8) used as a diffusion medium. The diffusion was carried out for 12 hours and 3 ml sample was withdrawn at an interval of 1, 2, 3, 4, 5, 6, 7, 8,9, 10,11 and 12 hour. The same volume of phosphate buffer pH 6.8 was added to receptor compartment to maintain sink conditions and the samples were analyzed at 232 nm in UV spectrophotometer.

III. RESULT AND DISCUSSION

A. Physical Interaction Study:

Visual interaction study were carried out there is no any visual difference observed. All polymer shows physical compatibility with drug.

Sr. No	Material	Initial observation	observation after 3 Weeks
1	Metformin Hydrochloride	White powder	White powder
2	Metformin Hcl + HPMC	White powder	White powder
3	Metformin Hcl + Ethyl cellulose	White powder	White powder
4	Metformin Hcl + Ethyl cellulose+ HPMC	White powder	White powder

Table 3:- observation of Physical interaction study

B. FTIR Interaction Study

Metformin hydrochloride powder is a white, crystalline in nature, it is insoluble in chloroform and freely soluble in water, methanol. FTIR characteristic peaks of pure drug are also observed in the spectra of physical mixture showing no modification for interaction between the drug and excipients. Metformin hydrochloride shows sharp peak value at 646.15, 937.4, 1060.85, 1546.91, 1620.21 and these peaks also shows into the physical mixture. This proves that there is potential compatibility of drug and excipients.

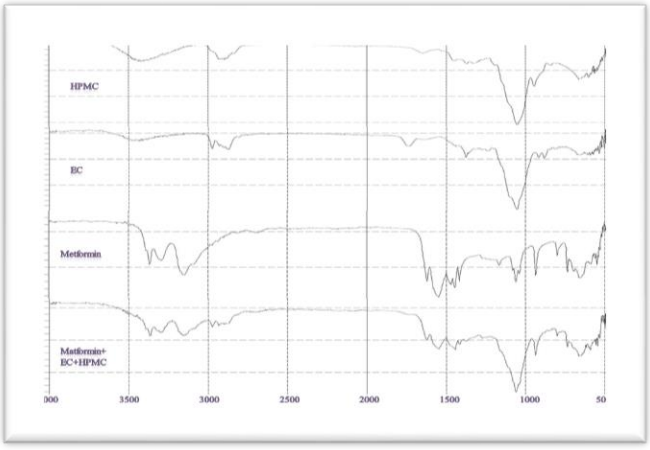

Fig 2:- IR graph of Ethyl cellulose + HPMC + Metformin Hydrochloride

C. XRD of Metformin hydrochloride

The characteristic peaks of metformin hydrochloride was appear at diffraction angle at 2theta at 17.7, 22.4, 23.3, 29.5, 29.6, 35.4 and 48.9 respectively with peak intensity of 510, 730, 733, 5273, 2885, 608 and 548.

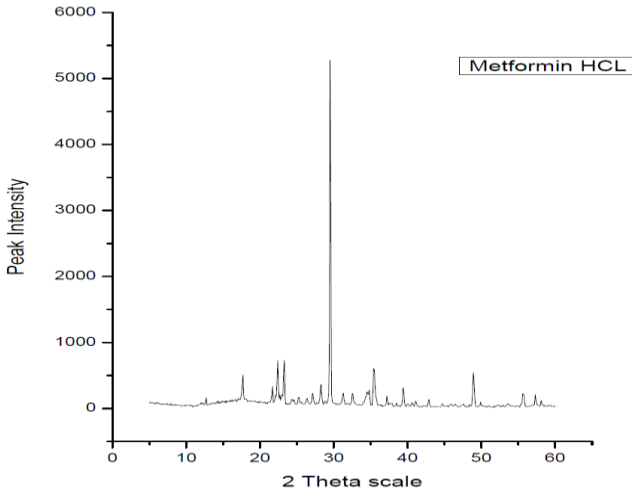

Fig 3:- XRD of Metformin hydrochloride

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Batch code	Thickness (mm)	Folding endurance (No)	Weight Uniformity (gm)	Moisture content (%)	Assay(%)
F1	0.16±0.025	103±5	1.14±0.017	1.79±0.02	90.45±0.041
F2	0.15±0.006	65±7.63	1.15±0.017	2.88±0.03	85.87±0.098
F3	0.15±0.023	98±7.63	1.15±0.031	1.36±1.03	87.65±0.087
F4	0.16±0.017	94±5.29	1.14±0.015	1.75±0.142	112.65±0.065
F5	0.16±0.006	108±5	1.16±0.020	1.72±0.85	102.65±0.0488
F6	0.14±0.006	107±5.77	1.13±0.021	2.19±0.20	88.78±0.087
F7	0.15±0.010	108±54	1.15±0.025	1.93±0.50	96.87±0.0504

Table 4:- Evaluation parameters of Metformin Transdermal Patch

D. In-vitro Drug Release:

Transdermal patches of all formulation was evaluated for drug release profile formulation F7 showimg good sustained release profile upto 12 hrs. Cumulative drug release after 12 hrs was observed 96.12%.

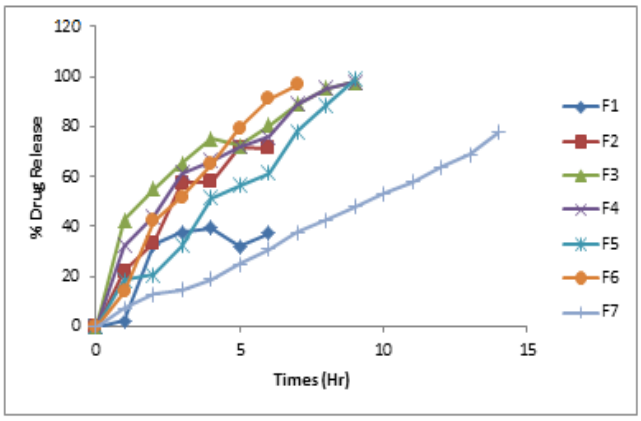

Fig 4:- *In-vitro* Drug Release profile of Formulations

IV. CONCLUSION

Metformin hydrochloride is anti- diabetic drug helps to maintain the sugar level. When it administered orally required more dose as compared to the transdermal drug delivery. In transdermal patch required less dose. The prepared transdermal patch consist of the ethyl cellulose and HPMC as a polymer, this combination of polymer was found to maintain the sustained release effect of the transdermal. PEG 400 used as plastisizer in the patch it produces good flexibility. It not produces any irritation at the site of application because of flexible and soft surface. Metformin hydrochloride containing transdermal drug delivery is very better for topical route. It may improve compliance of patient those unable to take drug orally.

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