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FORMULATION AND EVALUATION OF TRANSDERMAL PATCHES OF GLIBENCLAMIDE

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ABSTRACT

The objective of present study was to develop matrix type transdermal therapeutic systems of Glibenclamide using various hydrophilic (HPMC) and hydrophobic (EUDRAGID) polymers as matrix formers. Results revealed that prepared patches showed good physical characteristics, no drug-polymer interaction and no skin irritation was observed. The in vitro release study revealed that F3 formulation showed maximum release in 24hrs. Formulation F3 was subjected for accelerated stability studies. The F3 formulation was found to be stable as there was no drastic change in the Physico-chemical properties of the patches, which was also confirmed by FTIR. Thus conclusion can be made that stable transdermal patches of Glibenclamide has been developed. F1, F2, F3, F4 formulations showed highest cumulative percentage drug release of 98.13%, 95.50%, 98.65%, 97.21% were obtained during in vitro drug release studies after 24 hrs. The release of Glibenclamide appears to be dependent on lipophilicity of the matrix. Moderately lipophillic matrices showed best release. The predominant release mechanism of drug through the fabricated matrices was believed to be by diffusion mechanism. Based upon the in vitro dissolution data the F3 formulation was concluded as optimized formulation.

KEYWORDS: Glibenclamide, Ethyl cellulose, Sodium alginate, Poly ethylene glycol.

INTRODUCTION

Transdermal drug delivery is one of the most promising methods for drug application. Increasing numbers of drugs are being added to the list of therapeutic agents that can be delivered to the systemic circulation via skin.[1,2] The main advantages of this system are that there is controlled release of the drug and the medication is painless. The drug is mainly

delivered to the skin with the help of a transdermal patch which adheres to the skin.[3] The transdermal drug delivery system has potential advantages of avoiding hepatic first pass metabolism, maintaining constant blood level for longer period of time resulting in a reduction of dosing frequency, improved bioavailability, decreased gastrointestinal irritation that occur due to local contact with gastric mucosa and improved patient compliance.[4,5] Glibenclamide is a potent oral sulfonylurea hypoglycemic agent. It is currently available for treating hyperglycemia in Non-insulin dependent Diabetes Mellitus.[6] Plasma half-life is 4-6hrs. Which make frequent dosing necessary to maintain therapeutic blood level of the drug a long term treatment.[7,8] Therefore controlled released Transdermal preparation of Glibenclamide was prepare to give sustain effect as compared to conventional multiple oral dosing. It is highly accepted that membrane controlled transdermal systems have the distinct advantage that the drug release rate,[9] which is regulated by permeation through the rate controlling membrane, remain relatively constant as long as drug loading in the reservior is maintained at high level. Hence, the proposed work involves the development and evaluation of transdermal drug delivery systems containing Glibenclamide.[10,11,12]

MATERIALS AND METHODS[13,14]

Materials

Glibenclamide was obtained as gift sample from Hetero labs. Pvt india. Eudragit RS100 & Ethyl cellulose was procured from AR chemicals. Other excipients used were of standard pharmaceutical grade and all chemical reagents used were of analytical grade.

Method

Preparation of transdermal patch

Table 1: Formulation Design of Glibenclamide Transdermal Patches

S. No	Formulation code	Ingredients (gms)				
		Drug (mg)	HPMC	Ethylcellulose	Eudragit	Sodium alginate
1	F1	100	100	900	-	-
2	F2	100	900	100	-	-
3	F3	100	-	-	100	900
4	F4	100	-	-	900	100

Transdermal patches containing Glibenclamide were prepared by the solvent casting evaporation technique. The drug Glibenclamide was dissolved in methanol. Polymers HPMC, Ethyl cellulose, Sodium alginate and ERS100 were taken in a boiling tube, to this add Glibenclamide drug which was previously dissolved in methanol. About 30ml of solvent

mixture of dichloromethane: methanol (1:1) was added and vortexed. Sufficient care was taken to prevent the formation of lumps. The boiling tube was set aside for 4 hours to allow the polymer to swell. Polyethylene glycol was taken as a plasticizer (15%v/w of dry polymer weight), and added to the mixture and mixed well. It was set aside for 2 hours to exclude any entrapped air and was then transferred into a previously cleaned petri plate ($40cm^2$), drying of patches was carried out in vacuum oven at room temperature. Dried patches were packed in aluminium foil and stored in a desiccator for further evaluation[15,16,17]

Evaluation Parameters

Physical appearance

The prepared patches were found to be uniform, smooth, flexible and homogenous.

Folding endurance

The folding endurance numbers of all the Glibenclamide patches are 180 – 292. The folding endurance number gives the mechanical property of the patches, high folding endurance number indicate that has high mechanical property. The folding endurance number was increased with increasing the HPMC content. These results indicated that the patches would not break and maintain their integrity with general skin folding when applied.

Thickness of the film

Thickness was changed from batch to batch in individual strips of medicated patch carry uniform thickness, which indicates that total medicated patch carry uniform thickness.

Weight uniformity

The mean weights of all the prepared patches are shown in table 17. The weights are in the range of 401.9 – 539. The F11 formulation patches showed maximum weight.

Drug content

The drug content analysis of the prepared formulations have shown that the process employed to prepare the patches was capable of giving uniform drug content with minimum batch variability. All the patches were found to have drug content in the range of 90 – 101%. So the method employed i.e. solvent evaporation method is satisfactory for the preparation of Glibenclamide transdermal patches.

In vitro release study

Phosphate buffer pH 7.4 containing 0.5% SLS was used as medium for the release studies and good linearity was observed in the plotted standard graph with a correlation coefficient of 0.999. The drug release profiles of Glibenclamide patches containing different ratios of polymers HPMC, Eudragit E100, and Ethyl cellulose. It was cleared from the release profiles of formulations, that the drug release was governed by polymer nature and content. The formulations F1, F2, F3, and F4 showed the maximum release when comparing with other formulations due to the high concentration of HPMC polymer. The release was decreased as the concentration of hydrophobic polymer increase.

Stability studies

Optimized formulations F3 was selected for accelerated stability studies as per ICH guidelines. The patches were observed for colour, appearance and flexibility for a period of three months. The folding endurance, weight, drug content, % cumulative drug release of the formulation was found to be decreasing. This decrease may be attributed to the harsh environment (40^0C) maintained during the studies.

RESULTS

Table 2: Physicochemical evaluation of Glibenclamide patches

Formulation code	Weight (mg)	Thickness (mm)	Folding endurance	Drug content (%)
F1	473.9±1.66	0.89±1.88	292±4.72	101
F2	430±1.58	0.86±1.72	290±2.51	99
F3	486±0.89	0.81±1.55	289±3.46	99.64
F4	501.7±2.50	0.85±0.99	291±3.18	98.86

Table 3: *In vitro* drug release profiles of Glibenclamide transdermal patch (F1-F4).

Time (hrs)	% Cumulative drug released			
	F1	F2	F3	F4
0	0	0	0	0
0.5	13.56±1.43	10.65±1.44	13.48±1.27	11.79±2.1
1	22.72±1.87	19.27±1.49	26.50±1.33	24.67±1.8
2	34.94±1.26	25.49±1.77	31.71±1.45	26.627±1.22
3	41.16±1.33	30.28±1.29	34.36±1.72	30.18±1.38
4	47.88±1.89	33.63±1.39	40.25±1.63	36.71±1.59
5	51.33±2.0	37.46±2.1	41.07±1.82	39.20±1.66
6	53.46±2.3	41.60±1.27	45.53±1.25	43.76±1.91
8	62.87±1.67	49.35±1.71	52.15±1.19	50.92±1.83
10	69.01±1.31	53.61±1.33	60.71±1.32	55.08±1.77
12	74.93±1.56	63.49±1.92	68.30±1.83	62.48±1.45

14	79.70±1.19	70.45±1.68	76.11±1.95	70.81±1.21
16	87.64±1.88	79.33±1.18	80.27±1.18	79.23±1.07
18	92.49±1.3	83.80±1.22	85.93±2.5	84.16±1.55
20	97.08±1.99	88.34±1.82	91.44±2.41	89.42±1.91
22	98..01±1.25	92.20±2.39	95.09±1.85	93.82±1.05
24	98.93±1.71	95.50±2.81	98.65±1.90	97.21±1.02

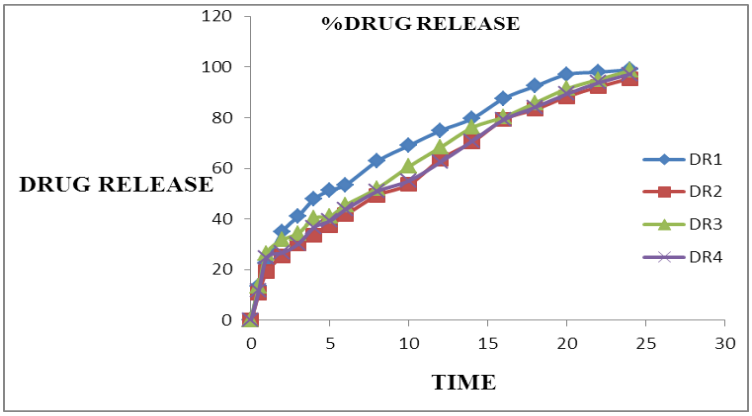

Figure 1: Drug release formulations.

Stability studies

Optimized formulations F3 was selected for accelerated stability studies as per ICH guidelines.

Table 4: Stability studies of optimized formulations at 40 ± 2 ^{0}C and 75 ± 5% RH for 3 months.

Time in days	Drug content (%)	Folding endurance	Physical appearance	% Cumulative drug release
0	98	285	No change in color	97
90	97.1	281	Slight yellowish color	96.35

CONCLUSION

Results revealed that prepared patches showed good physical characteristics, no drug-polymer interaction and no skin irritation was observed. The F3 formulation was found to be stable as there was no drastic change in the Physico-chemical properties of the patches, which was also confirmed by FTIR. Thus conclusion can be made that stable transdermal patches of Glibenclamide has been developed. F1, F2, F3, F4 formulations showed highest cumulative percentage drug release of 98.65%, 95.50%, 98.93%, 97.21% were obtained during *in vitro* drug release studies after 24 hrs. The release of Glibenclamide appears to be dependent on lipophilicity of the matrix. Moderately lipophillic matrices showed best release. The predominant release mechanism of drug through the fabricated matrices was believed to be

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