Formulation, Optimization And Characterization Of Root Extract Of Gloriosa Superba Linn. Loaded Transdermal Patch

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Abstract
The aim was to formulate and evaluate methanolic root extract of gloriosa superb linn. Containing herbal transdermal patch by solvent casting method using polymer ethyl cellulose, 0.35% and 0.45% and a total of eight formulations were prepared and study on effect of polymer concentration on in vitro drug release profile. Plasticizer used was dibutyl pthalate with penetration enhancer PEG-6000. The transdermal patches were evaluated for their physicochemical properties like thickness, weight variation, % moisture content, water vapor transmission, % drug content uniformity, in-vitro drug release studies were performed by using Franz diffusion cell. The optimized formulation F4 contains 0.35% ethyl cellulose with dibutyl phthalate as plasticizer showed a maximum release of 99.89 in 12 hours. Out of these eight formulations of 0.35% ethyl cellulose was optimized concentration they produced sustain and complete release over a period of 12 hours due to 0.035% of PEG-6000 as penetration enhancer. The study indicated that the optimized formulation F4 has good effect of polymer concentration on in vitro drug release profile.

Keywords: Gloriosa superb Linn. Transdermal, Ethylcellulose, PEG-6000

Introduction

Transdermal drug delivery systems are self contained, discrete dosage forms which, when applied to the intact skin, deliver the drugs, at controlled rate to the systemic circulation.[1,2] The transdermal delivery provides controlled, constant administration of the drug, it deliver therapeutically effective amount of drug across the skin when it placed on skin[3]. It is the dosage form in which the drug is administered topically in the form of a patch that delivers the drug at a controlled rate for systemic effects[4]. TDDS offers many advantages over conventional mode injection and oral methods. Numerous considerable advantages of TDD are limitation of hepatic first pass metabolism, enrichment of therapeutic efficiency and maintenance of steady plasma level of the drug[5]. It reduces the load that the oral route commonly places on the digestive tract and liver. It is safe, effective and may be withdrawn easily as per need of the patient[6].

Gloriosa superba Linn is tuberous root of the Liliaceae family[7]. It is considered as a rich source of colchicines and gloriosine. It has highly active alkaloid "Colchicine". This plant is a part of folk medicine from ancient time. It shows a number of important pharmacological activities.[8] *G. superb* considered as a medicinal plant because of its important pharmaceutical constituents known as colchicines, gloriosine[9] and other tropolone alkaloids. Colchicine, the main alkaloid of *G. superba*, is a useful agent chiefly in the treatment of acute attacks of gout but is also valuable in other inflammatory diseases such as gouty attacks, Arthritis, serositis related to familial Mediterranean fever, Behcet syndrome, and more recently use in acute and recurrent pericarditis and many more diseased conditions. In acute gout, colchicine is effective in alleviating the acute attack and as a prophylactic medication. Colchicine is used to prevent or treat attacks of gout (also called gouty arthritis). This condition is caused by too much uric acid in the blood. An attack of gout occurs when uric acid causes inflammation (pain, redness, swelling, and heat) in a joint. The tuberous root stocks of glory lily, *G. superba*boiled with *Sesamum*oil is applied twice a day on the joints, affected with arthritis reduces pain.[10]

The objective of the present study was to design and evaluate transdermal polymeric matrix films of EC and PEG -6000 containing methanolic extract of *Gloriosa superb Linn*. root use as anti-inflammatory to avoid the hepatic first pass metabolism and improve the therapeutic efficacy of the drug.

Materials and methods

Material

The Gloriosa superba roots were collected from supplier Indian jadibooti, Delhi. Root sample was authenticated by Dr. Sunita Garg, former chief scientist, Head, RHMD, CSIR-NISCAIR, Delhi. Polymer and plasticizer used were purchased by SD fine chemicals, india. Magnetic stirrer, hot air oven, waiging balance and franz diffusion cell were used in this study.

Methodology

Formulation of transdermal drug delivery system

TDDS was developed using solvent evaporation method. The polymer was dissolved in particular solvent and then the specified quantity of drug as well as plasicizer and penetration enhancer were added and was air dried for 24 h in petri dish with help of inverted funnel for controlled evaporation. A total of 8 formulations were made in as shown in table 1.

Preparation of transdermal patches:

The solvent casting technique was used to formulate the methanolic root extract of gloriosa superb Linn. containing transdermal patch. The adhesive patch prepared by dissolving polymer and methanolic extract in methanol 0.5 % w/v in ethanol and chloroform. To this PEG-6000 as penetration enhancer and dibutyl phthalate as plasticizer were added and mixed well. The polymeric dispersion was poured into a petri dish. To control the rate of evaporation of solvent, the mould was covered with a funnel of suitable size and the casting solvent was allowed to evaporate to obtain the dried films. The film was cut into small patches (4 cm^2) and stored between sheets of wax paper in desiccators for further evaluations[11].

Evaluation of transdermal patches:

1. Physical appearance

All the prepared patches were visually inspected for color, clarity, flexibility and smoothness[12].

2. Weight of patch:

Three patches from each batch were taken and weight of each patch was found by using electronic balance. Then average weight of single patch was determined[13].

3. Thickness of patch

The thickness of the formulated film was measured at 3 different point using a calliper and average thickness was calculated[13].

4. Percentage moisture content

The patch was weighed individually and kept in desiccator containing fused calcium chloride at room temperature for 72h. The patch was again weighed and the percentage moisture content was calculated using the formula[13].

% moisture content= [initial weight – final weight / final weight] × 100

5. Percentage moisture uptake

The weighed films were kept in a desiccator at room temperature for 72 hours and then exposed to 84 % relative humidity using a saturated solution of potassium chloride. Finally, the films were weighed and the percentage moisture uptake was calculated using the formula[13].

% moisture uptake = [Final weight - Initial weight / initial weight] × 100.

6. Folding endurance

Evaluation of folding endurance involves determining the folding capacity of the films subjected to frequent extreme condition of folding. Folding endurance was determined by repeatedly folding the film at the same place until it broke. The number of times the film could be folded at the same place without breaking was the folding endurance[14].

7. Drug content uniformity

A film of size 10 mm × 10 mm was cut into small pieces and put in a 50 ml phosphate buffer saline 7.4 pH. This was then shaken in a mechanical shaker for 2 hours to get a homogenous solution and filtered. Then appropriate dilution was done. Data for each and every experiment was obtained in triplicate and statistically analyzed. The drug was determined spectroscopically at 350 nm after suitable dilution[15-19].

8. In vitro drug release studies

In-vitro drug release studies were performed by using franz diffusion cell with a receptor compartment capacity of 20ml. the cellophane membrane was mounted between donor and receptor compartment of the diffusion cell. The formulated patches were cut into size of 1.4 cm radius and placed over the drug release membrane and the receptor compartment of the diffusion cell was filled with phosphate buffer pH 7.4. The whole assembly was fixed on a magnetic stirrer, and the solution in the receptor compartment was constantly and continuously stirred using magnetic beads. The samples of 2 ml were collected at predetermined time intervals and replace with same volume of phosphate buffer pH 7.4. Thesamples were analyzed for drug content using UV spectrophotometer at 350nm[15-19].

Results and discussion:

Preparation of transdermal patches

As per methodology transdermal polymeric metrix patches using EC and PEG-6000 were prepared by using solvent casting method.

Evaluation of prepared transdermal patches

Physical appearance

All the prepared patches were visually inspected for color, clarity, flexibility and smoothness.

Weight of patch:

The weight variation of formulated films was found to be in the range of 0.071±0.001 to 0.093±0.0015 cm^2 a low standard deviation (SD) value in the film weight variation measurement ensures uniformity of the films.

Thickness of patch

Thickness of formulated films was found to be in the range 0.205 to 0.224 mm a low standard deviation (SD) value in the film thickness measurement ensures uniformity of the films.

Percentage moisture content

Percentage moisture content was found to be in range 7.7 to 8.8 cm^2. The higher percentage of moisture content was found in formulation F6, F8, F3 and F1 in higher range compare to other formulations which may be due to the hydrophobic nature of polymer used. % moisture absorption decrease with increase in percentage of EC. Moisture loss increase with increase of EC.

Percentage moisture uptake

Percentage moisture uptake was found to be in range 5.7 to 6.8 cm^2. The higher percentage of moisture uptake was found in formulation F6, F8, F3 and F1in higher range compare to other formulations which may be due to the hydrophobic nature of polymer used. % moisture absorption is decrease with increase in percentage of EC.

Folding endurance

The values of folding endurance were found to vary from237.6 to 308 which indicates good strength and elasticity

Water vapour transmission rate

Water vapour transmission rates for EC was found in the range of 1.55 to 1.67 $g/cm^2/h$ water vapour transmission rate results were found to be similar to the results obtained in moisture absorption studies.

Drug content

The Percentage drug content of formulated films was found to be in the range of 98.67 to 99.36 per 4 cm^2 strip.

Table 1 Formulation of herbal patches

Ingredient	F1	F2	F3	F4	F5	F6	F7	F8
Methanolic extract	4.5 mg	4.5 mg	4.5 mg	4.5 mg	4.5 mg	4.5 mg	4.5 mg	4.5 mg
Ethylcellulose	0.45%	0.35%	0.45%	0.35%	0.35%	0.45%	0.35%	0.45%
PEG 6000	0.035%	0.045%	0.045%	0.035%	0.035%	0.035%	0.045%	0.045%
Dibutyl phthalate	0.17%	0.2%	0.17%	0.17%	0.2%	0.2%	0.17%	0.2%
Methanol 0.5 % w/v in ethanol	0.28 ml	0.28 ml	0.28 ml	0.28 ml	0.28 ml	0.28 ml	0.28 ml	0.28 ml
Chloroform	20 ml	20 ml	20 ml	20 ml	20 ml	20 ml	20 ml	20 ml

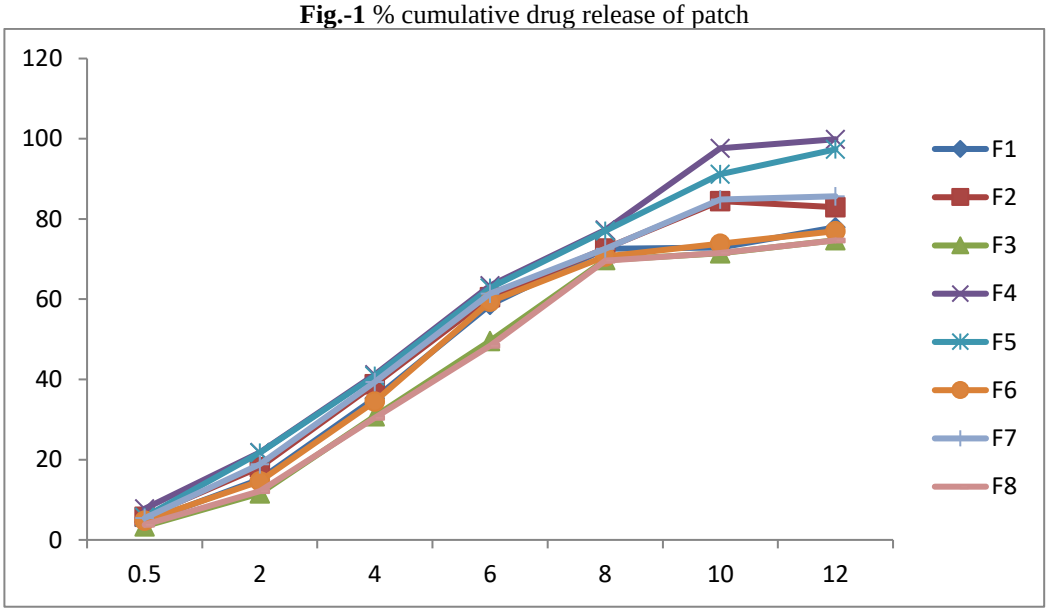
Table 2 Evaluation of prepared herbal patches

Formulations	Thickness (mm)	Weight variation	% Moisture content	% Moisture uptake	Folding endurance	Water vapor transmission	% Drug content
F1	0.215	0.091	8.6	6.6	296.6	1.62	99.31
F2	0.205	0.083	7.7	6.33	302.6	1.64	98.79
F3	0.224	0.092	8.7	6.7	245.6	1.55	99.32
F4	0.219	0.071	8.3	5.76	308	1.66	99.36
F5	0.222	0.072	8.3	6.06	304	1.67	99.35
F6	0.221	0.093	8.8	6.83	280.33	1.60	99.3
F7	0.219	0.071	8.06	6.3	303	1.66	98.67
F8	0.218	0.092	8.7	6.6	237.6	1.58	99.33

Table 3 In vitro % cumulative drug release of patch

Formulations code	In - vitro % cumulative Drug release						
	0.5 h	2h	4h	6h	8h	10h	12h
F1	4.47	15.12	35.34	58.57	72.55	72.87	77.92
F2	5.77	18.13	38.81	60.54	72.63	84.46	82.95
F3	3.40	11.56	30.85	49.59	69.79	71.46	74.71
F4	7.76	21.78	41.18	63.36	77.3	97.66	99.89
F5	5.71	21.77	40.85	62.85	77.01	91.16	97.36
F6	4.81	14.66	34.48	59.44	70.67	73.82	76.97
F7	5.43	18.83	39.37	61.38	72.60	84.85	85.66
F8	3.78	12.19	30.46	48.40	69.58	71.51	74.66

Fig.-1 % cumulative drug release of patch



Discussion

The present study was aimed at preparing transdermal patches containing methanolic extract of gloriosa superb linn. Root for sustained release of drug and studies the effect of polymer on rate of release. Transdermal patches composed of different polymers such as Ethyl cellulose and PEG-6000 as penetration enhancer at different concentration of 0.35% - 0.45% and 0.035% - 0.045% respectively using plasticizers dibutyl phthalate were prepared using solvent casting technique. A total of 8 formulations were made using ethyl cellulose and PEG-6000. The formulated patches were subjected to physicochemical evaluation parameter i.e. folding endurance, thickness, moisture loss, moisture absorption, water vapour transmission rate and drug content confirm the it integrity and physical stability. Folding endurance value of matrix films were found within 237.6 to 308 no. of folds indicating good strength and elasticity and that the patch would maintain the integrity with general skin folding when applied. The thickness of all the formulations indicates physical uniformity among the prepared patches. The drug content analysis value show minimum batch variability. Hydrophobic polymer like EC with increased concentration showed a decrease value, as it was able to repel water. Optimization of the formulated batches was done by performing in-vitro diffusion rate studies using Franz diffusion cell with cellophane membrane. In these studies the PEG-6000 show the effect of penetration enhancer with the value of maximum drug release at 12 h in the concentration 0.035%, when increase the concentration it was not high it may be the drug polymer ratio increase the drug release was not increase.

Conclusion

Delivery of drug into systemic circulation through skin has created lot of interest among pharmaceutical scientist during recent years. The transdermal system offers several advantages over oral dosage forms which include avoidance of hepatic first pass effect metabolism, decrease in frequency of administration, providing steady state plasma concentration and improves patient compliance. On evaluation of various parameters it was found that the polymers produced satisfactory results with respect to the physical characteristics of the film. Methanolic extract of gloriosa superb root was showed sustained and complete release at a period of 12 hours.

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